

From: [Nikolaas Tilkin-Franssens](#)
To: [DiFranco, Stephen](#)
Cc: [Justyna Palasińska](#)
Subject: [EXTERNAL] Re: GRN 1122 canola concentrate items for clarification - Reply
Date: Tuesday, July 11, 2023 11:05:27 AM
Attachments: [image001.png](#)
[image007.png](#)
[FDA GRN 1122 Concentrate 28JUNE2023 Napiferyn Answers.docx](#)
[Literature review GRAS years 2021-2023.pdf](#)
[Canola Protein Concentrate SDS v1.pdf](#)
[Additional suitability Report meat extensions.pdf](#)

CAUTION: This email originated from outside of the organization. Do not click links or open attachments unless you recognize the sender and know the content is safe.

Dear Stephen,

Thank you for reaching out with the questions for clarification.
We have worked closely with Napiferyn to close the doubts.

Kindly find attached a Word file including the Questions&Answers, a report on the requested literature review, a SDS sheet as requested by the USDA-FSIS, and a report on the suitability assessment.

We remain available for any further questions or updates.

Thanks for taking the application in further consideration,
best regards,

Nikolaas Tilkin-Franssens

Regulatory Affairs Manager | Pen & Tec Consulting

T [+34 936 758 015](tel:+34936758015) **M** [+34 649 840 417](tel:+34649840417) **F** [+34 936 758 016](tel:+34936758016) www.pentec-consulting.eu

Pl. Ausias March 1 | 4th floor D01 | 08195 Sant Cugat del Vallès | Barcelona | Spain

PEN + TEC
CONSULTING
PART OF THE ARGENTA GROUP

La información contenida en este mensaje y/o archivo(s) adjunto(s), enviada desde Pen & Tec Consulting SLU, es confidencial/privilegiada y está destinada a ser leída sólo por la(s) persona(s) a la(s) que va dirigida. Le recordamos que sus datos han sido incorporados en el sistema de tratamiento de Pen & Tec Consulting SLU y que siempre y cuando se cumplan los requisitos exigidos por la normativa, usted podrá ejercer sus derechos de acceso, rectificación, limitación de tratamiento, supresión, portabilidad y oposición/revocación, en los términos que establece la normativa vigente en materia de protección de datos, dirigiendo su petición a la dirección postal Pl. Ausias March 1, 4 planta 08195, Sant Cugat del Vallès (Barcelona) o bien a través de correo electrónico info@pentec-consulting.eu. Si usted lee este mensaje y no es el destinatario señalado, el empleado o el agente responsable de entregar el mensaje al destinatario, o ha recibido esta comunicación por error, le informamos que está totalmente prohibida, y puede ser ilegal, cualquier divulgación, distribución o reproducción de esta comunicación, y le rogamos que nos lo notifique inmediatamente y nos devuelva el mensaje original a la dirección arriba mencionada. Gracias.

The information contained in this message and/or attached file(s), sent by Pen & Tec Consulting SLU, is confidential/privileged and is intended to be read solely by the person(s) to whom it is addressed. We hereby inform you that your data will be incorporated into the processing system owned by Pen & Tec Consulting SLU, and that provided it complies with the requirements included in the law, you may exercise the rights of access, rectification, limitation of processing, deletion, portability and opposition by sending your request to the postal address Pl. Ausias March 1, 4 floor 08195, Sant Cugat del Valles (Barcelona) or to the email address info@pentec-consulting.eu. If you read this message and you are neither the intended recipient, employee or agent in charge of delivering the message to the recipient, or if you have received this message as the result of an error, we hereby inform you that distributing, sharing or reproducing any part of this message is totally forbidden and may be illegal. As a result, we request that you immediately inform us of the error and return this message to the address mentioned above. Thank you.

From: DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>
Date: Wednesday, 28 June 2023 at 17:41
To: Nicoleta Pasecinic <nicoleta@pentec-consulting.eu>
Cc: Nikolaas Tilkin-Franssens <niko@pentec-consulting.eu>
Subject: [EXTERNAL]: GRN 1122 canola concentrate items for clarification

CAUTION: This email originated from outside of the organization. Do not click links or open attachments unless you recognize the sender and know the content is safe.

Hello Ms. Pasecinic,

After evaluating NapiFeryn's GRAS Notice No. GRN 1122 on canola concentrate we noted a few issues that should be addressed. Please respond to the following points for clarification:

1. On p. 9, NapiFeryn states that the major storage proteins in canola seed are cruciferins and napins, and that canola concentrate consists of 30-45% protein and 40-70% dietary fiber. Please provide the typical cruciferin content and napin content in canola concentrate.
2. Please confirm that all raw materials and processing aids used in the manufacturing process are used in accordance with the U.S. regulations, are GRAS for their respective uses or are the subject of an effective food contact notification. For the record, we note that the food additive regulations cited in Table 4 (p. 15) for ascorbic acid (21 CFR 182.8013), ethanol (21 CFR 184.1293), and ethyl acetate (21 CFR 173.228) do not appear to be applicable to your intended uses of these substances.
3. In Table 6 (p. 18-19), NapiFeryn provides the results from the batch analyses for heavy metals. We would like to bring to your attention a relevant FDA's "[Closer to Zero](#)" initiative that focuses on reducing the levels of heavy metals in foods and recommend that you lower the specification limits for heavy metal to better reflect the batch analyses results and to be as low as possible.
4. In Table 10 (p. 22), NapiFeryn provides batch analyses data for residual solvents and processing aids. In addition, in Table 21 (p. 50), you provided the results from the batch analyses for erucic acid in your canola concentrate ranging from 0.37% to < 0.1%.
 - a. Please include limits for residual ethanol, ethyl acetate, and sulphur dioxide as well as a limit for erucic acid in the specifications for canola concentrate and specify the analytical methods used to test for these parameters.
 - b. In addition, please provide an updated Tables 5 and 6 (p. 16-19) to include the additional specification parameters mentioned above, corresponding analytical methods, and batch analyses.
5. Please state that all analytical methods used to test batches were validated and are fit for their respective purpose.
6. Please state that canola concentrate is not intended for use in infant formula or in foods

where standards of identity preclude its use.

7. In Table 15 (p.), NapiFeryn provides the results of the batch analyses for total plate count in the raw material (rapeseed press cake). Please address the significant variation in the results (from <10 to 28,000 CFU/g) and discuss whether this will impact safety of the final ingredient.
8. On p. 19, NapiFeryn states that the levels of mycotoxins in canola concentrate are below the limit of quantitation (LOQ) and provide the results from the analyses of five batches to support your statement. Please clarify whether you expect mycotoxins to be present in canola concentrate manufactured in accordance with good manufacturing practices.
9. In Part 1.4 (p. 6) and Part 3.1 (p. 33), NapiFeryn states that the intended use of canola concentrate is as a source of protein and/or fiber, thickener, or texturizer. However, we note that on p. 33 you also state the intended use of canola concentrate is as a flavoring agent or binder in various comminuted or whole muscle meat and poultry products. In addition, in Appendix 3 (p. 5) you state that canola concentrate may also be used “to create a flavored salt” or as “a flavor enhancer like monosodium glutamate”. Please confirm these additional uses of canola concentrate are within the scope of GRN 001122.
10. On p. 10, the notifier describes the protein composition of canola concentrate, being primarily cruciferins, napin, oleosin, and squalene monooxygenase. However, the pivotal safety data provided appear to only be relevant to the cruciferin and napin fractions of the canola concentrate. Please provide a brief narrative to confirm the safety of oleosin and squalene monooxygenase exposure from the intended uses.
11. On p. 31-32 of the notice, the notifier clearly establishes that canola concentrate is intended to be substitutive to protein and fiber consumption and will not contribute to additional exposure to protein or fiber in general. Please elaborate on this conclusion, and clarify if the intended uses of canola concentrate are additive or substitutive to other canola protein products currently on the market (i.e., GRNs 327, 386, and 683)?
12. On p. 37, the notifier concludes exposure to canola concentrate from the intended uses is safe since the EDI reported is “still much lower (approximately 7- to 22-fold lower) than the no-observed-adverse-effect level (NOAEL) values established” for cruciferin- and napin-rich protein isolates in male rats following a 13-week oral exposure regimen (Mejia *et al.*, 2009a & 2009b). We note that an uncertainty factor, or margin of safety (MOS), of 100 (10 for interindividual variability × 10 for interspecies variability) is normally used when assessing safety of a food ingredient by comparing estimated human exposure levels to the NOAEL from animal toxicology data. Therefore, it is not clear why MOS that is ~5-10-fold lower can be concluded as safe without proper justification. Additionally, we note that potential thyrotoxic effects were observed at the highest doses in these two rat studies, as well as for rapeseed products in general tested in other species, as cited in Table 20 of the GRAS notice. This effect was mostly attributed to the presence of glucosinolate; however, we note that since the level of glucosinolate was low or absent in both the test articles from Mejia *et al.* and the article of

commerce, the rationale used by the study authors to conclude that the observed NOAEL was not in fact the LOAEL may be questionable. Regardless, it appears that the provided safety narrative lacks sufficient basis to conclude MOS of 7-22 is adequate to reach the conclusion of “reasonable certainty of no harm.” Based on generally available data and information, please provide additional narrative to explain your rationale for your GRAS conclusion.

13. We note that when discussing the absorption, distribution, metabolism, and excretion of canola concentrate (p. 49), the notifier reports unpublished data from an EU Novel Foods application for “defatted rapeseed powder” to support their conclusion. Similarly, genotoxicity conclusions are made using unpublished data from an EFSA Panel conclusion on defatted rapeseed powder. Given other data and information have been used in prior GRAS notices for canola ingredients (e.g., GRN 327), please confirm that the EFSA Panel and EU Novel Foods conclusions are only considered as corroborative, not pivotal, to the safety determination of canola concentrate at its intended use level?
14. On p. 40, the notifier discusses the allergenicity potential of canola concentrate being determined via a “bioinformatics approach” and concludes that canola concentrate “may elicit possible allergenic effects.” Additionally, on p. 59 the notifier reiterates that the bioinformatics analysis indicated “possible allergenic effects” of canola concentrate, but no further discussion is provided. While data from an allergen online database search is provided as part of Appendix 4, no discussion of these data are included in the current GRAS notice. Please briefly detail the “possible allergenic effects” of canola concentrate similar to previous notices (e.g., GRN 683), and discuss why they would not be expected to pose a safety concern from the intended use.
15. We note that a recent study on rapeseed protein isolate was published (Xiong et al., 2022).
 - a. Please discuss if this study presents additional safety concerns for the article of commerce or contradicts the current GRAS conclusion.
 - b. Please also perform an updated literature review from 2021 to present and discuss if any additional studies relevant to the safety of canola concentrate were identified that would contradict the current GRAS conclusion.

References cited:

Xiong Z, Fu Y, Yao J, Zhang N, He R, Ju X, Wang Z. Removal of anti-nutritional factors of rapeseed protein isolate (RPI) and toxicity assessment of RPI. *Food Funct.* 2022 Jan 24;13(2):664-674. doi: 10.1039/d1fo03217h. PMID: 34933325.

Additionally, we received the following questions from USDA FSIS regarding their review of the uses of GRN 1122 concerning products within their purview. Please respond to the following and we will pass your responses along to them.

Please provide Safety Data Sheet (SDS) for the at use concentrations of the substance and include a description of how the use of this technology will not adversely affect the safety of FSIS inspectors. Workplace safety and health hazards include inhalation, direct skin contact (skin, eyes, mouth), and fire/explosion caused by exposure to the product, its working solution or dry mixture and potential by-products formed and/or off-gassed during the

application process. The employee safety information should demonstrate how the New Technology will not “jeopardize the safety of Federal inspection personnel” as specified in the [FSIS Compliance Guideline Procedures for New Technology Notifications and Protocols, April 2015](#). FSIS workplace and employee safety must be specifically addressed. Please refer to Appendix A on p. 17, Workplace Safety and Health Criteria, for clarification on what to provide in the response. For additional clarity with respect to employee safety, the following are examples of information that are typically needed by FSIS’ employee safety and health group;

1. Potential workplace exposures that could result from inhalation and direct contact during use of the substance/technology. This information is required in addition to a SDS to determine accurate hazard potential and recommended exposure control measures for IPP work areas in accordance with Occupational Safety and Health Administration (OSHA) regulations: 29 CFR 1910.1200, Hazard Communication, 29 CFR 1910.132, Personal Protective Equipment, and 29 CFR 1910.1000, Air Contaminants. The information should be included as a specific section in each of the protocols.
2. If the SDS workplace hazards/precautions do not apply to the type of exposure that would be expected for the FSIS IPP, please have the submitter provide specific information (per the April 2015 FSIS Compliance Guideline Procedures) for the actual type of exposures expected.
3. If no IPP workplace exposures are expected and no control measures are required, please have the submitter state this and provide the reasons why (e.g., such as the substance “as used” [for all concentrations] is not hazardous by inhalation or direct contact and/or IPP would not be exposed to the substance based on the system design, operation and/or control measures that will be in place).
4. Please also indicate how will FSIS IPP be informed of the above information so that it is clear that the information contained in the SDS for the concentrate does not apply to their actual workplace exposure.
5. Are there any potential hazards from chemical mixing or low pH as a result of discharges of the various solutions to floor drains? Are dedicated drain lines or any other enclosures required?
6. With respect to potential airborne exposures to FSIS IPP in the use/application areas, does the submitter have air sampling results taken during the use of the various concentrations of the technology in the listed mixture?
7. The intended use of this product in FSIS meat and poultry products is apparently as a binder/extender. The suitability support provided in Appendix 6 does sufficiently support no significant difference in yield and other organoleptic qualities when used as a partial replacement for another binder in a processed meat and poultry product, such as sausage. However, **additional suitability support is needed:**
 - a. No suitability data was provided for **whole muscle meat and poultry products at the maximum proposed use level**. We would need to see similar data as provided in Appendix 6 for:
 1. Whole muscle red meat control containing no other binders, extenders, or moisture retention agents, as compared to a whole muscle red meat product containing 15% isolated canola product.
 2. Whole muscle poultry control containing no other binders, extenders, or moisture

retention agents as compared to a whole muscle poultry product containing 15% isolated canola product.

Responses may be sent in an email or in a separate document. We respectfully request a response within 10 business days. If you are unable to complete the response within that time frame, please contact me to discuss further options.

If you have any additional questions or concerns, please don't hesitate to contact me at stephen.difranco@fda.hhs.gov or by phone at 240.402.2710.

Best,
Steve

Stephen DiFranco, PhD

Regulatory Review Scientist/Chemist

Center for Food Safety and Applied Nutrition
Office of Food Additive Safety
Division of Food Ingredients
U.S. Food and Drug Administration
Tel: 240-402-2710
stephen.difranco@fda.hhs.gov



CAUTION: This email, including any attachments, is confidential. If you are not the intended recipient, please notify the sender and delete the email and any attachments from your system. In addition, you must not use, distribute or reproduce this email or any attachments. Opinions and other information in this email and any attachments which do not relate to the official business of Argenta are neither given by nor endorsed by Argenta. While Argenta uses anti-virus software, Argenta accepts no liability for any viruses in this email or any attachment, or for any effects this email or any attachment may have on your network or computer system.

**GRN 1122 - Raptein™30 - Canola protein concentrate:
Replies to request for clarification of 28 June 2023**

1. On p. 9, NapiFeryn states that the major storage proteins in canola seed are cruciferins and napins, and that canola concentrate consists of 30-45% protein and 40-70% dietary fiber. Please provide the typical cruciferin content and napin content in canola concentrate.

Answer:

The typical method for cruciferin and napin content is the quantitative HPLC-UV method based on SEC (size-exclusion chromatography). This method is suitable for soluble samples and it is not applicable to canola concentrate due to interactions between fiber and protein and the general characteristics of the sample (e.g. poor solubility of the sample). Based on our knowledge and process parameters, the content of cruciferins significantly exceeds the content of napins in the concentrate. The qualitative analyses of protein with the use of LC-MS method confirmed the presence of cruciferins, napins and oleosins in Raptein™30.

2. Please confirm that all raw materials and processing aids used in the manufacturing process are used in accordance with the U.S. regulations, are GRAS for their respective uses or are the subject of an effective food contact notification. For the record, we note that the food additive regulations cited in Table 4 (p. 15) for ascorbic acid (21 CFR 182.8013), ethanol (21 CFR 184.1293), and ethyl acetate (21 CFR 173.228) do not appear to be applicable to your intended uses of these substances.

Answer:

Napiferyn hereby confirms that canola protein concentrate is manufactured in accordance with good manufacturing practices, using food-grade raw materials and processing aids. We acknowledge the CFR references included are not accurate on the intended uses, but merely support the identity of the used processing aids.

3. In Table 6 (p. 18-19), NapiFeryn provides the results from the batch analyses for heavy metals. We would like to bring to your attention a relevant FDA's "Closer to Zero" initiative that focuses on reducing the levels of heavy metals in foods and recommend that you lower the specification limits for heavy metal to better reflect the batch analyses results and to be as low as possible.

Answer:

Based on results from samples of several batches Napiferyn can commit to lower the limits for Lead and Arsenic.

	Arsenic (mg/kg)	Cadmium (mg/kg)	Lead (mg/kg)	Mercury (mg/kg)
Current	≤ 0,2	≤ 0,2	≤ 0,5	≤ 0,1
Concentrate (new)	≤ 0,15	≤ 0,2	≤ 0,35	≤ 0,1

4. In Table 10 (p. 22), NapiFeryn provides batch analyses data for residual solvents and processing aids. In addition, in Table 21 (p. 50), you provided the results from the batch analyses for erucic acid in your canola concentrate ranging from 0.37% to < 0.1%.
 - a. Please include limits for residual ethanol, ethyl acetate, and sulphur dioxide as well as a limit for erucic acid in the specifications for canola concentrate and specify the analytical methods used to test for these parameters.
 - b. In addition, please provide an updated Tables 5 and 6 (p. 16-19) to include the additional specification parameters mentioned above, corresponding analytical methods, and batch analyses.

Answer:

Please consider the updated tables 5 (Specifications) and 6 (Analytical results from 5 batches) below.

Napiferyn considers that Erucic acid would not need to be included in the specification. We do observe that the GRAS Notice dossier does not clearly specify that the percentage relates to % of total fatty acids. Accordingly, the results for 5 independent, non-consecutive batches are in fact 0,37% and <0.1% (<LOQ) of total fatty acids. The total fat level of canola protein isolate is $\leq 2\%$ DM. As such, there is no possibility of a higher presence of erucic acid. Napiferyn sources solely low erucic acid varieties of rapeseed/canola, in accordance with 21 CFR §184.1555.

Table 5. Product specifications for canola concentrate (Raptein™30)

Parameter	Unit	Value	Method
Appearance	-	white to off-white dried powder	Visual
Composition**			
Total protein (N*6.25)	%	30 - 45	ISO 1871:2009
Carbohydrates	%	≤ 65	By difference*
Fat (direct)	%	≤ 2	PB/CH/16 version 3 from 09.11.2018
Ash	%	≤ 5	PN-A-79011-8:1998
Moisture	%	≤ 7	PN-A-79011-3:1998
Total dietary fiber (TDF)	%	40 - 70	AOAC 2011.25-M
Total glucosinolates	mmol/kg	≤ 0.3	ISO 9167-1:1992; AOCS Ak 1-92
Purity**			

Phytates	%	≤ 2	Analytical Vol. 77:536-539 (1977)	Biochemistry
Lead	mg/kg	≤ 0.35	DIN EN 15763:2010 (2010-04), mod.	
Arsenic	mg/kg	≤ 0.15	§64 LFGB L 00.00-19/3	
Cadmium	mg/kg	≤ 0.2	DIN EN 15763:2010 (2010-04), mod.	
Mercury	mg/kg	≤ 0.1	DIN EN 15763:2010 (2010-04), mod.	
Microbiological criteria				
Total plate count	cfu/g	≤ 10 ⁴	PN-EN ISO 4833-1:2013-12	
<i>E. coli</i>	-	absence in 10 g	PN-ISO 7251:2006	
<i>Salmonella</i> spp.	-	absence in 25 g	PN-EN ISO 6579-1:2017-04	
Yeast and Molds	cfu/g	≤ 100	PN-ISO 21527-2:2009	
Total coliform count	cfu/g	≤ 10	PN-ISO 4831:2007	
<i>Enterobacteriaceae</i>	cfu/g	< 10	PN- EN ISO 21528-2:2017-08	
Potential contaminants				
Residual Ethanol**	mg/kg	<200	HH-MA-M 03-011, Headspace, GC-FID: 2019-01	
Residual Ethyl Acetate**	mg/kg	<200	HH-MA-M 03-011, Headspace, GC-FID: 2019-01	
Residual Sulphur Dioxide**	mg/kg	<10	PN-EN 1988-1:2001	

*Carbohydrates are calculated by difference as follows: 100 % - [protein (as is) % + moisture % + fat % + ash %] **On dry matter (except of moisture)

PN-A - polish standard; LFGB - Lebensmittel-und-Futtermittelgesetzbuch (German Food and Feed Act); DIN - Deutsches Institute für Normung (German institute for standardization); AOCS - American Oil Chemists' Society; AOAC - Association of Official Agricultural Chemists

**applicable only if used in the production process

Table 6. Analyses of 5 production batches of canola concentrate (Raptein™30)

Parameter	Specificati on	Lot No. R- 03#35	Lot No. R- 06#60	Lot No. R- 09#41	Lot No. R- 13#60	Lot No. R- 15#66
Appearance	white to off-white dried powder					
Composition**						
Total protein (N*6.25) [%]	30-45	41.26	33.10	32.28	31.65	35.49
Moisture [%]	≤ 7	2.9	5.6	2.8	6.0	4.9
Fat (direct) [%]	≤ 2	0.89	0.86	0.51	0.67	0.83
Ash [%]	≤ 5	2.82	2.87	2.89	3.81	3.23
Total dietary fiber (TDF) [%]	40-70	51.2	66.4	63.6	65.9	64.7
Carbohydrates* [%]	≤ 65	55.04	63.17	64.31	63.87	60.45
Total glucosinolates [mmol/kg]	≤ 0.3	<LOQ (<0.05)	<LOQ (<0.05)	<LOQ (<0.05)	<LOQ (<0.05)	<LOQ (<0.05)
Purity**						
Phytates [%]	≤ 2	1.44	1.09	1.38	1.60	1.49
Lead [mg/kg]	≤ 0.35	0.154	0.233	0.257	0.117	0.089

Arsenic [mg/kg]	≤ 0.15	<LOQ (<0.1)	<LOQ (<0.1)	<LOQ (<0.1)	<LOQ (<0.1)	<LOQ (<0.1)
Cadmium [mg/kg]	≤ 0.2	0.026	0.018	0.020	0.030	0.026
Mercury [mg/kg]	≤ 0.1	<LOQ (<0.005)	<LOQ (<0.005)	<LOQ (<0.005)	<LOQ (<0.005)	<LOQ (<0.005)
Microbiological criteria						
Total plate count [cfu/g]	≤ 10 ⁴	1 200	720	610	180	170
<i>E. coli</i>	absent in 10g	absent	absent	absent	absent	absent
<i>Salmonella</i> spp.	absent in 25 g	absent	absent	absent	absent	absent
Yeast and Molds [cfu/g]	≤ 100	<10	<10	<10	<10	<10
Total coliform count [cfu/g]	≤ 10	0	0	0	0	0
<i>Enterobacteriaceae</i> [cfu/g]	<10	<10	<10	<10	<10	<10
Potential contaminants						
Residual Ethanol [mg/kg]**	<200	17.5	117.0	12.3	14.1	<1.0
Residual Ethyl Acetate [mg/kg]**	<200	71.0	53.4	<1.0	29.8	14.9
Sulphur Dioxide [mg/kg]**	<10	<LOQ (<10)	<LOQ (<10)	<LOQ (<10)	<LOQ (<10)	<LOQ (<10)
<p>*Carbohydrates are calculated by difference as follows: 100 % - [protein (as is) % + moisture % + fat % + ash %];</p> <p>**On dry matter (except of moisture); <LOQ – below the Limit of Quantification</p> <p>**applicable only if used in the production process</p>						

5. Please state that all analytical methods used to test batches were validated and are fit for their respective purpose.

Answer:

Napiferyn confirms all analytical methods used to test batches were validated and are fit for their respective purpose.

6. Please state that canola concentrate is not intended for use in infant formula or in foods where standards of identity preclude its use.

Answer:

Canola concentrate is not intended for use in infant formula or in foods.

7. In Table 15 (p.), Napiferyn provides the results of the batch analyses for total plate count in the raw material (rapeseed press cake). Please address the significant variation in the results (from <10 to 28,000 CFU/g) and discuss whether this will impact safety of the final ingredient.

Answer:

The raw materials were different, e.g. different batches, hence the differences in the results. Regardless of the level of microbiology in the raw material, the product obtained is microbiologically clean and meets the specification limit.

8. On p. 19, Napiferyn states that the levels of mycotoxins in canola concentrate are below the limit of quantitation (LOQ) and provide the results from the analyses of five batches to support your statement. Please clarify whether you expect mycotoxins to be present in canola concentrate manufactured in accordance with good manufacturing practices.

Answer:

We don't expect mycotoxins to be present in canola concentrate manufactured in accordance with good manufacturing practices. The additional testing of five batches has confirmed that no mycotoxins were detected.

9. In Part 1.4 (p. 6) and Part 3.1 (p. 33), Napiferyn states that the intended use of canola concentrate is as a source of protein and/or fiber, thickener, or texturizer. However, we note that on p. 33 you also state the intended use of canola concentrate is as a flavoring agent or binder in various comminuted or whole muscle meat and poultry products. In addition, in Appendix 3 (p. 5) you state that canola concentrate may also be used "to create a flavored salt" or as "a flavor enhancer like monosodium glutamate". Please confirm these additional uses of canola concentrate are within the scope of GRN 001122.

Answer:

Napiferyn hereby confirms that canola protein isolate, as part of GRN 1103, is not intended for use as a flavored salt or flavor enhancer. Canola protein isolate can be used as an ingredient in spice and seasoning mixes (i.e. formulation aid, stabilizer and thickener, and texturizer) but does not have, by itself, the capacity to supplement, enhance, or modify the original taste and/or aroma of a food, nor to impart or help impart a taste or aroma in food.

10. On p. 10, the notifier describes the protein composition of canola concentrate, being primarily cruciferins, napin, oleosin, and squalene monooxygenase. However, the pivotal safety data provided appear to only be relevant to the cruciferin and napin fractions of the canola concentrate. Please provide a brief narrative to confirm the safety of oleosin and squalene monooxygenase exposure from the intended uses.

Answer:

Oleosins are protein compounds commonly found in seeds. Oleosins have been associated with allergic reactions for hazelnuts, peanuts and sesame^{[1][2][3]}. Allergenicity of these oil body proteins from Brassica napus is not clearly established. Oleosin S2-2 (OLES2_BRANA) identified in Raptein™30 shares less than 50% of protein amino acid sequence with oleosins from plants outside of the Brassicaceae family, except for oleosins in hazelnut and peanut with which it shares slightly above 50% (full-length FASTA). Cross-reactivity between oleosins may be primarily expected within Brassicaceae family but it also cannot be excluded against hazelnuts and peanuts, as noted in literature. Please also consider the elaboration on allergenicity of canola protein concentrate in reply to question 14.

Squalene monooxygenases (also known as squalene epoxidases) is a group of eukaryotic enzymes involved in cholesterol synthesis. While these enzymes are present in many eukaryotes, squalene monooxygenase 1,2 (ERG12_BRANA) identified in Raptein™30 shares more than 50% of its amino acid sequence exclusively with other members of the Brassicaceae family.

The inhibition of the enzyme has been considered for its potential in the treatment of hypercholesterolemia^[4]. Available publications and studies therefore mainly focus on the possible inhibitors^[5], while the effects of exposure to squalene monooxygenase through the consumption of food remain unexplored. Considering the long history of human consumption of crops in the Brassicaceae family and the expected low levels of the enzyme in the product, consumption of Raptein™30 containing a minor amount of squalene monooxygenase 1,2 is not considered to introduce any new safety concerns.

References cited:

- [1] Leduc V, Moneret-Vautrin DA, Tzen JT, Morisset M, Guerin L and Kanny G, 2006. Identification of oleosins as major allergens in sesame seed allergic patients. *Allergy*, 61, 349-356.
- [2] Akkerdaas JH, Schocker F, Vieths S, Versteeg S, Zuidmeer L, Hefle SL, Aalberse RC, Richter K, Ferreira F and van Ree R, 2006. Cloning of oleosin, a putative new hazelnut allergen, using a hazelnut cDNA library. *Mol Nutr Food Res*, 50, 18-23.
- [3] Zuidmeer-Jongejan, L., Fernández-Rivas, M., Winter, M.G. et al., 2014 Oil body-associated hazelnut allergens including oleosins are underrepresented in diagnostic extracts but associated with severe symptoms. *Clin Transl Allergy* 4, 4.
- [4] Belter A, Skupinska M, Giel-Pietraszuk M, Grabarkiewicz T, Rychlewski L, Barciszewski J. Squalene monooxygenase - a target for hypercholesterolemic therapy. *Biol Chem*. 2011 Dec;392(12):1053-75
- [5] Zou Y, Zhang H, Bi F, Tang Q, Xu H. Targeting the key cholesterol biosynthesis enzyme squalene monooxygenase for cancer therapy. *Front Oncol*. 2022 Aug 24.

11. On p. 31-32 of the notice, the notifier clearly establishes that canola concentrate is intended to be substitutive to protein and fiber consumption and will not contribute to additional exposure to protein or fiber in general. Please elaborate on this conclusion, and clarify if the intended uses of canola concentrate are additive or substitutive to other canola protein products currently on the market (i.e., GRNs 327, 386, and 683)?

Answer:

The canola concentrate (Raptein™30) will be added to food products as a protein or fiber substitute and therefore will not contribute to any additional exposure to protein and fiber for the consumers.

In terms of protein part of canola concentrate it is substitutive to other canola protein products currently on the market (i.e., GRNs 327, 386, and 683), but in case of the fiber part of canola concentrate it is additive, because GRN mentioned are not rich in fiber (they are canola proteins).

12. On p. 37, the notifier concludes exposure to canola concentrate from the intended uses is safe since the EDI reported is “still much lower (approximately 7- to 22-fold lower) than the no-observed-adverse-effect level (NOAEL) values established” for cruciferin- and napin-rich protein isolates in male rats following a 13-week oral exposure regimen (Mejia *et al.*, 2009a & 2009b). We note that an uncertainty factor, or margin of safety (MOS), of 100 (10 for interindividual variability × 10 for interspecies variability) is normally used when assessing safety of a food ingredient by comparing estimated human exposure levels to the NOAEL from animal toxicology data. Therefore, it is not clear why MOS that is ~5-10-fold lower can be concluded as safe without proper justification. Additionally, we note that potential thyrotoxic effects were observed at the highest doses in these two rat studies, as well as for rapeseed products in general tested in other species, as cited in Table 20 of the GRAS notice. This effect was mostly attributed to the presence of glucosinolate; however, we note that since the level of glucosinolate was low or absent in both the test articles from Mejia *et al.* and the article of commerce, the rationale used by the study authors to conclude that the observed NOAEL was not in fact the LOAEL may be questionable. Regardless, it appears that the provided safety narrative lacks sufficient basis to conclude MOS of 7-22 is adequate to reach the conclusion of “reasonable certainty of no harm.” Based on generally available data and information, please provide additional narrative to explain your rationale for your GRAS conclusion.

Answer:

The estimate exposure to canola protein concentrate ranges from 2.04 g/Kg BW/day for young children to 0.53 g/Kg BW/day for adults (considering 90th percentile). The applicant considers these are conservative values which are lower than the NOAEL of 11.24 g/Kg bd/day for male rats reported by Mejia et al. for the cruciferin-rich protein isolate and 12.46 g/Kg BW/day for male rats for the napin-rich protein isolate^{[1][2]}. The exposures are slightly above than those reported in one prior GRAS notices which ranged from 2.0 to 0.53 g/Kg BW/day (GRN 00068) and lower than those reported in GRN 327 which ranged from 3.1 to 0.75 g/Kg BW/day.

The canola protein concentrate is not expected to have 100% of the market share for canola protein products. Additionally, food intake databases from which the estimated exposures are derived usually overestimate consumption, since they do not reflect the true chronic exposure conditions. These factors will typically overestimate the exposure of a macronutrient by a factor of 2- to 10-fold^[3].

Taking these considerations into account all the aspects for evaluation of safe exposure, the applicant considers that canola protein concentrate intakes will be well below levels of any possible concern and thus is safe for human consumption.

Organ weights were not affected by the treatment with the possible exception of the relative thyroid plus parathyroid weight, which was slightly but significantly increased in females, but not in males, of the high dose napin protein isolate group^[2] and in both sexes of the high dose cruciferin protein isolate group^[1]. In the absence of histopathological changes of the thyroids, the thyroid weight was not considered of toxicological relevance^{[1][2][4]}.

References cited:

[1] Mejia, L.A., Korgaonkar, C.K., Schweizer, M., Chengelis, C., Marit, G., Ziemer, E., Grabiell, R. & Empie, M. 2009, "A 13-week sub-chronic dietary toxicity study of a cruciferin-rich canola protein isolate in rats", Food and chemical toxicology : an international journal published for the British Industrial Biological Research Association, vol. 47, no. 10, pp. 2645-2654.

- [2] Mejia, L.A., Korgaonkar, C.K., Schweizer, M., Chengelis, C., Novilla, M., Ziemer, E., Williamson-Hughes, P.S., Grabiél, R. & Empie, M. 2009, "A 13-week dietary toxicity study in rats of a Napin-Rich Canola Protein Isolate", *Regulatory toxicology and pharmacology* : RTP, vol. 55, no. 3, pp. 394-402.
- [3] Munro, I.C., McGirr, L.G., Nestmann, E.R. & Kille, J.W. 1996, "Alternative approaches to the safety assessment of macronutrient substitutes", *Regulatory Toxicology and Pharmacology*, vol. 23, no. 1, pp. S6-S14
- [4] EFSA NDA Panel (EFSA Panel on Dietetic Products, Nutrition and Allergies), 2013. Scientific Opinion on the safety of "rapeseed protein isolate" as a Novel Food ingredient. *EFSA Journal* 2013;11(10):3420, 23 pp. doi:10.2903/j.efsa.2013.3420

13. We note that when discussing the absorption, distribution, metabolism, and excretion of canola concentrate (p. 49), the notifier reports unpublished data from an EU Novel Foods application for "defatted rapeseed powder" to support their conclusion. Similarly, genotoxicity conclusions are made using unpublished data from an EFSA Panel conclusion on defatted rapeseed powder. Given other data and information have been used in prior GRAS notices for canola ingredients (e.g., GRN 327), please confirm that the EFSA Panel and EU Novel Foods conclusions are only considered as corroborative, not pivotal, to the safety determination of canola concentrate at its intended use level?

Answer:

Napiferyn confirms that the EFSA Panel conclusions are only corroborative and not pivotal to the safety determination of canola concentrate at its intended use level.

14. On p. 40, the notifier discusses the allergenicity potential of canola concentrate being determined via a "bioinformatics approach" and concludes that canola concentrate "may elicit possible allergenic effects." Additionally, on p. 59 the notifier reiterates that the bioinformatics analysis indicated "possible allergenic effects" of canola concentrate, but no further discussion is provided. While data from an allergen online database search is provided as part of Appendix 4, no discussion of these data are included in the current GRAS notice. Please briefly detail the "possible allergenic effects" of canola concentrate similar to previous notices (e.g., GRN 683), and discuss why they would not be expected to pose a safety concern from the intended use.

Answer:

The results of Mascot search on SwissProt database identified 3 cruciferins as the most abundant proteins found; cruciferin CRU4 (CRU4_BRANA), cruciferin CRU1 (CRU3_BRANA), and cruciferin BnC1 (CRU1_BRANA); with oleosin S2-2 (OLES2_BRANA), napin-3 (2SS3_BRANA), and squalene monooxygenase 1,2 (ERG12_BRANA) present in smaller amounts. This is consistent with publicly available data on the composition of proteins in rapeseed^{[1][2]}.

Bioinformatics searches for sequence similarity to known allergen proteins or celiac disease-eliciting proteins were performed using the FASTA3 algorithm and BLASTP. The identified proteins were searched in publicly available FARRP allergen protein database, FARRP Celiac Disease database, and NCBI Protein database.

All 3 cruciferins show a degree of identity match to 11S globulin proteins in white mustard (*Sinapis alba*). This was especially high (90-92%, full-length FASTA) for cruciferin CRU1 (CRU3_BRANA). Cruciferin is one of the major allergens in white mustard and hazelnut (*Corylus avellana*)^[3]. Because of such a high degree of identity matches with 11S globulin proteins in white mustard, not in hazelnut, cross-reactivity to mustard cruciferins is very likely.

Napin-3 (2SS3_BRANA, allergen Bra n 1) is known to cause allergenic reaction in humans and to bind to IgE^{[4][5]}. It also had high degrees of identity matches to 2S seed storage albumin proteins in oriental mustard (*Brassica juncea*) (allergen Bra j 1-E, 89.1%, full-length FASTA) and in turnip rape (*Brassica*

rapa) (allergen Bra r 1, 80.9%), known to cause allergic reactions in humans^{[6][7][5]}. Napin-3 also had a high degree of identity match (up to 83%) to multiple variants of Sin a 1 allergen in white mustard.

Full-length FASTA search has shown relatively high identity matches between oleosin S2-2 (OLES2_BRANA) and oleosins in hazelnut (up to 52.3%) and peanuts (*Arachis hypogaea*, up to 52.5%). Identity matches against all other major food allergen sources were below 50%.

The BLASTP searches performed against the NCBI Protein database did not include any allergenic proteins apart from 10 that were already found during the FARRP allergen protein database searches. Based on historical data, cross-reactivity is fairly common for proteins sharing greater than 70% identity. Then again, those sharing less than 50% identity over the entire protein sequence are not likely to demonstrate cross-reactivity^[8]. Therefore, it can be concluded that cross-reactions between members of the *Brassicaceae* family are highly possible^{[3][5]}.

Overall, RapteinTM30 canola concentrate (rapeseed concentrate) is not expected to be allergenic except for those individuals allergic to mustard or other plants in the *Brassicaceae* family, which currently are not listed as major food allergen sources in the USA. Although the product is not derived from a major food allergen source and is not required to be labelled as such, due to potential allergic cross-reactivity of 2S and 11S seed storage proteins, voluntary precautionary statement for mustard may be considered^[3].

Proteins in RapteinTM30 did not match any peptides using the word search against the Celiac Disease peptide dataset (version 2, released 21 September 2017). The full-length FASTA search against the Celiac Disease protein dataset also did not indicate high sequence similarity with the RapteinTM30 proteins. Although some matches were found, identity matches of less than 45% over at least one-half of the FASTA aligned celiac disease protein and those with an E-value higher than 1×10^{-15} are unlikely to present a risk of inducing celiac disease. The results indicate that the RapteinTM30 proteins are unlikely to elicit celiac disease.

References cited:

- [1] Murphy D.J. (2003). Seed development. Oil Deposition. *Encyclopedia of Applied Plant Sciences*, Elsevier, Editor(s): Brian Thomas, pp. 1256-1261.
- [2] Ottens M. and Chilamkurthi S. (2013). 4 - Advances in process chromatography and applications in the food, beverage and nutraceutical industries. *Separation, Extraction and Concentration Processes in the Food, Beverage and Nutraceutical Industries*, Woodhead Publishing, Editor(s): Syed S.H. Rizvi, pp. 109-147.
- [3] Fiocchi A., Dahdah L., Riccardi C., Mazzina C., and Fierro V. (2016). Precautionary labelling of cross-reactive foods: The case of rapeseed. *Asthma Res and Pract.* 2(13):1-8.
- [4] Monsalve R.I., González de la Peña M.A., López-Otín C., Fiandor A., Fernández C., Villalba M., and Rodríguez R. (1997). Detection, isolation and complete amino acid sequence of an aeroallergenic protein from rapeseed flour. *Clin Exp Allergy*, 27:833-41.
- [5] Puumalainen T.J., Poikonen S., Kotovuori A., Vaali K., Kalkkinen N., Reunala T., Turjanmaa K., and Palosuo T. (2006). Napins, 2S albumins, are major allergens in oilseed rape and turnip rape. *J Allergy Clin Immunol*, 117(2):426-432.
- [6] Monsalve R.I., Gonzalez de la Peña M.A., Menendez-Arias L., Lopez-Otin C., Villalba M., and Rodriguez R. (1993). Characterization of a new oriental-mustard (*Brassica juncea*) allergen, Bra j IE: detection of an allergenic epitope. *Biochem J*, 293(3):625-632.
- [7] Moreno F.J. and Clemente A. (2008). 2S albumin storage proteins: what makes them food allergens? *Open Biochem J*, 2:16-28.
- [8] Aalberse R.C. (2000). Structural biology of allergens. *J Allergy Clin Immunol*, 106(2):228-238.

15. We note that a recent study on rapeseed protein isolate was published (Xiong et al., 2022).
- a. Please discuss if this study presents additional safety concerns for the article of commerce or contradicts the current GRAS conclusion.

Answer:

The article titled “Removal of anti-nutritional factors of rapeseed protein isolate (RPI) and toxicity assessment of RPI” discusses the potential safety concerns raised, in relation to the presence of anti-nutritional factors (ANFs) in rapeseed protein isolate (RPI). The study compares a non-treated (or non-detoxified) rapeseed protein isolate with a treated (or detoxified) RPI and a commercial soybean protein isolate (SPI), in terms of level of anti-nutritional factors (i.e., glucosinolates, phenolics and phytic acid) and their respective effects on mice. The de-toxification of the RPI was a combined treatment based on alkaline extraction and acidic precipitation. Initially, the RPI was pre-treated with phytase, followed by double ethanol extraction in (ratio 1:5) for a duration of 1.5 hours. The de-toxification of the RPI led to a significant removal of the anti-nutrients.

Following administration to mice for 14 days, the results showed that RPI de-toxified with phytase/ethanol was safe, while a decrease of the thyroid/parathyroid index in mice treated with non-detoxified RPI was reported. The authors state that significant changes were observed in the weight of liver and kidneys between the group fed detoxified RPI and the control group, though no corresponding damage to liver or kidneys was observed.

Additionally, measurement of the thyroid-releasing hormone (TRH), showed higher concentrations of TRH in serum of mice fed detoxified RPI, which could be associated with thyroid gland complications, such as hypothyroidism. The authors conclude that the RPI ingestion could cause inflammation of the thyroid gland, although proper elaboration on their conclusion is missing. Further, the group of mice fed detoxified RPI did show lower levels of Alanine transaminase (ALT) and Aspartate aminotransferase (AST) compared to the control groups (fed non-detoxified RPI). Finally, as a general statement the authors argue that non-detoxified RPI could cause liver disease. Yet, the study concludes that there were no consistent or significant differences in toxicology-related parameters between the treatment groups.

Given article by Xiong et al. (2022) demonstrates that significant removal of antinutrients can be achieved and the resulting detoxified RPI was considered safe under the conditions tested. The article therefore supports that appropriate treatments can be considered to lower antinutrients in rapeseed protein products, but it does not permit to draw accurate conclusions on the toxicity of other rapeseed protein products (i.e., non-detoxified).

As regards to Napiferyn, in the production of the rapeseed/canola protein concentrate, which is the subject of GRAS Notice 1122, purposely designed steps are applied to reduce the content of antinutritional factors. As a result, the final levels of antinutrients are in line or lower than what is conventionally found in rapeseed protein isolates.

- b. Please also perform an updated literature review from 2021 to present and discuss if any additional studies relevant to the safety of canola concentrate were identified that would contradict the current GRAS conclusion.

Answer:

A literature review for the period of 2021-2023 (until 4 July 2023) has been conducted. The result, including discussion, can be found in the report titled ‘Literature_review_GRAS_years_2021-2023’.

References cited:

Xiong Z, Fu Y, Yao J, Zhang N, He R, Ju X, Wang Z. Removal of anti-nutritional factors of rapeseed protein isolate (RPI) and toxicity assessment of RPI. *Food Funct.* 2022 Jan 24;13(2):664-674. doi: 10.1039/d1fo03217h. PMID: 34933325.

Additionally, we received the following questions from USDA FSIS regarding their review of the uses of GRN 1122 concerning products within their purview. Please respond to the following and we will pass your responses along to them.

Please provide Safety Data Sheet (SDS) for the at use concentrations of the substance and include a description of how the use of this technology will not adversely affect the safety of FSIS inspectors. Workplace safety and health hazards include inhalation, direct skin contact (skin, eyes, mouth), and fire/explosion caused by exposure to the product, its working solution or dry mixture and potential by-products formed and/or off-gassed during the application process. The employee safety information should demonstrate how the New Technology will not “jeopardize the safety of Federal inspection personnel” as specified in the FSIS Compliance Guideline Procedures for New Technology Notifications and Protocols, April 2015. FSIS workplace and employee safety must be specifically addressed. Please refer to Appendix A on p. 17, Workplace Safety and Health Criteria, for clarification on what to provide in the response. For additional clarity with respect to employee safety, the following are examples of information that are typically needed by FSIS’ employee safety and health group;

Answer: A Safety Data Sheet for Canola Protein Concentrate has been included, titled ‘Canola_Protein_Concentrate_SDS_v1’.

1. Potential workplace exposures that could result from inhalation and direct contact during use of the substance/technology. This information is required in addition to a SDS to determine accurate hazard potential and recommended exposure control measures for IPP work areas in accordance with Occupational Safety and Health Administration (OSHA) regulations: 29 CFR 1910.1200, Hazard Communication, 29 CFR 1910.132, Personal Protective Equipment, and 29 CFR 1910.1000, Air Contaminants. The information should be included as a specific section in each of the protocols.

Answer:

Raptein™30 is not classified as hazardous according to OSHA Hazard Communication Standard (29 CFR 1910.1200). Nonetheless, since the product is a powder, depending on how it is used, dust can be generated, which can be both a health and a fire hazard. Also, there is a potential for allergen cross-reactivity with mustard, other members of the *Brassicaceae* family, some tree nuts and peanuts.

Therefore, the safety data sheet includes relevant precautions for safe handling, such as wearing protective gloves, protective clothing, eye and/or face protection; avoiding the formation/deposition of dust and static charges; providing for good ventilation of the room when handling the material, and, in case of inadequate ventilation, wearing respiratory protection. Breathing dust should be avoided. Also, it is advisable to prevent the powder from getting into the eyes, on skin, or on clothing as this may lead to either ingestion or adversely affect the eyes. Not eating, drinking or smoking in work areas and proper handling of contaminated clothing and protective equipment are part of normal hygiene practices.

The material is not specifically listed in 29 CFR 1910.1000. Since dust can potentially be generated, depending on how the material is used, the SDS includes 8-hour total weight average (TWA) permissible exposure limit (PEL) applicable to particulates not otherwise regulated

(PNOR), which is 15 mg/m³ (measured as total dust) and 5 mg/m³ (measured as respirable fraction).

2. If the SDS workplace hazards/precautions do not apply to the type of exposure that would be expected for the FSIS IPP, please have the submitter provide specific information (per the April 2015 FSIS Compliance Guideline Procedures) for the actual type of exposures expected.

Answer: Precautions for safe handling in the SDS are relevant to the type of exposure that could be expected for the FSIS IPP.

3. If no IPP workplace exposures are expected and no control measures are required, please have the submitter state this and provide the reasons why (e.g., such as the substance “as used” [for all concentrations] is not hazardous by inhalation or direct contact and/or IPP would not be exposed to the substance based on the system design, operation and/or control measures that will be in place).

Answer: Whether IPP workplace exposures could be expected will depend on how the material is used on site. Therefore, an assessment on a case-by-case basis is recommended.

4. Please also indicate how will FSIS IPP be informed of the above information so that it is clear that the information contained in the SDS for the concentrate does not apply to their actual workplace exposure.

Answer: It is our view that the information contained in the SDS may potentially apply to the IPP’s actual workplace exposure. Therefore, an assessment on a case-by-case basis is recommended.

5. Are there any potential hazards from chemical mixing or low pH as a result of discharges of the various solutions to floor drains? Are dedicated drain lines or any other enclosures required?

Answer: Not applicable

6. With respect to potential airborne exposures to FSIS IPP in the use/application areas, does the submitter have air sampling results taken during the use of the various concentrations of the technology in the listed mixture?

Answer: Such testing has not been conducted. An assessment on a case-by-case basis is recommended.

7. The intended use of this product in FSIS meat and poultry products is apparently as a binder/extender. The suitability support provided in Appendix 6 does sufficiently support no significant difference in yield and other organoleptic qualities when used as a partial replacement for another binder in a processed meat and poultry product, such as sausage. However, additional suitability support is needed:
 - a. No suitability data was provided for whole muscle meat and poultry products at the maximum proposed use level. We would need to see similar data as provided in Appendix 6 for:
 1. Whole muscle red meat control containing no other binders, extenders, or moisture retention agents, as compared to a whole muscle red meat product containing 15% isolated canola product.
 2. Whole muscle poultry control containing no other binders, extenders, or moisture retention agents as compared to a whole muscle poultry product containing 15% isolated canola product.

Answer: Additional suitability testing has been performed, results are described in the attached report titled 'Additional_suitability_Report_meat_extensions'.

Literature Search Strategy protocol: Safety of Raptein™30 and Raptein™90 in support of GRAS Notices

Product: Rapeseed/canola protein concentrate and isolate

Client: NapiFeryn BioTech

Prepared by: Pen&Tec Consulting

Date: 10 July 2023

Executive summary:

A comprehensive search of the scientific literature was conducted to review the safety of NapiFeryn's rapeseed/canola protein-fibre concentrate Raptein™30 and rapeseed/canola protein isolate Raptein™90 and their components, destined for human consumption. Two databases were searched: CAB Abstracts® and the Food Science and Technology Abstracts (FSTA®). The search was limited to the last two years since submission of the GRAS notice (years 2021-2023 to date of search: 04 July 2023)).

1. Background and Introduction

NapiFeryn BioTech (NFB) is interested to bring its rapeseed/canola protein-fibre concentrate Raptein™30 and rapeseed/canola protein isolate Raptein™90 to the United States market, to be used as a food ingredient in a variety of foods and beverages at use levels ranging from 5% to 100%. (*e.g.*, bakery products, breakfast cereals, grain products, pastas, bars, protein-fiber and nutritional powders, beverages and beverage bases non-alcoholic, milk products and dairy analogs, coffee and tea etc.).

2. Question and objective

Question

Does the consumption of rapeseed/canola proteins, either isolate or concentrate form, raise any health safety issues, specifically due to the potential presence of undesirable substances (i.e. contaminants or anti-nutritional factors (ANFs))?

N.B.: the presence of potential undesirable substances is controlled as part of the manufacturing process and applicable food safety and quality management systems in the production of Raptein™30 and Raptein™90.

3. Topics of interest

The topic of interest for this literature search is the safety for humans (i.e., human safety data and *in vitro* and *in vivo* (from experimental animals) toxicity data).

3.1. Inclusion/Exclusion criteria

The following inclusion and exclusion criteria were defined *a priori*.

Inclusion criteria:

- Studies, publications, or case reports (human studies/testing, immunological tests, relevant protein analysis) that investigate the safety and any potential toxicity of rapeseed/canola proteins, or concentrates or isolates thereof specifically;
- Toxicological studies, reports and case studies related to the safety of *Brassica napus*, *Brassica rapa* and *Brassica juncea* (including those for humans, if any);
- Consider studies in all languages

- Studies analysing chemical residues of concern or anti-nutritional factors in the interested *Brassica* species.

Exclusion criteria:

- Publications not relevant to the safety and toxicity topics of the literature search
- Abstracts related to patent registration of description
- Biocidal studies
- Ecotoxicology studies (e.g., plant growth/ plant disease/ soil crops studies)
- Therapeutical/positive effect: reported effects can be regarded as favourable rather than adverse (positive effects) e.g.: studies addressing health benefits (e.g., activity against cancer cell lines, diabetes or present protective aspect against some pathologies)
- Studies on pesticides
- Abstracts whose full- text pdfs are not retrievable
- Duplicates

The search terms and details of the literature search are specified in Table 1. The outcome of the search was exported as an EndNote library and the file is available upon request in .ciw (EndNote) format.

4. Search strategy

4.1. Study selection and assessment

EndNote was used for the selection process, which was performed in the steps indicated below:

- The search was conducted using the WebofScience platform and covered two databases (FSTA and CABI) using the key terms as described in Table 1.
- Importation of hits in EndNote
- Screening of titles and abstracts against inclusion/exclusion criteria (First screening)
- Full-text screening of selected references considered up for inclusion (Second screening)
- Write-up literature review

4.2. Search strategy

A search was conducted using the following databases: CAB Abstracts® and the Food Science Resource (FSTA®). The time-period searched was limited to two years (2021-2023 [up to 4 July]), while there was no limitation related to the language of publication. The search terms used are defined in Table 1 and the outcome for the literature search is described in section 5 below.

In brief, the results of the literature search were copied into an EndNote™ file and the titles and abstracts were independently screened for relevance. References for which only a title was available and/or abstracts for which the reviewer could not make a decision were included by default in the list of full manuscripts to be obtained. For the references that could not be obtained at the first attempt, follow-up attempts were made to obtain the full manuscript. References meeting the inclusion criteria were considered relevant. Data from abstracts were used only where it was unlikely that the information contained in the full manuscript would change the conclusions of this review in a clinically meaningful way.

Search terms were chosen specific to the research question. Descriptors were used to identify relevant articles in both databases, as shown below. Descriptors are specific to each database, hence the differences between the search criteria in Table 1 below.

Table 1: Search for safety and toxicity, of Canola proteins (concentrate or isolates) in CAB Abstracts® and FSTA®. Interface: Web of Science		
Period searched: 2021 – 2023. Search was carried out 4 July 2023		
Search set: CABI: CAB Abstracts® FSTA® - the food science resource		
Search combinations and number of items found		
Subject areas	Search sets	Number of items found
CAB Abstracts®	<p>#Descriptors: (rapeseed OR rapeseed protein OR canola OR brassica napus OR brassica rapa OR brassica juncea))</p> <p>AND #Topic:("protein*" OR concentrate or isolate))</p> <p>AND #Descriptors: (food safety OR toxicity OR toxic substances OR antinutritional factors)</p> <p>Filter: years 2021-2023 (up to 3 July 2023)</p>	47
FSTA®	<p># Descriptors: (canola OR rapeseeds OR brassica napus OR brassica rapa OR brassica juncea)</p> <p>AND #Descriptors: (protein isolates OR protein concentrates OR proteins)</p> <p>AND #Descriptors: (food safety plant foods OR food safety animal foods OR toxins OR anti-nutritional compounds OR anti-nutritional factors OR antinutritional factors)</p> <p>Filter: years 2021-2023 (up to 3 July 2023)</p>	11

5. Literature search outcome

5.1. Literature retrieved from databases

The literature search identified a total of 58 publications in a combined CABI Abstracts and FSTA search. Results from each database were individually screened for relevance. Ultimately, 11 publications were considered relevant from both databases and included in the discussion for the safety assessment of the rapeseed proteins for human consumption.

5.2. Results and discussion

The exclusion criteria leading to the greatest number of papers excluded are provided along with the number of papers affected:

- Publications not relevant to the safety or toxicity topics of the literature search: 22 (CABI abstracts) / 7 (FSTA)
- Species not relevant: 2 (CABI abstracts) / not applicable (FSTA)
- Ecotoxicology/plant studies (e.g., plant growth/ plant disease/ soil crops studies): 2 (CABI abstracts) / not applicable (FSTA)
- Therapeutical/positive effect: 3 (CABI abstracts) / 1 (FSTA)
- Studies on pesticides: 2 (CABI abstracts) / 1 (FSTA)
- Abstracts whose full- text pdfs are not retrievable: 2 (CABI abstracts) / 1 (FSTA)
- Duplicates: 1 (CABI abstracts) / not applicable (FSTA)

Rapeseed safety and residues of concern

Rapeseed is characterised as the second largest and an excellent source of plant proteins across the globe, with an ideal profile of essential amino acids, while is used widely in human and animal nutrition. Chmielewska A. and colleagues, presented in 2021 a comprehensive review of oilseeds of *Brassica* family (mainly consisting of canola/rapeseed proteins: cruciferin and napin), focusing on their possible applications in food, while also addressing the need to obtain rapeseed protein products free from anti-nutritional factors. The outcome of their research showed that rapeseed proteins demonstrate beneficial nutritional value (and functional properties). However, the authors, do mention the need of paying attention to the allergenic potential of predominant canola/rapeseed proteins, such as 2S napin, as well as to the presence of undesirable anti-nutritional factors such as glucosinolates, phenolic compounds including sinapine and condensed tannis, phytates, or fibre, which are formed during different metabolic processes as side products and could affect the safety of the rapeseed products used in human or animal nutrition. The study concluded that although the abovementioned anti-nutritional factors are still considered to be the main disadvantage of rapeseed proteins use for human food applications, current technological processes allow elimination up to 100% of tannic acid, 92% of phytic acid and 95% of glucosinolates.

The latter anti-nutritional elements and their role in feed safety were also described by K. Golebiewska et al. in 2022. Overall, the published review study explains that although few of these elements (e.g., glucosinolates) may not be toxic to animals in their original form, products of their hydrolysis may be harmful to animals and lead to lower feed intake. Therefore, the review concluded that the presence of these elements, constitute a limitation in the use of rapeseed meal (RSM) in monogastric animal nutrition, and is essential for the feed safety to be significantly reduced through the fermentation process applied.

In another recent review study published in 2022, F.Kaiser and his colleagues investigated the use of rapeseed proteins as alternative to fish meals, since rapeseed protein products are highly available on a global scale and provide one of the most balanced amino acid composition among plant-based protein sources. However, this review study also identified the presence of anti-nutritional factors in rapeseed products, such as phytic acid, protease inhibitors and tannins, which although can be considered negligible at low concentrations, their negative impact on animal safety, besides their undesirable effects on nutrient digestibility and diet palatability, can be influenced by multiple factors and should be taken into consideration.

According to the study, several of the anti-nutritive substances including glucosinolates, phytic acid, sinapine and tannins are responsible for multiple issues concerning the health status of animals, such as liver haemorrhage, toxicity for liver and kidney, increased organ weight, disturbed thyroid function like goitre, neurotoxicity, mutagenicity and even mortality. Consequently, the authors concluded that potential dietary tolerance levels for anti-nutritive substances in rapeseed protein products appear to be roughly 0.7 $\mu\text{mol/g}$ for glucosinolates, 0.4% for phytic acid, 0.5% for proteinase inhibitors, 0.2% for tannins and 3% for crude fibre in multiple species of fish according to experimental results from current literature. On the contrary, due to the variety of influencing factors involved, accurate safe thresholds for other animal species and humans were impossible to be predicted from the current review and more research is required (F.Kaiser et al.2022)¹.

Additionally, F.Kaiser and his team investigated in more detail the effect of certain supplemented anti-nutritive substances from rapeseed such as phytic acid and glucosinolates on fish health. During this study, growth and health performance of rainbow trout (*Oncorhynchus mykiss*) was evaluated after 38 and 56 days of feeding, with diets rich in glucosinolates and phytic acid respectively. The results of the study showed that high inclusion levels of phytic acid supplemented for 56 days led to impaired feed intake (and consequently decreased animal growth) and therefore was concluded that phytic acid should be kept at lowest inclusion level possible until further research is done. With regards to supplementation of glucosinolates for the designated period (38 days), no significant negative effect was observed in the health status of *Oncorhynchus mykiss*. However, it is highlighted that the short experimental duration should be considered for the above conclusions (F.Kaiser et al., 2021)².

According to Liu S. and his colleagues, high amounts of glucosinolates (GSLs) which are found in rapeseed by-products, could negatively affect the health of animals, such as pigs, since they are degraded by myrosinase enzymes to produce a variety of anti-nutritional factors, like isothiocyanates (ITCs), tannins, thiocyanates and phytic acid. The authors advocate that several studies have found that long-term intake of feedstuff containing high doses of ITCs reduced intake and growth, induced liver and thyroid hypertrophy, and caused acute gastroenteritis, such as diarrhea, colic and mouth-foaming in pigs.

Xiong Z. and his team highlighted in their study the potential safety concerns raised for humans related to the presence of anti-nutritional factors (ANFs) in rapeseed protein isolate (RPI) and stressed the importance of their removal, prior to human consumption. For this purpose, a treatment combining phytase and ethanol was applied. The de-toxification treatment of the rapeseed protein isolate led to significant removal of ANFs and the no-observed-effect level (NOEL) for detoxified RPI was established at 10 g kg⁻¹ of detoxified RPI, whereas the no-observed-adverse-effect-level (NOAEL) was the highest fed level of 20 g kg⁻¹ of detoxified RPI. The study concluded that rapeseed protein isolate was safe for human consumption, after the de-toxification treatment and the significant removal of anti-nutritional factors.

Another study, (F. Kaiser et al., 2021)³ tested a highly purified rapeseed protein isolate with high protein content and low levels of both Nitrogen-free extracts (NfE) and anti-nutritive substances (ANFs), to assess its suitability as fish meal replacement. The outcome of this study, where control diet was gradually replaced by rapeseed protein isolate to 33%, 66% and 100% of digestible protein and

¹ F. Kaiser, H. Harbach and C. Schulz. Rapeseed proteins as fishmeal alternatives: a review. *Reviews in aquaculture*. Vol.14, P.1887-1911, 2022.

²F. Kaiser, H. J. Harloff, R. P. Tressel, D. Steffens, H. Seibel, C. Jung and C. Schulz. Effects of supplemented anti-nutritive substances from rapeseed on growth and health performance of rainbow trout (*Oncorhynchus mykiss*). *Aquaculture nutrition*. 2021.

³F. Kaiser, H. J. Harloff, R. P. Tressel, T. Kock and C. Schulz. Effects of highly purified rapeseed protein isolate as fishmeal alternative on nutrient digestibility and growth performance in diets fed to rainbow trout (*Oncorhynchus mykiss*). *Aquaculture nutrition*. Vol.27, P.1352-1362, 2021.

energy, showed no significant effect on fish health parameters (e.g., viscerosomatic index, fish weight, hepatosomatic index, spleen somatic index and Fulton's condition factor), after 56 days observation.

Liwei Liu et al., described the adverse physiological and toxicological impacts of anti-nutritional factors and toxicants, such as tannin, identified in rapeseed on fish (*Ctenopharyngodon idellus*). Different concentrations of dietary tannin (1.5, 7.2, 19.9, 39.4, 83.2 and 162.0 g kg⁻¹ diet) were tested and the outcome of this study showed that high levels of dietary tannin (≥ 39.4 g kg⁻¹ diet) lowered immunity (serum superoxide dismutase and catalase activities and the contents of total protein, albumin, complement component C3 and C4) ($p < .05$) and damaged the hepatic structure of grass carp (*Ctenopharyngodon idellus*), leading to attenuated growth. The study suggested that grass carp could not tolerate dietary tannin of >19.9 g kg⁻¹.

Liping Zhu and his team reported fatty liver hemorrhage syndrome (FLHS) observed in hens after fed with rapeseed meal (RSM). The results of their study indicated that from overall 600 laying hens tested, 3 hens died due to liver hemorrhage after ingesting 14% RSM diet. The 14% RSM decreased serum low-density lipoprotein cholesterol (LDL-C) content ($P < 0.01$) while tended to increase serum trimethylamine N-oxide (TMAO) content compared to the control group ($P = 0.08$). The 14% RSM diet also increased total cholesterol (TC) and LDL-C content in the liver ($P < 0.01$, and $P < 0.01$, respectively). The liver total bile acid (TBA) content was decreased compared to the control ($P < 0.01$). Recent metabolomic approaches have identified that plasma trimethylamine-N-oxide (TMAO), is a novel and independent risk factor for promoting incidence of cardiovascular diseases (CVD), such as atherosclerosis (AS) both in humans and mice.

In the European Union, rapeseed products (i.e., oil), are regularly consumed by the population while other forms such as protein isolates and oilseed rape powders are not yet as common. The European Food Safety Authority (EFSA), has recently assessed the safety of genetically modified rapeseed product from *Brassica napus* (MON 94100), and has issued positive scientific opinion supporting its safety for humans, animals and the environment (under the proposed conditions of use), as similarly indicated for its conventional non-GM counterparts (Advanta Hyola 575 CL, Brett Young 5535 CL, Brett Young 5545 CL, Dekalb 71–30 CL, Mycogen 2020 CL, Mycogen 2022 CL, Mycogen 2024 CL, Pioneer 45H76, Pioneer 46H75, Rubisco Atomic TT, Rubisco DL1501 CL and Rubisco Trapper). Similar conclusions were presented by EFSA after the safety assessment of genetically modified oilseed rape 73496 and its conventional non-GM counterpart, which was found to be safe for human, animal consumption and the environment, under the proposed conditions of use.

6. Conclusions

The current search of the literature, conducted for the years between 2021-2023, identified several published studies describing the wide use of rapeseed products in human and animal nutrition. Although no significant evidence of safety concerns or adverse effects directly related to rapeseed protein-fibres were described, in the available publications, the literature search detected multiple indications for safety concerns related to the presence of residues and anti-nutritional factors (e.g., glucosinolates, phenolic compounds including sinapine and condensed tannin, phytates etc), in rapeseed isolates and by-products, such as rapeseed meals.

Overall, although no direct relationship of such anti-nutritional factors with Raptein™30 and Raptein™90 was reported, this review concludes that the presence of residues and anti-nutritional factors should be monitored and be reduced with appropriate treatments (e.g., by de-toxification following combined treatment of phytase and ethanol), before human consumption. Therefore, following significant removal of any ANFs, rapeseed/canola protein-fibre concentrate Raptein™30 and rapeseed/canola protein isolate Raptein™90 should be considered safe to be used as food for humans,

with a limited likelihood of causing adverse reactions or safety issues, at the proposed conditions of use.

7. References

7.1. Databases and software used

- CABI: CAB Abstracts®
- FSTA® - the food science resource
- EndNote X9.3.3 Clarivate, Desktop application

7.2. Bibliography

A. Chmielewska, M. Kozłowska, D. Rachwał, P. Wnukowski, R. Amarowicz, E. Nebesny and J. Rosicka-Kaczmarek. Canola/rapeseed protein - nutritional value, functionality and food application: a review. *Critical Reviews in Food Science and Nutrition*. 2020.

EFSA Panel on Genetically Modified Organisms (GMO). Assessment of genetically modified oilseed rape MON 94100 for food and feed uses, under regulation (EC) No 1829/2003 (application EFSA-GMO-NL-2020-169). *EFSA Journal*.2022.

EFSA Panel on Genetically Modified Organisms (GMO). Assessment of genetically modified oilseed rape 73496 for food and feed uses, under Regulation (EC) No 1829/2003 (application EFSA-GMO-NL-2012-109). *EFSA Journal*. 2021.

F. Kaiser, H. Harbach and C. Schulz. Rapeseed proteins as fishmeal alternatives: a review. *Reviews in aquaculture*. Vol.14, P.1887-1911, 2022.

F. Kaiser, H. J. Harloff, R. P. Tressel, D. Steffens, H. Seibel, C. Jung and C. Schulz. Effects of supplemented anti-nutritive substances from rapeseed on growth and health performance of rainbow trout (*Oncorhynchus mykiss*). *Aquaculture nutrition*. 2021.

F. Kaiser, H. J. Harloff, R. P. Tressel, T. Kock and C. Schulz. Effects of highly purified rapeseed protein isolate as fishmeal alternative on nutrient digestibility and growth performance in diets fed to rainbow trout (*Oncorhynchus mykiss*). *Aquaculture nutrition*. Vol.27, P.1352-1362, 2021.

K. Golebiewska, A. Frasz and D. Golebiewski. Rapeseed meal as a feed component in monogastric animal nutrition - a review. *Annals of animal science*. Vol.22, No. 4, P.1163-1183, 2022.

L. Liu, X. Liang, J. Fang, X. Yuan, B. Li and J. Li. Tannase alleviates the adverse physiological and toxicological impacts of supplementing tannin in the diet of grass carp (*Ctenopharyngodon idellus*). *Aquaculture nutrition*. P.1-14, 2021.

L. Zhu, J. Wang, X. Ding, S. Bai, Q. Zeng, Y. Xuan, G. S. Fraley and K. Zhang. Serum trimethylamine-N-oxide and gut microbiome alterations are associated with cholesterol deposition in the liver of laying hens fed with rapeseed meal. *Animal nutrition*. Vol.7, P.1258-1270. 2021

S. Liu, Z. Lin, X. Mao, L. Ge, L. Hou, G. Le, F. Gan, L. Wen and K. Huang. Nontoxic dose of phenethyl isothiocyanate ameliorates deoxynivalenol-induced cytotoxicity and inflammation in IPEC-J2 cells. *Research in veterinary science*. Vol.136, P.66-73, 2021.

Z. Xiong, Y. Fu, J. Yao, N. Zhang, R. He, X. Ju and Z. Wang. Removal of anti-nutritional factors of rapeseed protein isolate (RPI) and toxicity assessment of RPI. *Food function*. Vol.13, P.664-674, 2022.

 NAPIFERYN BIOTECH®	Safety Data Sheet	Page 1 of 6
	Raptein™30 Rapeseed Protein Concentrate	July 11, 2023
		Version 1

1. Identification

1.1. Product identifier

Trade name: Raptein™30

Product description: Rapeseed protein concentrate (canola protein concentrate), protein powder

1.2. Recommended use of the chemical and restrictions on use

Intended use: Food ingredient

Restrictions on use: No specific uses advised against are identified

Method of use: Incorporation into foods, including meat and poultry

1.3. Details of the supplier of the safety data sheet

Manufacturer/supplier: NapiFeryn BioTech Sp. z o.o.
 Dubois 114/116
 93-465 Łódź
 POLAND
 Phone: +48 503 542 475

1.4. Emergency phone number:

1-800-262-8200 (within the U.S.)
 1-703-741-5500 (Worldwide)

2. Hazard(s) identification

2.1. Classification of the substance or mixture

Not a hazardous substance or mixture according to OSHA Hazard Communication Standard (29 CFR 1910.1200)

2.2. Label elements

Hazard symbols	Not required
Signal word	Not required
Hazard statements	Not required
Precautionary statements	Not required

2.3. Other hazards

Can create dust and/or flammable dust hazard if handled improperly. Use in ventilated areas and provide adequate dust control.

3. Composition/information on ingredients

3.1. Substance

Chemical name	Rapeseed protein concentrate (canola protein concentrate)
CAS number	Not available

4. First-aid measures

4.1. Description of first-aid measures

Eye contact	Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing. If irritation persists, call a doctor.
-------------	---

 NAPIFERYN BIOTECH®	Safety Data Sheet	Page 2 of 6
	Raptein™30 Rapeseed Protein Concentrate	July 11, 2023
		Version 1

Skin contact	Brush off loose particles from skin. Wash with plenty of water.
Ingestion	Product is fit for consumption as food. After ingestion drink sufficient water. Consult a physician if feeling unwell.
Inhalation	If breathing is difficult, quickly remove victim away from the contaminated area to fresh air and keep at rest in a position comfortable for breathing. If experiencing respiratory symptoms, call a doctor.
General advice	Call a doctor for treatment advice. Show this safety data sheet to the doctor in attendance.

4.2. Most important symptoms and effects, both acute and delayed

Due to dusting potential, the powder may cause irritation to eyes and nasal passageway. May cause allergy or asthma symptoms or breathing difficulties if inhaled. May cause an allergic reaction if ingested.

4.3. Indication of immediate medical attention and special treatment needed

Treat symptomatically. No special treatment required.

5. Fire-fighting measures

5.1. Extinguishing media

Suitable extinguishing media	Use carbon dioxide, dry chemical, alcohol-resistant foam or water spray depending on requirements of surrounding conditions.
Unsuitable extinguishing media	Do not use water jet as this may spread the fire.

5.2. Specific hazards arising from the substance or mixture

Non-combustible material. Any fine powder is susceptible to fire risk so keep away from combustion sources. Product dust is potentially explosive if present at high enough concentration. Thermal decomposition products may include harmful gases or vapors.

5.3. Advice for firefighters

During all firefighting activities, wear appropriate personal protective equipment consistent with the requirements of the surrounding conditions, including self-contained breathing apparatus.

6. Accidental release measures

6.1. Personal precautions, protective equipment, and emergency procedures

Avoid formation of dust as it can produce an explosion hazard at high enough concentrations. Wear suitable personal protective clothing. Use breathing apparatus if exposed to dust. Wash thoroughly after dealing with a spillage.

6.2. Environmental precautions

Prevent large quantities of this material getting into drains/surface water/groundwater.

6.3. Methods and materials for containment and cleaning up

Take up mechanically with a dustpan and broom or shovel. Water can be used to flush spill areas. Keep in suitable, closed containers for disposal. Dispose of spilled material by approved solid waste disposal measures.

6.4. Reference to other sections

- See Section 7 for information on safe handling.
- See Section 8 for information on personal protective equipment.
- See Section 13 for disposal information.

 NAPIFERYN BIOTECH®	Safety Data Sheet	Page 3 of 6
	Raptein™30 Rapeseed Protein Concentrate	July 11, 2023
		Version 1

7. Handling and storage

7.1. Precautions for safe handling

Wear protective gloves, protective clothing, eye and/or face protection. Avoid the formation/deposition of dust and static charges. Provide for good ventilation of the room when handling the material. In case of inadequate ventilation wear respiratory protection. Do not breathe dust. Do not get in eyes, on skin, or on clothing. Do not eat, drink and smoke in work areas. Wash hands thoroughly after handling. Remove contaminated clothing and protective equipment before entering eating areas. Contaminated work clothing should not be allowed out of the workplace.

Releases to the environment should be avoided. Review and implement appropriate technical and procedural wastewater and waste disposal measures to prevent occupational exposure or environmental releases.

7.2. Conditions for safe storage, including any incompatibilities

Keep in tightly closed container in a cool, dry and dark place.

8. Exposure controls/personal protection

8.1. Control parameters

8-hour TWA PEL (OSHA PNOR): 15 mg/m³ (measured as total particulate)

8-hour TWA PEL (OSHA PNOR): 5 mg/m³ (measured as respirable fraction)

TWA: total weight average; PEL: permissible exposure limit; OSHA: Occupational Safety and Health Administration; PNOR: Particulate Not Otherwise Regulated.

8.2. Appropriate engineering controls

Provide adequate ventilation. Good general ventilation should be adequate to control worker exposure to airborne contaminants.

8.3. Individual protection measures, such as personal protective equipment

Eyes/face protection	Use gloves and appropriate safety glasses in the workplace when exposure to eyes can be expected to occur.
Skin and body protection	Wear protective gloves and protective work clothing (uniforms, laboratory coats, disposable coveralls, etc.).
Respiratory protection	Respiratory protection should be provided in instances where exposure to dust can be expected to occur (dust masks with P2 type filters are recommended).
Hygiene measures	Wash hands before breaks and at the end of work. Routinely wash work clothing and protective equipment to remove contaminants.

9. Physical and chemical properties

Physical state:	Solid (powder)
Color:	White to off-white
Odor:	Neutral
Odor threshold:	No data available
Dusting potential:	No data available
pH:	No data available
Melting/freezing point:	Not applicable
Initial boiling point and boiling range:	Not applicable
Flash point:	No data available

 NAPIFERYN BIOTECH®	Safety Data Sheet	Page 4 of 6
	Raptein™30	July 11, 2023
	Rapeseed Protein Concentrate	Version 1

Evaporation rate:	Not applicable
Flammability:	No data available
Upper/lower flammability or explosive limits:	No data available
Vapor pressure and density:	Not applicable
Auto-ignition and decomposition temperature:	No data available
Explosive and oxidizing properties:	No data available
Vapor pressure:	Not applicable
Viscosity:	Not applicable
Partition coefficient: n-octanol/water:	No data available
Solubility:	No data available
Decomposition temperature:	No data available
Oxidizing properties:	No data available
Density:	≥ 0,1 g/cm ³

10. Stability and reactivity

10.1. Reactivity

This product is stable and hazardous reactions will not occur under the recommended conditions for handling and storage.

10.2. Chemical stability

Stable at normal ambient temperatures and when used as recommended. Stable under the prescribed storage conditions.

10.3. Possibility of hazardous reactions

No potentially hazardous reactions known.

10.4. Conditions to avoid

Exposure to moisture may affect product quality.

10.5. Incompatible materials

No data available.

10.6. Hazardous decomposition products

No hazardous decomposition products known.

11. Toxicological information

11.1. Information on toxicological effects

Acute toxicity	Based on available data, the classification criteria are not met.
Skin corrosion/irritation	Based on available data, the classification criteria are not met.
Eye damage/irritation	No information available.
Respiratory or skin sensitization	No information available.
Germ cell mutagenicity	Based on available data, the classification criteria are not met.
Carcinogenicity	Based on available data, the classification criteria are not met.

 NAPIFERYN BIOTECH®	Safety Data Sheet	Page 5 of 6
	Raptein™30 Rapeseed Protein Concentrate	July 11, 2023
		Version 1

Reproductive toxicity	Based on available data, the classification criteria are not met.
STOT – single exposure	No information available.
STOT – repeated exposure	No information available.
Aspiration hazard	No information available.

12. Ecological information

12.1. Toxicity

No further relevant information available.

12.2. Persistence and degradability

No further relevant information available.

12.3. Bioaccumulative potential

No further relevant information available.

12.4. Mobility in soil

No further relevant information available.

12.5. Results of PBT and vPvB assessment

PBT/vPvB assessment not available as chemical safety assessment not required and therefore not conducted.

12.6. Other adverse effects

No further information available.

13. Disposal considerations

13.1. Waste treatment methods:

The generation of waste should be avoided or minimized wherever possible. The disposal of this product, packaging, and waste should at all times comply with the applicable requirements of local/regional/national/international environmental protection and waste disposal legislation and any requirements of relevant authorities. Waste should not be disposed of untreated to the sewer unless fully compliant with the requirements of all authorities with jurisdiction. Waste packaging should be recycled. Incineration or landfill should only be considered when recycling is not feasible.

14. Transport information

14.1. UN number	Not applicable (not regulated as a dangerous good)
14.2. UN proper shipping name	Not applicable
14.3. Transport hazard classes	Not applicable (not regulated as a dangerous good)
14.4. Packing group	Not applicable
14.5. Environmental hazards	Not applicable
14.6. Special precautions for user	Not applicable
14.7. Transport in bulk according to Annex II of MARPOL and the IBC Code	Not applicable

 NAPIFERYN BIOTECH®	Safety Data Sheet	Page 6 of 6
	Raptein™30 Rapeseed Protein Concentrate	July 11, 2023
		Version 1

15. Regulatory information

15.1. Safety, health and environmental regulations/legislation specific for the substance or mixture

OSHA (Occupational Safety and Health Administration)	Not applicable
CERCLA (Comprehensive Environmental Response, Compensation and Liability Act)	Not applicable
Clean Air Act Section (112)	None of the ingredients are listed
SARA (Superfund Amendments and Reauthorization) Title III Section 311/312 Hazard Categories	Not applicable
SARA (Superfund Amendments and Reauthorization) Title III Section 313 Reportable Substances	Not applicable
Toxic Substances Control Act (TSCA)	None of the ingredients are listed
California Proposition 65	None of the ingredients are listed. Product may contain trace amounts of lead which is known to the State of California to cause cancer and birth defects or other reproductive harm.
Massachusetts Right-to-Know List	None of the ingredients are listed
New Jersey Right-to-Know List	None of the ingredients are listed
New Jersey Special Hazardous Substance List	None of the ingredients are listed
Pennsylvania Right-to-Know List	None of the ingredients are listed
Pennsylvania Special Hazardous Substance List	None of the ingredients are listed

15.2. Chemical Safety Assessment

Not applicable

16. Other information

Issued by	NapiFeryn
Revision date	July 11, 2023
Revision	1

General disclaimer

The information provided in this Safety Data Sheet is correct to the best of our knowledge, information and belief at the date of its publication. The information is gathered from internal sources, raw material suppliers or published literature and is provided in good faith. It is designed only as a guidance for safe handling, use, processing, storage, transportation, disposal, and release and is not to be considered a warranty or quality specification of any kind, expressed or implied. The information relates only to the specific material designated and may not be valid for such material used in combination with any other materials or in any process, unless specified in the text. If data for a hazard are not included in this document there is no known information at this time.

End of safety data sheet

Use of canola concentrate as a functional ingredient as extender in sausage meat product

Objectives

The objectives of this study were to evaluate the quality characteristics of sausages containing 15% Raptein™ 30 canola concentrate.

Materials and Methods

Pork shoulder mixed with pork ham (50:50) <15% fat, turkey leg 7% fat and chicken drumstick 10% fat were sourced from local supermarket in Lodz, Poland. Raptein™30 was provided by NapiFeryn BioTech, Lodz, Poland. Raptein™ 30 is a canola concentrate product with a composition of 34.34% total protein and 60.87% total fiber. Four treatments were formulated shown in Table 1 and 2.

Table 1 shows one control treatment using whole muscle red meat containing no other binders, extenders, or moisture retention agents and one test treatment containing 15,0% canola concentrate.

Table 2 shows one control treatment using whole muscle poultry containing no other binders, extenders, or moisture retention agents and one test treatment containing 15,0% canola concentrate.

Table 1. Sausage Link Formulation with red meat

	Control	Test
Pork shoulder with pork ham (50:50) - <15% fat	78.50%	63.50%
Canola Concentrate	0.00%	15.00%
Salt	1.50%	1.50%
Water	20.00%	20.00%
Total	100.00%	100.00%

Table 2. Sausage Link Formulation with poultry

	Control	Test
Turkey leg meat - 7% fat	39.25%	31.75%
Chicken drumstick meat - 10% fat	39.25%	31.75%
Canola Concentrate	0.00%	15.00%
Salt	1.50%	1.50%
Water	20.00%	20.00%
Total	100.00%	100.00%

Evaluations

Cooked yield

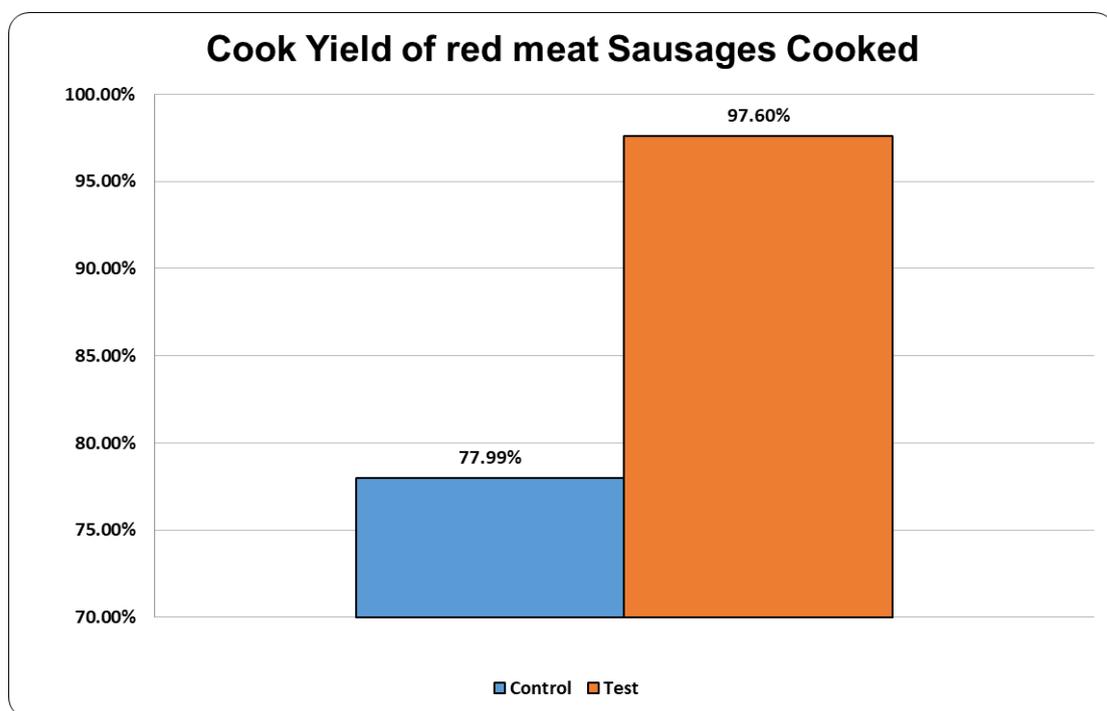
For each individual treatment, product cooked yield was calculated by dividing the chilled product weight 24h by the uncooked product weight (cooked product weight/uncooked product weight x 100). Cooked yield, therefore, represented product weight losses that occurred primarily during thermal processing and chilling. Comparison yields for red meat treatments and poultry treatments are shown in Chart 1 and 2, respectively. Individual yield values for control and test product are shown in Tables 3 and 4 for red meat treatments, and in Tables 5 and 6 for poultry treatments.

Texture analysis

Texture analysis was conducted using Brookfield CT3 Texture Analyzer. Texture analysis comparison data for red meat treatment and poultry treatment are shown in Chart 3 and 4, respectively. Individual texture values for control and test for both red meat and poultry treatments are shown in Tables 7 and 8, respectively.

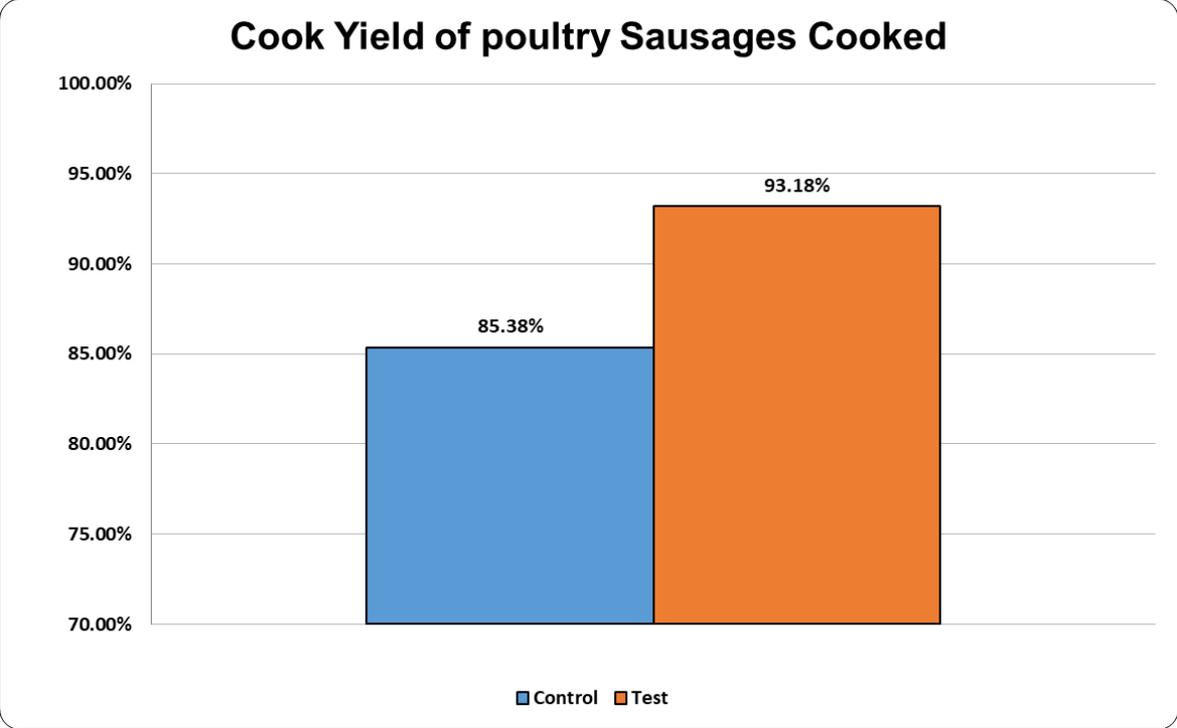
Results and Discussion

Chart 1. Cook Yield of red meat sausages.



Red meat sausages formulated with canola concentrate had a trend toward higher cooked yield compared to the control.

Chart 2. Cook Yield of poultry sausages.



Poultry sausages formulated with canola concentrate had a trend toward higher cooked yield compared to the control.

Table 3. Control Yields (red meat)

Control	Pre-cook weight g	Post cook weight g	% yield
Test 1	166.13	119.72	72.06
Test 2	145.81	119.80	82.16
Test 3	184.39	147.04	79.74
		AVG	77.99

Table 4. Test Yields (red meat)

Control	Pre-cook weight g	Post cook weight g	% yield
Test 1	130.53	125.30	95.99
Test 2	121.28	120.96	99.74
Test 3	126.31	122.60	97.06
		AVG	97.60

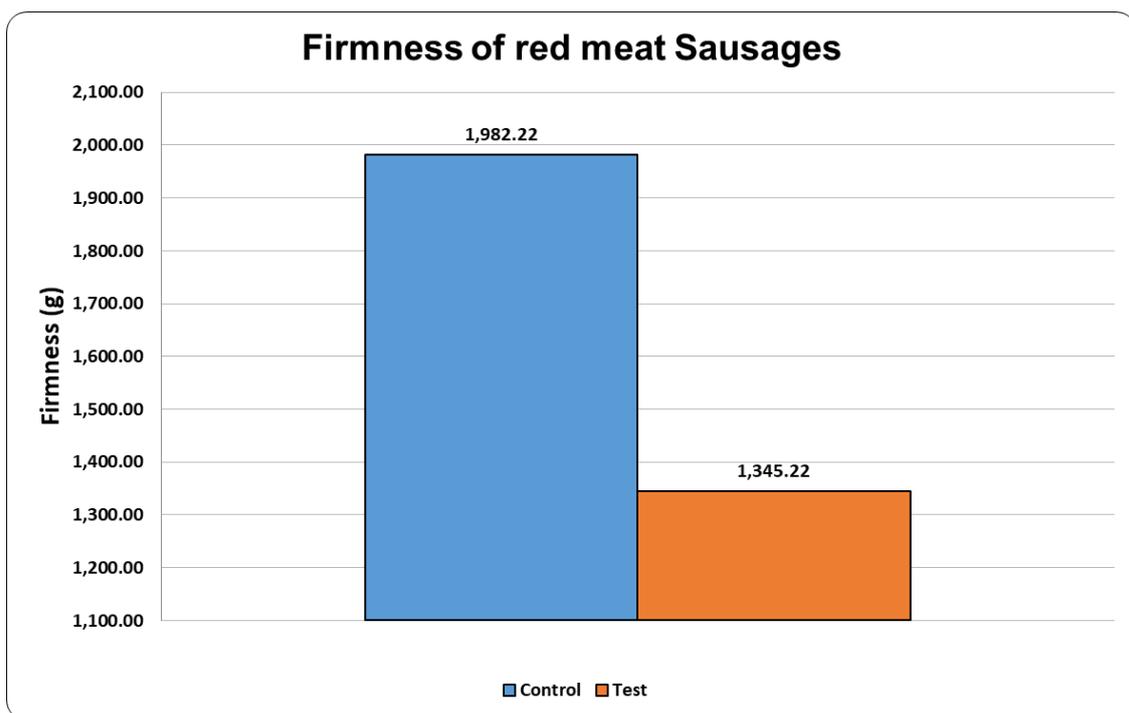
Table 5. Control Yields (poultry)

Control	Pre-cook weight g	Post cook weight g	% yield
Test 1	110.91	93.54	84.34
Test 2	100.86	85.91	85.18
Test 3	94.92	82.21	86.61
		AVG	85.38

Table 6. Test Yields (poultry)

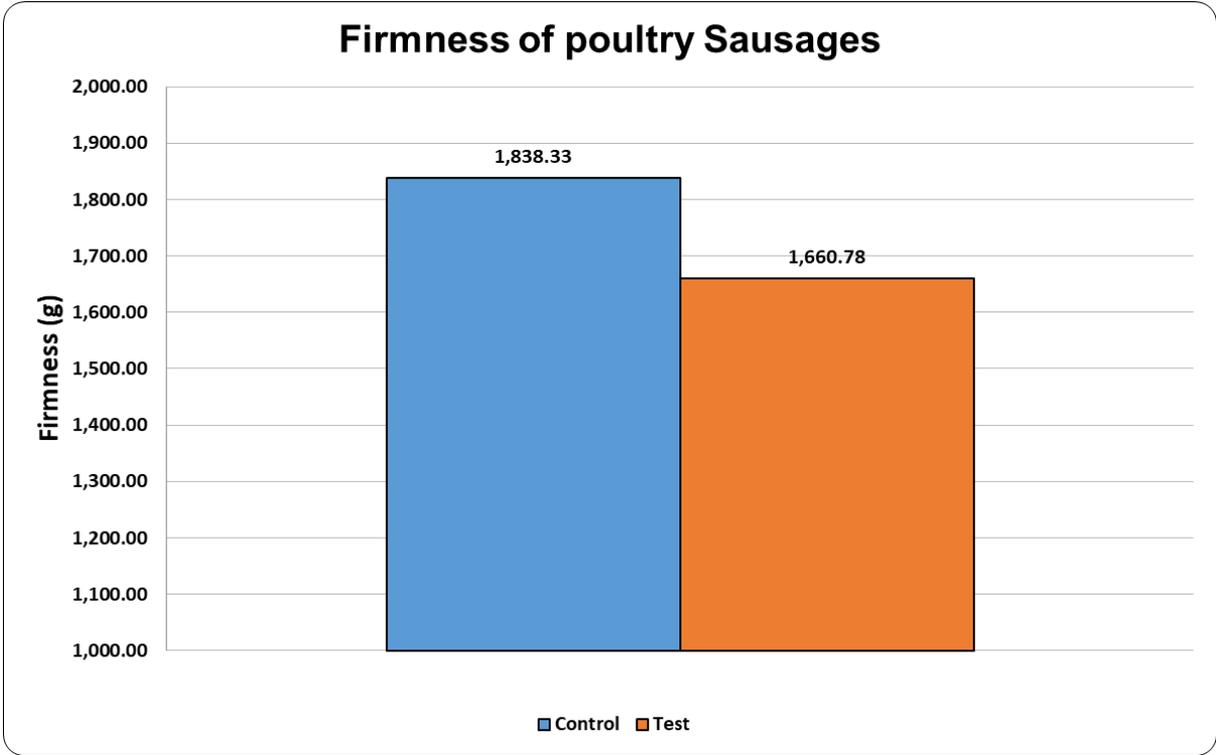
Control	Pre-cook weight g	Post cook weight g	% yield
Test 1	116.67	110.10	94.37
Test 2	110.87	101.69	91.72
Test 3	119.74	111.90	93.45
		AVG	93.18

Chart 3. Texture analysis of red meat sausages



Red meat sausages formulated with canola concentrate had a trend toward lower firmness compared to the control.

Chart 4. Texture analysis of poultry sausages



Poultry sausages formulated with canola concentrate had a trend toward lower firmness (non-significant) compared to the control.

Table 7. Texture analysis of red meat sausages

	Control	Test
#1	2 215.00	1 540.00
#2	1 864.00	1 276.00
#3	1 867.67	1 219.67
Average	1 982.22	1 345.22

Table 8. Texture analysis of poultry meat sausages

	Control	Test
#1	1 622.33	1 558.67
#2	1 643.33	1 785.00
#3	2 249.33	1 638.67
Average	1 838.33	1 660.78

Figure 1. Pre-formed red meat blend



Pre-formed red meat with canola concentrate test samples appeared slightly more dark and brown in color than the red meat without canola concentrate control.

Figure 2. Pre-formed poultry blend



Pre-formed poultry with canola concentrate test samples appeared slightly more dark and brown in color than the poultry without canola concentrate control.

Figure 3. Formed and Cooked red meat product



The red meat with canola concentrate test product appeared dryer on the surface than the control.

Figure 4. Formed and Cooked poultry product



The poultry with canola concentrate test product appeared dryer on the surface than the control.

Conclusions

The canola concentrate with red meat performed slightly different to red meat control without canola concentrate. Post-cook yield averages for control and test were 77.99% and 97.60%, respectively. Post-cook yield for red meat control was lower than for red meat with canola concentrate test. Texture analysis shows firmness is slightly lower for the canola concentrate samples compared to the red meat control. The canola concentrate sausages were slightly dryer than the red meat control. No major off notes or flavors were detected in the canola concentrate sausages. There were no significant differences between the test and red meat control sausages in terms of flavor.

The canola concentrate with poultry performed similar to poultry control without canola concentrate. Post-cook yield averages for control and test were 85.38% and 93.18%,

respectively. Post-cook yield for poultry control was lower than for poultry with canola concentrate test. Texture analysis shows firmness is similar for the canola concentrate samples compared to the poultry control. The canola concentrate sausages were slightly dryer than the poultry control. No major off notes or flavors were detected in the canola concentrate sausages. There were no significant differences between the test and poultry control sausages in terms of flavor.

From: [Nikolaas Tilkin-Franssens](#)
To: [DiFranco, Stephen](#)
Subject: [EXTERNAL] Re: GRN 1122 canola concentrate items for clarification - Reply
Date: Monday, July 17, 2023 10:35:23 AM
Attachments: [image001.png](#)
[image007.png](#)
[image008.png](#)
[FDA GRN 1122 Concentrate 28JUNE2023 Napiferyn Answers correction.docx](#)

CAUTION: This email originated from outside of the organization. Do not click links or open attachments unless you recognize the sender and know the content is safe.

Hi Stephen,

Apologies for this inconvenience.

We noticed that the reply to question 9 refers to Canola protein isolate (as per GRN 1103). I have updated the answer for it to be mentioning Canola protein concentrate (GRN 1122).

We hope this can be taken into consideration.

Kind regards,

Nikolaas Tilkin-Franssens

Regulatory Affairs Manager | Pen & Tec Consulting

T +34 936 758 015 **M** +34 649 840 417 **F** +34 936 758 016 www.pentec-consulting.eu

Pl. Ausias March 1 | 4th floor D01 | 08195 Sant Cugat del Vallès | Barcelona | Spain

PEN + TEC
CONSULTING
PART OF THE ARGENTA GROUP

La información contenida en este mensaje y/o archivo(s) adjunto(s), enviada desde Pen & Tec Consulting SLU, es confidencial/privilegiada y está destinada a ser leída sólo por la(s) persona(s) a la(s) que va dirigida. Le recordamos que sus datos han sido incorporados en el sistema de tratamiento de Pen & Tec Consulting SLU y que siempre y cuando se cumplan los requisitos exigidos por la normativa, usted podrá ejercer sus derechos de acceso, rectificación, limitación de tratamiento, supresión, portabilidad y oposición/revocación, en los términos que establece la normativa vigente en materia de protección de datos, dirigiendo su petición a la dirección postal Pl. Ausias March 1, 4 planta 08195, Sant Cugat del Vallès (Barcelona) o bien a través de correo electrónico info@pentec-consulting.eu. Si usted lee este mensaje y no es el destinatario señalado, el empleado o el agente responsable de entregar el mensaje al destinatario, o ha recibido esta comunicación por error, le informamos que está totalmente prohibida, y puede ser ilegal, cualquier divulgación, distribución o reproducción de esta comunicación, y le rogamos que nos lo notifique inmediatamente y nos devuelva el mensaje original a la dirección arriba mencionada. Gracias.

The information contained in this message and/or attached file(s), sent by Pen & Tec Consulting SLU, is confidential/privileged and is intended to be read solely by the person(s) to whom it is addressed. We hereby inform you that your data will be incorporated into the processing system owned by Pen & Tec Consulting SLU, and that provided it complies with the requirements included in the law, you may exercise the rights of access, rectification, limitation of processing, deletion, portability and opposition by sending your request to the postal address Pl. Ausias March 1, 4 floor 08195, Sant Cugat del Valles (Barcelona) or to the email address info@pentec-consulting.eu. If you read this message and you are neither the intended recipient, employee or agent in charge of delivering the message to the recipient, or if you have received this message as the result of an error, we hereby inform you that distributing, sharing or reproducing any part of this message is totally forbidden and may be illegal. As a result, we request that you immediately inform us of the error and return this message to the address mentioned above. Thank you.

From: Nikolaas Tilkin-Franssens <niko@pentec-consulting.eu>

Date: Tuesday, 11 July 2023 at 17:03

To: DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>
Cc: Justyna Pałasińska <justyna@pentec-consulting.eu>
Subject: Re: GRN 1122 canola concentrate items for clarification - Reply

Dear Stephen,

Thank you for reaching out with the questions for clarification.
We have worked closely with Napiferyn to close the doubts.

Kindly find attached a Word file including the Questions&Answers, a report on the requested literature review, a SDS sheet as requested by the USDA-FSIS, and a report on the suitability assessment.

We remain available for any further questions or updates.

Thanks for taking the application in further consideration,
best regards,

Nikolaas Tilkin-Franssens

Regulatory Affairs Manager | Pen & Tec Consulting

T +34 936 758 015 M +34 649 840 417 F +34 936 758 016 www.pentec-consulting.eu

Pl. Ausias March 1 | 4th floor D01 | 08195 Sant Cugat del Vallès | Barcelona | Spain

PEN + TEC
CONSULTING
PART OF THE ARGENTA GROUP

La información contenida en este mensaje y/o archivo(s) adjunto(s), enviada desde Pen & Tec Consulting SLU, es confidencial/privilegiada y está destinada a ser leída sólo por la(s) persona(s) a la(s) que va dirigida. Le recordamos que sus datos han sido incorporados en el sistema de tratamiento de Pen & Tec Consulting SLU y que siempre y cuando se cumplan los requisitos exigidos por la normativa, usted podrá ejercer sus derechos de acceso, rectificación, limitación de tratamiento, supresión, portabilidad y oposición/revocación, en los términos que establece la normativa vigente en materia de protección de datos, dirigiendo su petición a la dirección postal Pl. Ausias March 1, 4 planta 08195, Sant Cugat del Vallès (Barcelona) o bien a través de correo electrónico info@pentec-consulting.eu. Si usted lee este mensaje y no es el destinatario señalado, el empleado o el agente responsable de entregar el mensaje al destinatario, o ha recibido esta comunicación por error, le informamos que está totalmente prohibida, y puede ser ilegal, cualquier divulgación, distribución o reproducción de esta comunicación, y le rogamos que nos lo notifique inmediatamente y nos devuelva el mensaje original a la dirección arriba mencionada. Gracias.

The information contained in this message and/or attached file(s), sent by Pen & Tec Consulting SLU, is confidential/privileged and is intended to be read solely by the person(s) to whom it is addressed. We hereby inform you that your data will be incorporated into the processing system owned by Pen & Tec Consulting SLU, and that provided it complies with the requirements included in the law, you may exercise the rights of access, rectification, limitation of processing, deletion, portability and opposition by sending your request to the postal address Pl. Ausias March 1, 4 floor 08195, Sant Cugat del Valles (Barcelona) or to the email address info@pentec-consulting.eu. If you read this message and you are neither the intended recipient, employee or agent in charge of delivering the message to the recipient, or if you have received this message as the result of an error, we hereby inform you that distributing, sharing or reproducing any part of this message is totally forbidden and may be illegal. As a result, we request that you immediately inform us of the error and return this message to the address mentioned above. Thank you.

From: DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>
Date: Wednesday, 28 June 2023 at 17:41
To: Nicoleta Pasecinic <nicoleta@pentec-consulting.eu>
Cc: Nikolaas Tilkin-Franssens <niko@pentec-consulting.eu>
Subject: [EXTERNAL]: GRN 1122 canola concentrate items for clarification

CAUTION: This email originated from outside of the organization. Do not click links or open attachments unless you recognize the sender and know the content is safe.

Hello Ms. Pasecinic,

After evaluating NapiFeryn's GRAS Notice No. GRN 1122 on canola concentrate we noted a few issues that should be addressed. Please respond to the following points for clarification:

1. On p. 9, NapiFeryn states that the major storage proteins in canola seed are cruciferins and napins, and that canola concentrate consists of 30-45% protein and 40-70% dietary fiber. Please provide the typical cruciferin content and napin content in canola concentrate.
2. Please confirm that all raw materials and processing aids used in the manufacturing process are used in accordance with the U.S. regulations, are GRAS for their respective uses or are the subject of an effective food contact notification. For the record, we note that the food additive regulations cited in Table 4 (p. 15) for ascorbic acid (21 CFR 182.8013), ethanol (21 CFR 184.1293), and ethyl acetate (21 CFR 173.228) do not appear to be applicable to your intended uses of these substances.
3. In Table 6 (p. 18-19), NapiFeryn provides the results from the batch analyses for heavy metals. We would like to bring to your attention a relevant FDA's ["Closer to Zero"](#) initiative that focuses on reducing the levels of heavy metals in foods and recommend that you lower the specification limits for heavy metal to better reflect the batch analyses results and to be as low as possible.
4. In Table 10 (p. 22), NapiFeryn provides batch analyses data for residual solvents and processing aids. In addition, in Table 21 (p. 50), you provided the results from the batch analyses for erucic acid in your canola concentrate ranging from 0.37% to < 0.1%.
 - a. Please include limits for residual ethanol, ethyl acetate, and sulphur dioxide as well as a limit for erucic acid in the specifications for canola concentrate and specify the analytical methods used to test for these parameters.
 - b. In addition, please provide an updated Tables 5 and 6 (p. 16-19) to include the additional specification parameters mentioned above, corresponding analytical methods, and batch analyses.
5. Please state that all analytical methods used to test batches were validated and are fit for their respective purpose.
6. Please state that canola concentrate is not intended for use in infant formula or in foods where standards of identity preclude its use.
7. In Table 15 (p.), NapiFeryn provides the results of the batch analyses for total plate count in the raw material (rapeseed press cake). Please address the significant variation in the results (from <10 to 28,000 CFU/g) and discuss whether this will impact safety of the final ingredient.
8. On p. 19, NapiFeryn states that the levels of mycotoxins in canola concentrate are below the limit of quantitation (LOQ) and provide the results from the analyses of five batches to support your statement. Please clarify whether you expect mycotoxins to be present in canola

concentrate manufactured in accordance with good manufacturing practices.

9. In Part 1.4 (p. 6) and Part 3.1 (p. 33), NapiFeryn states that the intended use of canola concentrate is as a source of protein and/or fiber, thickener, or texturizer. However, we note that on p. 33 you also state the intended use of canola concentrate is as a flavoring agent or binder in various comminuted or whole muscle meat and poultry products. In addition, in Appendix 3 (p. 5) you state that canola concentrate may also be used “to create a flavored salt” or as “a flavor enhancer like monosodium glutamate”. Please confirm these additional uses of canola concentrate are within the scope of GRN 001122.
10. On p. 10, the notifier describes the protein composition of canola concentrate, being primarily cruciferins, napin, oleosin, and squalene monooxygenase. However, the pivotal safety data provided appear to only be relevant to the cruciferin and napin fractions of the canola concentrate. Please provide a brief narrative to confirm the safety of oleosin and squalene monooxygenase exposure from the intended uses.
11. On p. 31-32 of the notice, the notifier clearly establishes that canola concentrate is intended to be substitutive to protein and fiber consumption and will not contribute to additional exposure to protein or fiber in general. Please elaborate on this conclusion, and clarify if the intended uses of canola concentrate are additive or substitutive to other canola protein products currently on the market (i.e., GRNs 327, 386, and 683)?
12. On p. 37, the notifier concludes exposure to canola concentrate from the intended uses is safe since the EDI reported is “still much lower (approximately 7- to 22-fold lower) than the no-observed-adverse-effect level (NOAEL) values established” for cruciferin- and napin-rich protein isolates in male rats following a 13-week oral exposure regimen (Mejia *et al.*, 2009a & 2009b). We note that an uncertainty factor, or margin of safety (MOS), of 100 (10 for interindividual variability × 10 for interspecies variability) is normally used when assessing safety of a food ingredient by comparing estimated human exposure levels to the NOAEL from animal toxicology data. Therefore, it is not clear why MOS that is ~5-10-fold lower can be concluded as safe without proper justification. Additionally, we note that potential thyrotoxic effects were observed at the highest doses in these two rat studies, as well as for rapeseed products in general tested in other species, as cited in Table 20 of the GRAS notice. This effect was mostly attributed to the presence of glucosinolate; however, we note that since the level of glucosinolate was low or absent in both the test articles from Mejia *et al.* and the article of commerce, the rationale used by the study authors to conclude that the observed NOAEL was not in fact the LOAEL may be questionable. Regardless, it appears that the provided safety narrative lacks sufficient basis to conclude MOS of 7-22 is adequate to reach the conclusion of “reasonable certainty of no harm.” Based on generally available data and information, please provide additional narrative to explain your rationale for your GRAS conclusion.
13. We note that when discussing the absorption, distribution, metabolism, and excretion of canola concentrate (p. 49), the notifier reports unpublished data from an EU Novel Foods application for “defatted rapeseed powder” to support their conclusion. Similarly, genotoxicity conclusions are made using unpublished data from an EFSA Panel conclusion on

defatted rapeseed powder. Given other data and information have been used in prior GRAS notices for canola ingredients (e.g., GRN 327), please confirm that the EFSA Panel and EU Novel Foods conclusions are only considered as corroborative, not pivotal, to the safety determination of canola concentrate at its intended use level?

14. On p. 40, the notifier discusses the allergenicity potential of canola concentrate being determined via a “bioinformatics approach” and concludes that canola concentrate “may elicit possible allergenic effects.” Additionally, on p. 59 the notifier reiterates that the bioinformatics analysis indicated “possible allergenic effects” of canola concentrate, but no further discussion is provided. While data from an allergen online database search is provided as part of Appendix 4, no discussion of these data are included in the current GRAS notice. Please briefly detail the “possible allergenic effects” of canola concentrate similar to previous notices (e.g., GRN 683), and discuss why they would not be expected to pose a safety concern from the intended use.
15. We note that a recent study on rapeseed protein isolate was published (Xiong et al., 2022).
 - a. Please discuss if this study presents additional safety concerns for the article of commerce or contradicts the current GRAS conclusion.
 - b. Please also perform an updated literature review from 2021 to present and discuss if any additional studies relevant to the safety of canola concentrate were identified that would contradict the current GRAS conclusion.

References cited:

Xiong Z, Fu Y, Yao J, Zhang N, He R, Ju X, Wang Z. Removal of anti-nutritional factors of rapeseed protein isolate (RPI) and toxicity assessment of RPI. *Food Funct.* 2022 Jan 24;13(2):664-674. doi: 10.1039/d1fo03217h. PMID: 34933325.

Additionally, we received the following questions from USDA FSIS regarding their review of the uses of GRN 1122 concerning products within their purview. Please respond to the following and we will pass your responses along to them.

Please provide Safety Data Sheet (SDS) for the at use concentrations of the substance and include a description of how the use of this technology will not adversely affect the safety of FSIS inspectors. Workplace safety and health hazards include inhalation, direct skin contact (skin, eyes, mouth), and fire/explosion caused by exposure to the product, its working solution or dry mixture and potential by-products formed and/or off-gassed during the application process. The employee safety information should demonstrate how the New Technology will not “jeopardize the safety of Federal inspection personnel” as specified in the [FSIS Compliance Guideline Procedures for New Technology Notifications and Protocols, April 2015](#). FSIS workplace and employee safety must be specifically addressed. Please refer to Appendix A on p. 17, Workplace Safety and Health Criteria, for clarification on what to provide in the response. For additional clarity with respect to employee safety, the following are examples of information that are typically needed by FSIS’ employee safety and health group;

1. Potential workplace exposures that could result from inhalation and direct contact during use

of the substance/technology. This information is required in addition to a SDS to determine accurate hazard potential and recommended exposure control measures for IPP work areas in accordance with Occupational Safety and Health Administration (OSHA) regulations: 29 CFR 1910.1200, Hazard Communication, 29 CFR 1910.132, Personal Protective Equipment, and 29 CFR 1910.1000, Air Contaminants. The information should be included as a specific section in each of the protocols.

2. If the SDS workplace hazards/precautions do not apply to the type of exposure that would be expected for the FSIS IPP, please have the submitter provide specific information (per the April 2015 FSIS Compliance Guideline Procedures) for the actual type of exposures expected.
3. If no IPP workplace exposures are expected and no control measures are required, please have the submitter state this and provide the reasons why (e.g., such as the substance “as used” [for all concentrations] is not hazardous by inhalation or direct contact and/or IPP would not be exposed to the substance based on the system design, operation and/or control measures that will be in place).
4. Please also indicate how will FSIS IPP be informed of the above information so that it is clear that the information contained in the SDS for the concentrate does not apply to their actual workplace exposure.
5. Are there any potential hazards from chemical mixing or low pH as a result of discharges of the various solutions to floor drains? Are dedicated drain lines or any other enclosures required?
6. With respect to potential airborne exposures to FSIS IPP in the use/application areas, does the submitter have air sampling results taken during the use of the various concentrations of the technology in the listed mixture?
7. The intended use of this product in FSIS meat and poultry products is apparently as a binder/extender. The suitability support provided in Appendix 6 does sufficiently support no significant difference in yield and other organoleptic qualities when used as a partial replacement for another binder in a processed meat and poultry product, such as sausage. However, **additional suitability support is needed:**
 - a. No suitability data was provided for **whole muscle meat and poultry products at the maximum proposed use level**. We would need to see similar data as provided in Appendix 6 for:
 1. Whole muscle red meat control containing no other binders, extenders, or moisture retention agents, as compared to a whole muscle red meat product containing 15% isolated canola product.
 2. Whole muscle poultry control containing no other binders, extenders, or moisture retention agents as compared to a whole muscle poultry product containing 15% isolated canola product.

Responses may be sent in an email or in a separate document. We respectfully request a response within 10 business days. If you are unable to complete the response within that time frame, please contact me to discuss further options.

If you have any additional questions or concerns, please don't hesitate to contact me at stephen.difranco@fda.hhs.gov or by phone at 240.402.2710.

Best,

Steve

Stephen DiFranco, PhD

Regulatory Review Scientist/Chemist

Center for Food Safety and Applied Nutrition

Office of Food Additive Safety

Division of Food Ingredients

U.S. Food and Drug Administration

Tel: 240-402-2710

stephen.difranco@fda.hhs.gov



CAUTION: This email, including any attachments, is confidential. If you are not the intended recipient, please notify the sender and delete the email and any attachments from your system. In addition, you must not use, distribute or reproduce this email or any attachments. Opinions and other information in this email and any attachments which do not relate to the official business of Argenta are neither given by nor endorsed by Argenta. While Argenta uses anti-virus software, Argenta accepts no liability for any viruses in this email or any attachment, or for any effects this email or any attachment may have on your network or computer system.

**GRN 1122 - Raptein™30 - Canola protein concentrate:
Replies to request for clarification of 28 June 2023**

1. On p. 9, NapiFeryn states that the major storage proteins in canola seed are cruciferins and napins, and that canola concentrate consists of 30-45% protein and 40-70% dietary fiber. Please provide the typical cruciferin content and napin content in canola concentrate.

Answer:

The typical method for cruciferin and napin content is the quantitative HPLC-UV method based on SEC (size-exclusion chromatography). This method is suitable for soluble samples and it is not applicable to canola concentrate due to interactions between fiber and protein and the general characteristics of the sample (e.g. poor solubility of the sample). Based on our knowledge and process parameters, the content of cruciferins significantly exceeds the content of napins in the concentrate. The qualitative analyses of protein with the use of LC-MS method confirmed the presence of cruciferins, napins and oleosins in Raptein™30.

2. Please confirm that all raw materials and processing aids used in the manufacturing process are used in accordance with the U.S. regulations, are GRAS for their respective uses or are the subject of an effective food contact notification. For the record, we note that the food additive regulations cited in Table 4 (p. 15) for ascorbic acid (21 CFR 182.8013), ethanol (21 CFR 184.1293), and ethyl acetate (21 CFR 173.228) do not appear to be applicable to your intended uses of these substances.

Answer:

Napiferyn hereby confirms that canola protein concentrate is manufactured in accordance with good manufacturing practices, using food-grade raw materials and processing aids. We acknowledge the CFR references included are not accurate on the intended uses, but merely support the identity of the used processing aids.

3. In Table 6 (p. 18-19), NapiFeryn provides the results from the batch analyses for heavy metals. We would like to bring to your attention a relevant FDA's "Closer to Zero" initiative that focuses on reducing the levels of heavy metals in foods and recommend that you lower the specification limits for heavy metal to better reflect the batch analyses results and to be as low as possible.

Answer:

Based on results from samples of several batches Napiferyn can commit to lower the limits for Lead and Arsenic.

	Arsenic (mg/kg)	Cadmium (mg/kg)	Lead (mg/kg)	Mercury (mg/kg)
Current	≤ 0,2	≤ 0,2	≤ 0,5	≤ 0,1
Concentrate (new)	≤ 0,15	≤ 0,2	≤ 0,35	≤ 0,1

4. In Table 10 (p. 22), NapiFeryn provides batch analyses data for residual solvents and processing aids. In addition, in Table 21 (p. 50), you provided the results from the batch analyses for erucic acid in your canola concentrate ranging from 0.37% to < 0.1%.
 - a. Please include limits for residual ethanol, ethyl acetate, and sulphur dioxide as well as a limit for erucic acid in the specifications for canola concentrate and specify the analytical methods used to test for these parameters.
 - b. In addition, please provide an updated Tables 5 and 6 (p. 16-19) to include the additional specification parameters mentioned above, corresponding analytical methods, and batch analyses.

Answer:

Please consider the updated tables 5 (Specifications) and 6 (Analytical results from 5 batches) below.

Napiferyn considers that Erucic acid would not need to be included in the specification. We do observe that the GRAS Notice dossier does not clearly specify that the percentage relates to % of total fatty acids. Accordingly, the results for 5 independent, non-consecutive batches are in fact 0,37% and <0.1% (<LOQ) of total fatty acids. The total fat level of canola protein isolate is $\leq 2\%$ DM. As such, there is no possibility of a higher presence of erucic acid. Napiferyn sources solely low erucic acid varieties of rapeseed/canola, in accordance with 21 CFR §184.1555.

Table 5. Product specifications for canola concentrate (Raptein™30)

Parameter	Unit	Value	Method
Appearance	-	white to off-white dried powder	Visual
Composition**			
Total protein (N*6.25)	%	30 - 45	ISO 1871:2009
Carbohydrates	%	≤ 65	By difference*
Fat (direct)	%	≤ 2	PB/CH/16 version 3 from 09.11.2018
Ash	%	≤ 5	PN-A-79011-8:1998
Moisture	%	≤ 7	PN-A-79011-3:1998
Total dietary fiber (TDF)	%	40 - 70	AOAC 2011.25-M
Total glucosinolates	mmol/kg	≤ 0.3	ISO 9167-1:1992; AOCS Ak 1-92
Purity**			

Phytates	%	≤ 2	Analytical Vol. 77:536-539 (1977) Biochemistry
Lead	mg/kg	≤ 0.35	DIN EN 15763:2010 (2010-04), mod.
Arsenic	mg/kg	≤ 0.15	§64 LFGB L 00.00-19/3
Cadmium	mg/kg	≤ 0.2	DIN EN 15763:2010 (2010-04), mod.
Mercury	mg/kg	≤ 0.1	DIN EN 15763:2010 (2010-04), mod.
Microbiological criteria			
Total plate count	cfu/g	≤ 10 ⁴	PN-EN ISO 4833-1:2013-12
<i>E. coli</i>	-	absence in 10 g	PN-ISO 7251:2006
<i>Salmonella</i> spp.	-	absence in 25 g	PN-EN ISO 6579-1:2017-04
Yeast and Molds	cfu/g	≤ 100	PN-ISO 21527-2:2009
Total coliform count	cfu/g	≤ 10	PN-ISO 4831:2007
<i>Enterobacteriaceae</i>	cfu/g	< 10	PN- EN ISO 21528-2:2017-08
Potential contaminants			
Residual Ethanol**	mg/kg	<200	HH-MA-M 03-011, Headspace, GC-FID: 2019-01
Residual Ethyl Acetate**	mg/kg	<200	HH-MA-M 03-011, Headspace, GC-FID: 2019-01
Residual Sulphur Dioxide**	mg/kg	<10	PN-EN 1988-1:2001

*Carbohydrates are calculated by difference as follows: 100 % - [protein (as is) % + moisture % + fat % + ash %] **On dry matter (except of moisture)

PN-A - polish standard; LFGB - Lebensmittel-und-Futtermittelgesetzbuch (German Food and Feed Act); DIN - Deutsches Institute für Normung (German institute for standardization); AOCS - American Oil Chemists' Society; AOAC - Association of Official Agricultural Chemists

**applicable only if used in the production process

Table 6. Analyses of 5 production batches of canola concentrate (Raptein™30)

Parameter	Specificati on	Lot No. R- 03#35	Lot No. R- 06#60	Lot No. R- 09#41	Lot No. R- 13#60	Lot No. R- 15#66
Appearance	white to off-white dried powder					
Composition**						
Total protein (N*6.25) [%]	30-45	41.26	33.10	32.28	31.65	35.49
Moisture [%]	≤ 7	2.9	5.6	2.8	6.0	4.9
Fat (direct) [%]	≤ 2	0.89	0.86	0.51	0.67	0.83
Ash [%]	≤ 5	2.82	2.87	2.89	3.81	3.23
Total dietary fiber (TDF) [%]	40-70	51.2	66.4	63.6	65.9	64.7
Carbohydrates* [%]	≤ 65	55.04	63.17	64.31	63.87	60.45
Total glucosinolates [mmol/kg]	≤ 0.3	<LOQ (<0.05)	<LOQ (<0.05)	<LOQ (<0.05)	<LOQ (<0.05)	<LOQ (<0.05)
Purity**						
Phytates [%]	≤ 2	1.44	1.09	1.38	1.60	1.49
Lead [mg/kg]	≤ 0.35	0.154	0.233	0.257	0.117	0.089

Arsenic [mg/kg]	≤ 0.15	<LOQ (<0.1)	<LOQ (<0.1)	<LOQ (<0.1)	<LOQ (<0.1)	<LOQ (<0.1)
Cadmium [mg/kg]	≤ 0.2	0.026	0.018	0.020	0.030	0.026
Mercury [mg/kg]	≤ 0.1	<LOQ (<0.005)	<LOQ (<0.005)	<LOQ (<0.005)	<LOQ (<0.005)	<LOQ (<0.005)
Microbiological criteria						
Total plate count [cfu/g]	≤ 10 ⁴	1 200	720	610	180	170
<i>E. coli</i>	absent in 10g	absent	absent	absent	absent	absent
<i>Salmonella</i> spp.	absent in 25 g	absent	absent	absent	absent	absent
Yeast and Molds [cfu/g]	≤ 100	<10	<10	<10	<10	<10
Total coliform count [cfu/g]	≤ 10	0	0	0	0	0
<i>Enterobacteriaceae</i> [cfu/g]	<10	<10	<10	<10	<10	<10
Potential contaminants						
Residual Ethanol [mg/kg]**	<200	17.5	117.0	12.3	14.1	<1.0
Residual Ethyl Acetate [mg/kg]**	<200	71.0	53.4	<1.0	29.8	14.9
Sulphur Dioxide [mg/kg]**	<10	<LOQ (<10)	<LOQ (<10)	<LOQ (<10)	<LOQ (<10)	<LOQ (<10)
<p>*Carbohydrates are calculated by difference as follows: 100 % - [protein (as is) % + moisture % + fat % + ash %];</p> <p>**On dry matter (except of moisture); <LOQ – below the Limit of Quantification</p> <p>**applicable only if used in the production process</p>						

5. Please state that all analytical methods used to test batches were validated and are fit for their respective purpose.

Answer:

Napiferyn confirms all analytical methods used to test batches were validated and are fit for their respective purpose.

6. Please state that canola concentrate is not intended for use in infant formula or in foods where standards of identity preclude its use.

Answer:

Canola concentrate is not intended for use in infant formula or in foods.

7. In Table 15 (p.), Napiferyn provides the results of the batch analyses for total plate count in the raw material (rapeseed press cake). Please address the significant variation in the results (from <10 to 28,000 CFU/g) and discuss whether this will impact safety of the final ingredient.

Answer:

The raw materials were different, e.g. different batches, hence the differences in the results. Regardless of the level of microbiology in the raw material, the product obtained is microbiologically clean and meets the specification limit.

8. On p. 19, Napiferyn states that the levels of mycotoxins in canola concentrate are below the limit of quantitation (LOQ) and provide the results from the analyses of five batches to support your statement. Please clarify whether you expect mycotoxins to be present in canola concentrate manufactured in accordance with good manufacturing practices.

Answer:

We don't expect mycotoxins to be present in canola concentrate manufactured in accordance with good manufacturing practices. The additional testing of five batches has confirmed that no mycotoxins were detected.

9. In Part 1.4 (p. 6) and Part 3.1 (p. 33), Napiferyn states that the intended use of canola concentrate is as a source of protein and/or fiber, thickener, or texturizer. However, we note that on p. 33 you also state the intended use of canola concentrate is as a flavoring agent or binder in various comminuted or whole muscle meat and poultry products. In addition, in Appendix 3 (p. 5) you state that canola concentrate may also be used "to create a flavored salt" or as "a flavor enhancer like monosodium glutamate". Please confirm these additional uses of canola concentrate are within the scope of GRN 001122.

Answer:

~~Napiferyn hereby confirms that canola protein isolate, as part of GRN 1103, is not intended for use as a flavored salt or flavor enhancer. Canola protein isolate can be used as an ingredient in spice and seasoning mixes (i.e. formulation aid, stabilizer and thickener, and texturizer) but does not have, by itself, the capacity to supplement, enhance, or modify the original taste and/or aroma of a food, nor to impart or help impart a taste or aroma in food.~~

Napiferyn hereby confirms that canola protein concentrate, as part of GRN 1122, is not intended for use as a flavored salt or flavor enhancer. Canola protein concentrate can be used as an ingredient in spice and seasoning mixes (i.e. formulation aid, stabilizer and thickener, and texturizer) but does not have, by itself, the capacity to supplement, enhance, or modify the original taste and/or aroma of a food, nor to impart or help impart a taste or aroma in food.

10. On p. 10, the notifier describes the protein composition of canola concentrate, being primarily cruciferins, napin, oleosin, and squalene monooxygenase. However, the pivotal safety data provided appear to only be relevant to the cruciferin and napin fractions of the canola concentrate. Please provide a brief narrative to confirm the safety of oleosin and squalene monooxygenase exposure from the intended uses.

Answer:

Oleosins are protein compounds commonly found in seeds. Oleosins have been associated with allergic reactions for hazelnuts, peanuts and sesame^{[1][2][3]}. Allergenicity of these oil body proteins from Brassica napus is not clearly established. Oleosin S2-2 (OLES2_BRANA) identified in RapteinTM30 shares less than 50% of protein amino acid sequence with oleosins from plants outside of the Brassicaceae family, except for oleosins in hazelnut and peanut with which it shares slightly above 50% (full-length FASTA). Cross-reactivity between oleosins may be primarily expected within Brassicaceae family but it also cannot be excluded against hazelnuts and peanuts, as noted in literature. Please also consider the elaboration on allergenicity of canola protein concentrate in reply to question 14.

Squalene monooxygenases (also known as squalene epoxidases) is a group of eukaryotic enzymes involved in cholesterol synthesis. While these enzymes are present in many eukaryotes, squalene monooxygenase 1,2 (ERG12_BRANA) identified in RapteinTM30 shares more than 50% of its amino acid sequence exclusively with other members of the Brassicaceae family.

The inhibition of the enzyme has been considered for its potential in the treatment of hypercholesterolemia^[4]. Available publications and studies therefore mainly focus on the possible inhibitors^[5], while the effects of exposure to squalene monooxygenase through the consumption of food remain unexplored. Considering the long history of human consumption of crops in the Brassicaceae family and the expected low levels of the enzyme in the product, consumption of RapteinTM30 containing a minor amount of squalene monooxygenase 1,2 is not considered to introduce any new safety concerns.

References cited:

- [1] Leduc V, Moneret-Vautrin DA, Tzen JT, Morisset M, Guerin L and Kanny G, 2006. Identification of oleosins as major allergens in sesame seed allergic patients. *Allergy*, 61, 349-356.
- [2] Akkerdaas JH, Schocker F, Vieths S, Versteeg S, Zuidmeer L, Hefle SL, Aalberse RC, Richter K, Ferreira F and van Ree R, 2006. Cloning of oleosin, a putative new hazelnut allergen, using a hazelnut cDNA library. *Mol Nutr Food Res*, 50, 18-23.
- [3] Zuidmeer-Jongejan, L., Fernández-Rivas, M., Winter, M.G. et al., 2014 Oil body-associated hazelnut allergens including oleosins are underrepresented in diagnostic extracts but associated with severe symptoms. *Clin Transl Allergy* 4, 4.
- [4] Belter A, Skupinska M, Giel-Pietraszuk M, Grabarkiewicz T, Rychlewski L, Barciszewski J. Squalene monooxygenase - a target for hypercholesterolemic therapy. *Biol Chem*. 2011 Dec;392(12):1053-75
- [5] Zou Y, Zhang H, Bi F, Tang Q, Xu H. Targeting the key cholesterol biosynthesis enzyme squalene monooxygenase for cancer therapy. *Front Oncol*. 2022 Aug 24.

11. On p. 31-32 of the notice, the notifier clearly establishes that canola concentrate is intended to be substitutive to protein and fiber consumption and will not contribute to additional exposure to protein or fiber in general. Please elaborate on this conclusion, and clarify if the intended uses of canola concentrate are additive or substitutive to other canola protein products currently on the market (i.e., GRNs 327, 386, and 683)?

Answer:

The canola concentrate (Raptein™30) will be added to food products as a protein or fiber substitute and therefore will not contribute to any additional exposure to protein and fiber for the consumers.

In terms of protein part of canola concentrate it is substitutive to other canola protein products currently on the market (i.e., GRNs 327, 386, and 683), but in case of the fiber part of canola concentrate it is additive, because GRN mentioned are not rich in fiber (they are canola proteins).

12. On p. 37, the notifier concludes exposure to canola concentrate from the intended uses is safe since the EDI reported is “still much lower (approximately 7- to 22-fold lower) than the no-observed-adverse-effect level (NOAEL) values established” for cruciferin- and napin-rich protein isolates in male rats following a 13-week oral exposure regimen (Mejia *et al.*, 2009a & 2009b). We note that an uncertainty factor, or margin of safety (MOS), of 100 (10 for interindividual variability × 10 for interspecies variability) is normally used when assessing safety of a food ingredient by comparing estimated human exposure levels to the NOAEL from animal toxicology data. Therefore, it is not clear why MOS that is ~5-10-fold lower can be concluded as safe without proper justification. Additionally, we note that potential thyrotoxic effects were observed at the highest doses in these two rat studies, as well as for rapeseed products in general tested in other species, as cited in Table 20 of the GRAS notice. This effect was mostly attributed to the presence of glucosinolate; however, we note that since the level of glucosinolate was low or absent in both the test articles from Mejia *et al.* and the article of commerce, the rationale used by the study authors to conclude that the observed NOAEL was not in fact the LOAEL may be questionable. Regardless, it appears that the provided safety narrative lacks sufficient basis to conclude MOS of 7-22 is adequate to reach the conclusion of “reasonable certainty of no harm.” Based on generally available data and information, please provide additional narrative to explain your rationale for your GRAS conclusion.

Answer:

The estimate exposure to canola protein concentrate ranges from 2.04 g/Kg BW/day for young children to 0.53 g/Kg BW/day for adults (considering 90th percentile). The applicant considers these are conservative values which are lower than the NOAEL of 11.24 g/Kg bd/day for male rats reported by Mejia et al. for the cruciferin-rich protein isolate and 12.46 g/Kg BW/day for male rats for the napin-rich protein isolate^{[1][2]}. The exposures are slightly above than those reported in one prior GRAS notices which ranged from 2.0 to 0.53 g/Kg BW/day (GRN 00068) and lower than those reported in GRN 327 which ranged from 3.1 to 0.75 g/Kg BW/day.

The canola protein concentrate is not expected to have 100% of the market share for canola protein products. Additionally, food intake databases from which the estimated exposures are derived usually overestimate consumption, since they do not reflect the true chronic exposure conditions. These factors will typically overestimate the exposure of a macronutrient by a factor of 2- to 10-fold^[3].

Taking these considerations into account all the aspects for evaluation of safe exposure, the applicant considers that canola protein concentrate intakes will be well below levels of any possible concern and thus is safe for human consumption.

Organ weights were not affected by the treatment with the possible exception of the relative thyroid plus parathyroid weight, which was slightly but significantly increased in females, but not in males, of the high dose napin protein isolate group^[2] and in both sexes of the high dose cruciferin protein isolate group^[1]. In the absence of histopathological changes of the thyroids, the thyroid weight was not considered of toxicological relevance^{[1][2][4]}.

References cited:

- [1] Mejia, L.A., Korgaonkar, C.K., Schweizer, M., Chengelis, C., Marit, G., Ziemer, E., Grabiell, R. & Empie, M. 2009, "A 13-week sub-chronic dietary toxicity study of a cruciferin-rich canola protein isolate in rats", *Food and chemical toxicology* : an international journal published for the British Industrial Biological Research Association, vol. 47, no. 10, pp. 2645-2654.
- [2] Mejia, L.A., Korgaonkar, C.K., Schweizer, M., Chengelis, C., Novilla, M., Ziemer, E., Williamson-Hughes, P.S., Grabiell, R. & Empie, M. 2009, "A 13-week dietary toxicity study in rats of a Napin-Rich Canola Protein Isolate", *Regulatory toxicology and pharmacology* : RTP, vol. 55, no. 3, pp. 394-402.
- [3] Munro, I.C., McGirr, L.G., Nestmann, E.R. & Kille, J.W. 1996, "Alternative approaches to the safety assessment of macronutrient substitutes", *Regulatory Toxicology and Pharmacology*, vol. 23, no. 1, pp. S6-S14
- [4] EFSA NDA Panel (EFSA Panel on Dietetic Products, Nutrition and Allergies), 2013. Scientific Opinion on the safety of "rapeseed protein isolate" as a Novel Food ingredient. *EFSA Journal* 2013;11(10):3420, 23 pp. doi:10.2903/j.efsa.2013.3420

13. We note that when discussing the absorption, distribution, metabolism, and excretion of canola concentrate (p. 49), the notifier reports unpublished data from an EU Novel Foods application for "defatted rapeseed powder" to support their conclusion. Similarly, genotoxicity conclusions are made using unpublished data from an EFSA Panel conclusion on defatted rapeseed powder. Given other data and information have been used in prior GRAS notices for canola ingredients (e.g., GRN 327), please confirm that the EFSA Panel and EU Novel Foods conclusions are only considered as corroborative, not pivotal, to the safety determination of canola concentrate at its intended use level?

Answer:

Napiferyn confirms that the EFSA Panel conclusions are only corroborative and not pivotal to the safety determination of canola concentrate at its intended use level.

14. On p. 40, the notifier discusses the allergenicity potential of canola concentrate being determined via a "bioinformatics approach" and concludes that canola concentrate "may elicit possible allergenic effects." Additionally, on p. 59 the notifier reiterates that the bioinformatics analysis indicated "possible allergenic effects" of canola concentrate, but no further discussion is provided. While data from an allergen online database search is provided as part of Appendix 4, no discussion of these data are included in the current GRAS notice. Please briefly detail the "possible allergenic effects" of canola concentrate similar to previous notices (e.g., GRN 683), and discuss why they would not be expected to pose a safety concern from the intended use.

Answer:

The results of Mascot search on SwissProt database identified 3 cruciferins as the most abundant proteins found; cruciferin CRU4 (CRU4_BRANA), cruciferin CRU1 (CRU3_BRANA), and cruciferin BnC1 (CRU1_BRANA); with oleosin S2-2 (OLES2_BRANA), napin-3 (2SS3_BRANA), and squalene monooxygenase 1,2 (ERG12_BRANA) present in smaller amounts. This is consistent with publicly available data on the composition of proteins in rapeseed^{[1][2]}.

Bioinformatics searches for sequence similarity to known allergen proteins or celiac disease-eliciting proteins were performed using the FASTA3 algorithm and BLASTP. The identified proteins were searched in publicly available FARRP allergen protein database, FARRP Celiac Disease database, and NCBI Protein database.

All 3 cruciferins show a degree of identity match to 11S globulin proteins in white mustard (*Sinapis alba*). This was especially high (90-92%, full-length FASTA) for cruciferin CRU1 (CRU3_BRANA). Cruciferin is one of the major allergens in white mustard and hazelnut (*Corylus avellana*)^[3]. Because of such a high degree of identity matches with 11S globulin proteins in white mustard, not in hazelnut, cross-reactivity to mustard cruciferins is very likely.

Napin-3 (2SS3_BRANA, allergen Bra n 1) is known to cause allergenic reaction in humans and to bind to IgE^{[4][5]}. It also had high degrees of identity matches to 2S seed storage albumin proteins in oriental mustard (*Brassica juncea*) (allergen Bra j 1-E, 89.1%, full-length FASTA) and in turnip rape (*Brassica rapa*) (allergen Bra r 1, 80.9%), known to cause allergic reactions in humans^{[6][7][5]}. Napin-3 also had a high degree of identity match (up to 83%) to multiple variants of Sin a 1 allergen in white mustard.

Full-length FASTA search has shown relatively high identity matches between oleosin S2-2 (OLES2_BRANA) and oleosins in hazelnut (up to 52.3%) and peanuts (*Arachis hypogaea*, up to 52.5%). Identity matches against all other major food allergen sources were below 50%.

The BLASTP searches performed against the NCBI Protein database did not include any allergenic proteins apart from 10 that were already found during the FARRP allergen protein database searches. Based on historical data, cross-reactivity is fairly common for proteins sharing greater than 70% identity. Then again, those sharing less than 50% identity over the entire protein sequence are not likely to demonstrate cross-reactivity^[8]. Therefore, it can be concluded that cross-reactions between members of the *Brassicaceae* family are highly possible^{[3][5]}.

Overall, RapteinTM30 canola concentrate (rapeseed concentrate) is not expected to be allergenic except for those individuals allergic to mustard or other plants in the *Brassicaceae* family, which currently are not listed as major food allergen sources in the USA. Although the product is not derived from a major food allergen source and is not required to be labelled as such, due to potential allergic cross-reactivity of 2S and 11S seed storage proteins, voluntary precautionary statement for mustard may be considered^[3].

Proteins in RapteinTM30 did not match any peptides using the word search against the Celiac Disease peptide dataset (version 2, released 21 September 2017). The full-length FASTA search against the Celiac Disease protein dataset also did not indicate high sequence similarity with the RapteinTM30 proteins. Although some matches were found, identity matches of less than 45% over at least one-half of the FASTA aligned celiac disease protein and those with an E-value higher than 1×10^{-15} are unlikely to present a risk of inducing celiac disease. The results indicate that the RapteinTM30 proteins are unlikely to elicit celiac disease.

References cited:

- [1] Murphy D.J. (2003). Seed development. Oil Deposition. *Encyclopedia of Applied Plant Sciences*, Elsevier, Editor(s): Brian Thomas, pp. 1256-1261.
- [2] Ottens M. and Chilamkurthi S. (2013). 4 - Advances in process chromatography and applications in the food, beverage and nutraceutical industries. *Separation, Extraction and Concentration Processes in the Food, Beverage and Nutraceutical Industries*, Woodhead Publishing, Editor(s): Syed S.H. Rizvi, pp. 109-147.
- [3] Fiocchi A., Dahdah L., Riccardi C., Mazzina C., and Fierro V. (2016). Precautionary labelling of cross-reactive foods: The case of rapeseed. *Asthma Res and Pract.* 2(13):1-8.
- [4] Monsalve R.I., González de la Peña M.A., López-Otín C., Fiandor A., Fernández C., Villalba M., and Rodríguez R. (1997). Detection, isolation and complete amino acid sequence of an aeroallergenic protein from rapeseed flour. *Clin Exp Allergy*, 27:833-41.
- [5] Puumalainen T.J., Poikonen S., Kotovuori A., Vaali K., Kalkkinen N., Reunala T., Turjanmaa K., and Palosuo T. (2006). Napins, 2S albumins, are major allergens in oilseed rape and turnip rape. *J Allergy Clin Immunol*, 117(2):426-432.
- [6] Monsalve R.I., Gonzalez de la Peña M.A., Menendez-Arias L., Lopez-Otin C., Villalba M., and Rodriguez R. (1993). Characterization of a new oriental-mustard (*Brassica juncea*) allergen, Bra j 1E: detection of an allergenic epitope. *Biochem J*, 293(3):625-632.
- [7] Moreno F.J. and Clemente A. (2008). 2S albumin storage proteins: what makes them food allergens? *Open Biochem J*, 2:16-28.
- [8] Aalberse R.C. (2000). Structural biology of allergens. *J Allergy Clin Immunol*, 106(2):228-238.

15. We note that a recent study on rapeseed protein isolate was published (Xiong et al., 2022).
- a. Please discuss if this study presents additional safety concerns for the article of commerce or contradicts the current GRAS conclusion.

Answer:

The article titled “Removal of anti-nutritional factors of rapeseed protein isolate (RPI) and toxicity assessment of RPI” discusses the potential safety concerns raised, in relation to the presence of anti-nutritional factors (ANFs) in rapeseed protein isolate (RPI). The study compares a non-treated (or non-detoxified) rapeseed protein isolate with a treated (or detoxified) RPI and a commercial soybean protein isolate (SPI), in terms of level of anti-nutritional factors (i.e., glucosinolates, phenolics and phytic acid) and their respective effects on mice. The de-toxification of the RPI was a combined treatment based on alkaline extraction and acidic precipitation. Initially, the RPI was pre-treated with phytase, followed by double ethanol extraction in (ratio 1:5) for a duration of 1.5 hours. The de-toxification of the RPI led to a significant removal of the anti-nutrients.

Following administration to mice for 14 days, the results showed that RPI de-toxified with phytase/ethanol was safe, while a decrease of the thyroid/parathyroid index in mice treated with non-detoxified RPI was reported. The authors state that significant changes were observed in the weight of liver and kidneys between the group fed detoxified RPI and the control group, though no corresponding damage to liver or kidneys was observed.

Additionally, measurement of the thyroid-releasing hormone (TRH), showed higher concentrations of TRH in serum of mice fed detoxified RPI, which could be associated with thyroid gland complications, such as hypothyroidism. The authors conclude that the RPI ingestion could cause inflammation of the thyroid gland, although proper elaboration on their conclusion is missing. Further, the group of mice fed detoxified RPI did show lower levels of Alanine transaminase (ALT) and Aspartate aminotransferase (AST) compared to the control groups (fed non-detoxified RPI). Finally, as a general statement the authors argue that non-detoxified RPI could cause liver disease. Yet, the study concludes that there were no consistent or significant differences in toxicology-related parameters between the treatment groups.

Given article by Xiong et al. (2022) demonstrates that significant removal of antinutrients can be achieved and the resulting detoxified RPI was considered safe under the conditions tested. The article therefore supports that appropriate treatments can be considered to lower antinutrients in rapeseed protein products, but it does not permit to draw accurate conclusions on the toxicity of other rapeseed protein products (i.e., non-detoxified).

As regards to Napiferyn, in the production of the rapeseed/canola protein concentrate, which is the subject of GRAS Notice 1122, purposely designed steps are applied to reduce the content of antinutritional factors. As a result, the final levels of antinutrients are in line or lower than what is conventionally found in rapeseed protein isolates.

- b. Please also perform an updated literature review from 2021 to present and discuss if any additional studies relevant to the safety of canola concentrate were identified that would contradict the current GRAS conclusion.

Answer:

A literature review for the period of 2021-2023 (until 4 July 2023) has been conducted. The result, including discussion, can be found in the report titled ‘Literature_review_GRAS_years_2021-2023’.

References cited:

Xiong Z, Fu Y, Yao J, Zhang N, He R, Ju X, Wang Z. Removal of anti-nutritional factors of rapeseed protein isolate (RPI) and toxicity assessment of RPI. *Food Funct.* 2022 Jan 24;13(2):664-674. doi: 10.1039/d1fo03217h. PMID: 34933325.

Additionally, we received the following questions from USDA FSIS regarding their review of the uses of GRN 1122 concerning products within their purview. Please respond to the following and we will pass your responses along to them.

Please provide Safety Data Sheet (SDS) for the at use concentrations of the substance and include a description of how the use of this technology will not adversely affect the safety of FSIS inspectors. Workplace safety and health hazards include inhalation, direct skin contact (skin, eyes, mouth), and fire/explosion caused by exposure to the product, its working solution or dry mixture and potential by-products formed and/or off-gassed during the application process. The employee safety information should demonstrate how the New Technology will not “jeopardize the safety of Federal inspection personnel” as specified in the FSIS Compliance Guideline Procedures for New Technology Notifications and Protocols, April 2015. FSIS workplace and employee safety must be specifically addressed. Please refer to Appendix A on p. 17, Workplace Safety and Health Criteria, for clarification on what to provide in the response. For additional clarity with respect to employee safety, the following are examples of information that are typically needed by FSIS’ employee safety and health group;

Answer: A Safety Data Sheet for Canola Protein Concentrate has been included, titled ‘Canola_Protein_Concentrate_SDS_v1’.

1. Potential workplace exposures that could result from inhalation and direct contact during use of the substance/technology. This information is required in addition to a SDS to determine accurate hazard potential and recommended exposure control measures for IPP work areas in accordance with Occupational Safety and Health Administration (OSHA) regulations: 29 CFR 1910.1200, Hazard Communication, 29 CFR 1910.132, Personal Protective Equipment, and 29 CFR 1910.1000, Air Contaminants. The information should be included as a specific section in each of the protocols.

Answer:

Raptein™30 is not classified as hazardous according to OSHA Hazard Communication Standard (29 CFR 1910.1200). Nonetheless, since the product is a powder, depending on how it is used, dust can be generated, which can be both a health and a fire hazard. Also, there is a potential for allergen cross-reactivity with mustard, other members of the *Brassicaceae* family, some tree nuts and peanuts.

Therefore, the safety data sheet includes relevant precautions for safe handling, such as wearing protective gloves, protective clothing, eye and/or face protection; avoiding the formation/deposition of dust and static charges; providing for good ventilation of the room when handling the material, and, in case of inadequate ventilation, wearing respiratory protection. Breathing dust should be avoided. Also, it is advisable to prevent the powder from getting into the eyes, on skin, or on clothing as this may lead to either ingestion or adversely affect the eyes. Not eating, drinking or smoking in work areas and proper handling of contaminated clothing and protective equipment are part of normal hygiene practices.

The material is not specifically listed in 29 CFR 1910.1000. Since dust can potentially be generated, depending on how the material is used, the SDS includes 8-hour total weight average (TWA) permissible exposure limit (PEL) applicable to particulates not otherwise regulated

(PNOR), which is 15 mg/m³ (measured as total dust) and 5 mg/m³ (measured as respirable fraction).

2. If the SDS workplace hazards/precautions do not apply to the type of exposure that would be expected for the FSIS IPP, please have the submitter provide specific information (per the April 2015 FSIS Compliance Guideline Procedures) for the actual type of exposures expected.

Answer: Precautions for safe handling in the SDS are relevant to the type of exposure that could be expected for the FSIS IPP.

3. If no IPP workplace exposures are expected and no control measures are required, please have the submitter state this and provide the reasons why (e.g., such as the substance “as used” [for all concentrations] is not hazardous by inhalation or direct contact and/or IPP would not be exposed to the substance based on the system design, operation and/or control measures that will be in place).

Answer: Whether IPP workplace exposures could be expected will depend on how the material is used on site. Therefore, an assessment on a case-by-case basis is recommended.

4. Please also indicate how will FSIS IPP be informed of the above information so that it is clear that the information contained in the SDS for the concentrate does not apply to their actual workplace exposure.

Answer: It is our view that the information contained in the SDS may potentially apply to the IPP’s actual workplace exposure. Therefore, an assessment on a case-by-case basis is recommended.

5. Are there any potential hazards from chemical mixing or low pH as a result of discharges of the various solutions to floor drains? Are dedicated drain lines or any other enclosures required?

Answer: Not applicable

6. With respect to potential airborne exposures to FSIS IPP in the use/application areas, does the submitter have air sampling results taken during the use of the various concentrations of the technology in the listed mixture?

Answer: Such testing has not been conducted. An assessment on a case-by-case basis is recommended.

7. The intended use of this product in FSIS meat and poultry products is apparently as a binder/extender. The suitability support provided in Appendix 6 does sufficiently support no significant difference in yield and other organoleptic qualities when used as a partial replacement for another binder in a processed meat and poultry product, such as sausage. However, additional suitability support is needed:
 - a. No suitability data was provided for whole muscle meat and poultry products at the maximum proposed use level. We would need to see similar data as provided in Appendix 6 for:
 1. Whole muscle red meat control containing no other binders, extenders, or moisture retention agents, as compared to a whole muscle red meat product containing 15% isolated canola product.
 2. Whole muscle poultry control containing no other binders, extenders, or moisture retention agents as compared to a whole muscle poultry product containing 15% isolated canola product.

Answer: Additional suitability testing has been performed, results are described in the attached report titled 'Additional_suitability_Report_meat_extensions'.

From: [Nikolaas Tilkin-Franssens](#)
To: [DiFranco, Stephen](#)
Subject: Re: [EXTERNAL] Re: GRN 1122 canola concentrate items for clarification - Reply
Date: Monday, August 28, 2023 4:43:17 AM
Attachments: [image001.png](#)
[image007.png](#)
[image008.png](#)

CAUTION: This email originated from outside of the organization. Do not click links or open attachments unless you recognize the sender and know the content is safe.

Hi Steve,

Hope you are having a productive start of the week.

Please find the answers to raised questions + 1 additional request from Napiferyn's side (for a minor amendment).

0. Request from Napiferyn: following the requests for clarification, it has been noticed there is a minor inconsistency in the GRAS Notice of Canola Protein Concentrate (GRN 1122).

The carbohydrate specification indicates "65%" which would need to be "70%" in order to be consistent with the Fibre level (40-70%) (being part of total carbohydrates).

Could we take the opportunity of this request for clarification to propose this amendment to the specifications of Canola Protein Concentrate (GRN 1122)?

Questions and Answers

Our reviewers have a few follow up questions regarding your notice. Please comment on the following:

1. In Appendix 1, you provide the results from the batch analyses for pesticide residues in canola concentrate that show glyphosate levels in the range of 0.012-0.020 mg/kg two batches of canola concentrate (Lots R-06#60 and R-09#41) and a phosphine level of 0.008 mg/kg in one batch (Lot R-06#60). In addition, you state that thiophanate-methyl and isofetamid were detected in the raw material (rapeseed cake) at a level of concern; however, the batch analyses of the final ingredient showed no pesticide residues at any level of concern (page 28 of GRN 001122).
 - a. Please address the types of pesticides (other than those mentioned above) that may be used in production (growth and post-harvest) of canola seeds, discuss what steps are taken to minimize pesticide residues in the starting material (rapeseed cake) used in production of canola concentrate, and how the batches of the rapeseed cake with the pesticide residues at a level of concern are handled.

Answer: *The pesticides being of the most concern are listed as follows:*

Acetamiprid, Azoxystrobin, Benzovindiflupyr, Bifenthrin, Boscalid, Captan, Carboxin, Carfentrazone-ethyl, Chlorantraniliprole, Clethodim, Clomazone, Clothianidin, Cyantraniliprole, Cyprodinil, Deltamethrin, Dichlorvos, Difenoconazole, Diquat dibromide, Ethalfluralin, Ethametsulfuron-methyl, Etofenprox, Flonicamid, Fludioxonil, Flumioxazin, Fluopyram, Fluoride, Fluoxastrobil, Flupyradifurone, Fluxapyroxad, Gamma Cyhalothrin, Glufosinate-ammonium, Glyphosate, Imidacloprid, Isofetamid, Lambda

Cyhalothrin, Mefentrifluconazole, Metalaxyl-M (Mefenoxam), Metconazole, Methyl bromide, Nitrpyrin, Penflufen, Penthiopyrad, Phosphine, Picoxystrobin, Propiconazole, Prothioconazole, Pydiflumetofen, Pyraclostrobin, Pyriproxyfen, Quinclorac, Quizalofop-ethyl, Saflufenacil, Sedaxane, Sethoxydim, Spinosad, Sulfoxaflor, Sulfuryl fluoride, Tebufenozide, Tetraconazole, Thiamethoxam, Thifensulfuron-methyl, Thiophanate-methyl, Tribenuron Methyl, Trifluralin, Zeta-Cypermethrin.

Each batch of starting material is analyzed for pesticide residues prior to the production process to ascertain the material meets legal requirements for pesticides content. If the limits are exceeded, this batch would be rejected. Additionally, to reduce the load of pesticide in the starting material upfront dehulling prior to cold-pressing is preferable. If this step is not taken, further in the production process hull fraction removal would be applied.

- b. On page 14 of GRN 001122, you state that canola concentrate is manufactured using rapeseed cake preferably devoid of hull fraction. On page 15 of GRN 001122, you state, "Optionally, to remove residues of hull fraction from the final product, a separation step can be employed...". Please clarify if a separation step is optional or required in the case where canola seeds are not dehulled prior to processing. If the separation step is not required, please discuss how this would impact the pesticide levels in the final ingredient.

Answer:

A separation step is required in the case where canola seeds are not dehulled before processing.

- c. Please clarify whether the results from the batch analyses in Appendix 1 are for canola concentrate manufactured using rapeseed cake that devoid hull fraction. If the rapeseed cake contained hulls, please clarify whether the batches were subjected to the separation step to remove hull fraction residue.

Answer:

Results from the batch analyses in Appendix 1 are for canola concentrate manufactured using both non-dehulled rapeseed cake (R-06#60, R-09#41, R-08#64) and dehulled rapeseed cake (R-03#35, R-13#60, R-15#66). The batches manufactured using non-dehulled rapeseed cake were subjected to the separation step to remove hull fraction residue.

Raptein™30					
R-03#35	R-06#60	R-09#41	R-13#60*	R-15#66	R-08#64
A-00#58 DRC	P-00#16 RC	P-00#16 RC	A-00#59 DRC	A-00#59 DRC	P-00#16 RC

*pesticides not analyzed

DRC - dehulled rapeseed cake

RC - rapeseed cake (non-dehulled)

Kind regards,

Nikolaas Tilkin-Franssens

Regulatory Affairs Manager | Pen & Tec Consulting

T +34 936 758 015 M +34 649 840 417 F +34 936 758 016 www.pentec-consulting.eu

Pl. Ausias March 1 | 4th floor D01 | 08195 Sant Cugat del Vallès | Barcelona | Spain



La información contenida en este mensaje y/o archivo(s) adjunto(s), enviada desde Pen & Tec Consulting SLU, es confidencial/privilegiada y está destinada a ser leída sólo por la(s) persona(s) a la(s) que va dirigida. Le recordamos que sus datos han

sido incorporados en el sistema de tratamiento de Pen & Tec Consulting SLU y que siempre y cuando se cumplan los requisitos exigidos por la normativa, usted podrá ejercer sus derechos de acceso, rectificación, limitación de tratamiento, supresión, portabilidad y oposición/revocación, en los términos que establece la normativa vigente en materia de protección de datos, dirigiendo su petición a la dirección postal Pl. Ausias March 1, 4 planta 08195, Sant Cugat del Vallès (Barcelona) o bien a través de correo electrónico info@pentec-consulting.eu. Si usted lee este mensaje y no es el destinatario señalado, el empleado o el agente responsable de entregar el mensaje al destinatario, o ha recibido esta comunicación por error, le informamos que está totalmente prohibida, y puede ser ilegal, cualquier divulgación, distribución o reproducción de esta comunicación, y le rogamos que nos lo notifique inmediatamente y nos devuelva el mensaje original a la dirección arriba mencionada. Gracias.

The information contained in this message and/or attached file(s), sent by Pen & Tec Consulting SLU, is confidential/privileged and is intended to be read solely by the person(s) to whom it is addressed. We hereby inform you that your data will be incorporated into the processing system owned by Pen & Tec Consulting SLU, and that provided it complies with the requirements included in the law, you may exercise the rights of access, rectification, limitation of processing, deletion, portability and opposition by sending your request to the postal address Pl. Ausias March 1, 4 floor 08195, Sant Cugat del Valles (Barcelona) or to the email address info@pentec-consulting.eu. If you read this message and you are neither the intended recipient, employee or agent in charge of delivering the message to the recipient, or if you have received this message as the result of an error, we hereby inform you that distributing, sharing or reproducing any part of this message is totally forbidden and may be illegal. As a result, we request that you immediately inform us of the error and return this message to the address mentioned above. Thank you.

From: DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>

Date: Thursday, 17 August 2023 at 21:10

To: Nikolaas Tilkin-Franssens <niko@pentec-consulting.eu>

Subject: RE: [EXTERNAL] Re: GRN 1122 canola concentrate items for clarification - Reply

Hello Niko,

Our reviewers have a few follow up questions regarding your notice. Please comment on the following:

1. In Appendix 1, you provide the results from the batch analyses for pesticide residues in canola concentrate that show glyphosate levels in the range of 0.012-0.020 mg/kg two batches of canola concentrate (Lots R-06#60 and R-09#41) and a phosphine level of 0.008 mg/kg in one batch (Lot R-06#60). In addition, you state that thiophanate-methyl and isofetamid were detected in the raw material (rapeseed cake) at a level of concern; however, the batch analyses of the final ingredient showed no pesticide residues at any level of concern (page 28 of GRN 001122).
 - a. Please address the types of pesticides (other than those mentioned above) that may be used in production (growth and post-harvest) of canola seeds, discuss what steps are taken to minimize pesticide residues in the starting material (rapeseed cake) used in production of canola concentrate, and how the batches of the rapeseed cake with the pesticide residues at a level of concern are handled.
 - b. On page 14 of GRN 001122, you state that canola concentrate is manufactured using rapeseed cake preferably devoid of hull fraction. On page 15 of GRN 001122, you state, "Optionally, to remove residues of hull fraction from the final product, a separation step can be employed...". Please clarify if a separation step is optional or required in the case where canola seeds are not dehulled prior to processing. If the separation step is not required, please discuss how this would impact the pesticide levels in the final ingredient.
 - c. Please clarify whether the results from the batch analyses in Appendix 1 are for canola concentrate manufactured using rapeseed cake that devoid hull fraction. If the rapeseed cake contained hulls, please clarify whether the batches were subjected to the separation step to remove hull fraction residue.

If you have any questions on the above or otherwise, please don't hesitate to reach out.

Best,

Steve

Stephen DiFranco, PhD

Regulatory Review Scientist/Chemist

Center for Food Safety and Applied Nutrition

Office of Food Additive Safety

Division of Food Ingredients

U.S. Food and Drug Administration

Tel: 240-402-2710

stephen.difranco@fda.hhs.gov



From: Nikolaas Tilkin-Franssens <niko@pentec-consulting.eu>

Sent: Monday, July 17, 2023 11:05 AM

To: DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>

Subject: Re: [EXTERNAL] Re: GRN 1122 canola concentrate items for clarification - Reply

CAUTION: This email originated from outside of the organization. Do not click links or open attachments unless you recognize the sender and know the content is safe.

Hi Stephen,

Thanks a lot for the quick confirmation.

Have a good work week ahead.

KR

Nikolaas Tilkin-Franssens

Regulatory Affairs Manager | Pen & Tec Consulting

T [+34 936 758 015](tel:+34936758015) **M** [+34 649 840 417](tel:+34649840417) **F** [+34 936 758 016](tel:+34936758016) www.pentec-consulting.eu

Pl. Ausias March 1 | 4th floor D01 | 08195 Sant Cugat del Vallès | Barcelona | Spain

PEN + TEC
CONSULTING

PART OF THE ARGENTA GROUP

La información contenida en este mensaje y/o archivo(s) adjunto(s), enviada desde Pen & Tec Consulting SLU, es confidencial/privilegiada y está destinada a ser leída sólo por la(s) persona(s) a la(s) que va dirigida. Le recordamos que sus datos han sido incorporados en el sistema de tratamiento de Pen & Tec Consulting SLU y que siempre y cuando se cumplan los requisitos exigidos por la normativa, usted podrá ejercer sus derechos de acceso, rectificación, limitación de tratamiento, supresión, portabilidad y

oposición/revocación, en los términos que establece la normativa vigente en materia de protección de datos, dirigiendo su petición a la dirección postal Pl. Ausias March 1, 4 planta 08195, Sant Cugat del Vallès (Barcelona) o bien a través de correo electrónico info@pentec-consulting.eu. Si usted lee este mensaje y no es el destinatario señalado, el empleado o el agente responsable de entregar el mensaje al destinatario, o ha recibido esta comunicación por error, le informamos que está totalmente prohibida, y puede ser ilegal, cualquier divulgación, distribución o reproducción de esta comunicación, y le rogamos que nos lo notifique inmediatamente y nos devuelva el mensaje original a la dirección arriba mencionada. Gracias.

The information contained in this message and/or attached file(s), sent by Pen & Tec Consulting SLU, is confidential/privileged and is intended to be read solely by the person(s) to whom it is addressed. We hereby inform you that your data will be incorporated into the processing system owned by Pen & Tec Consulting SLU, and that provided it complies with the requirements included in the law, you may exercise the rights of access, rectification, limitation of processing, deletion, portability and opposition by sending your request to the postal address Pl. Ausias March 1, 4 floor 08195, Sant Cugat del Valles (Barcelona) or to the email address info@pentec-consulting.eu. If you read this message and you are neither the intended recipient, employee or agent in charge of delivering the message to the recipient, or if you have received this message as the result of an error, we hereby inform you that distributing, sharing or reproducing any part of this message is totally forbidden and may be illegal. As a result, we request that you immediately inform us of the error and return this message to the address mentioned above. Thank you.

From: DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>
Date: Monday, 17 July 2023 at 17:01
To: Nikolaas Tilkin-Franssens <niko@pentec-consulting.eu>
Subject: RE: [EXTERNAL] Re: GRN 1122 canola concentrate items for clarification - Reply

Hello Niko,

No problem—Ill distribute this to the team for review.

Best,

Steve

Stephen DiFranco, PhD

Regulatory Review Scientist/Chemist

Center for Food Safety and Applied Nutrition

Office of Food Additive Safety

Division of Food Ingredients

U.S. Food and Drug Administration

Tel: 240-402-2710

stephen.difranco@fda.hhs.gov



From: Nikolaas Tilkin-Franssens <niko@pentec-consulting.eu>
Sent: Monday, July 17, 2023 10:35 AM
To: DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>
Subject: [EXTERNAL] Re: GRN 1122 canola concentrate items for clarification - Reply

CAUTION: This email originated from outside of the organization. Do not click links or open attachments unless you recognize the sender and know the content is safe.

Hi Stephen,

Apologies for this inconvenience.

We noticed that the reply to question 9 refers to Canola protein isolate (as per GRN 1103). I have updated the answer for it to be mentioning Canola protein concentrate (GRN 1122).

We hope this can be taken into consideration.

Kind regards,

Nikolaas Tilkin-Franssens

Regulatory Affairs Manager | Pen & Tec Consulting

T +34 936 758 015 **M** +34 649 840 417 **F** +34 936 758 016 www.pentec-consulting.eu

Pl. Ausias March 1 | 4th floor D01 | 08195 Sant Cugat del Vallès | Barcelona | Spain

PEN + TEC
CONSULTING
PART OF THE ARGENTA GROUP

La información contenida en este mensaje y/o archivo(s) adjunto(s), enviada desde Pen & Tec Consulting SLU, es confidencial/privilegiada y está destinada a ser leída sólo por la(s) persona(s) a la(s) que va dirigida. Le recordamos que sus datos han sido incorporados en el sistema de tratamiento de Pen & Tec Consulting SLU y que siempre y cuando se cumplan los requisitos exigidos por la normativa, usted podrá ejercer sus derechos de acceso, rectificación, limitación de tratamiento, supresión, portabilidad y oposición/revocación, en los términos que establece la normativa vigente en materia de protección de datos, dirigiendo su petición a la dirección postal Pl. Ausias March 1, 4 planta 08195, Sant Cugat del Vallès (Barcelona) o bien a través de correo electrónico info@pentec-consulting.eu. Si usted lee este mensaje y no es el destinatario señalado, el empleado o el agente responsable de entregar el mensaje al destinatario, o ha recibido esta comunicación por error, le informamos que está totalmente prohibida, y puede ser ilegal, cualquier divulgación, distribución o reproducción de esta comunicación, y le rogamos que nos lo notifique inmediatamente y nos devuelva el mensaje original a la dirección arriba mencionada. Gracias.

The information contained in this message and/or attached file(s), sent by Pen & Tec Consulting SLU, is confidential/privileged and is intended to be read solely by the person(s) to whom it is addressed. We hereby inform you that your data will be incorporated into the processing system owned by Pen & Tec Consulting SLU, and that provided it complies with the requirements included in the law, you may exercise the rights of access, rectification, limitation of processing, deletion, portability and opposition by sending your request to the postal address Pl. Ausias March 1, 4 floor 08195, Sant Cugat del Valles (Barcelona) or to the email address info@pentec-consulting.eu. If you read this message and you are neither the intended recipient, employee or agent in charge of delivering the message to the recipient, or if you have received this message as the result of an error, we hereby inform you that distributing, sharing or reproducing any part of this message is totally forbidden and may be illegal. As a result, we request that you immediately inform us of the error and return this message to the address mentioned above. Thank you.

From: Nikolaas Tilkin-Franssens <niko@pentec-consulting.eu>

Date: Tuesday, 11 July 2023 at 17:03

To: DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>

Cc: Justyna Pałasińska <justyna@pentec-consulting.eu>

Subject: Re: GRN 1122 canola concentrate items for clarification - Reply

Dear Stephen,

Thank you for reaching out with the questions for clarification.
We have worked closely with Napiferyn to close the doubts.

Kindly find attached a Word file including the Questions&Answers, a report on the requested literature review, a SDS sheet as requested by the USDA-FSIS, and a report on the suitability assessment.

We remain available for any further questions or updates.

Thanks for taking the application in further consideration,
best regards,

Nikolaas Tilkin-Franssens

Regulatory Affairs Manager | Pen & Tec Consulting

T +34 936 758 015 M +34 649 840 417 F +34 936 758 016 www.pentec-consulting.eu

Pl. Ausias March 1 | 4th floor D01 | 08195 Sant Cugat del Vallès | Barcelona | Spain

PEN + TEC
CONSULTING

PART OF THE ARGENTA GROUP

La información contenida en este mensaje y/o archivo(s) adjunto(s), enviada desde Pen & Tec Consulting SLU, es confidencial/privilegiada y está destinada a ser leída sólo por la(s) persona(s) a la(s) que va dirigida. Le recordamos que sus datos han sido incorporados en el sistema de tratamiento de Pen & Tec Consulting SLU y que siempre y cuando se cumplan los requisitos exigidos por la normativa, usted podrá ejercer sus derechos de acceso, rectificación, limitación de tratamiento, supresión, portabilidad y oposición/revocación, en los términos que establece la normativa vigente en materia de protección de datos, dirigiendo su petición a la dirección postal Pl. Ausias March 1, 4 planta 08195, Sant Cugat del Vallès (Barcelona) o bien a través de correo electrónico info@pentec-consulting.eu. Si usted lee este mensaje y no es el destinatario señalado, el empleado o el agente responsable de entregar el mensaje al destinatario, o ha recibido esta comunicación por error, le informamos que está totalmente prohibida, y puede ser ilegal, cualquier divulgación, distribución o reproducción de esta comunicación, y le rogamos que nos lo notifique inmediatamente y nos devuelva el mensaje original a la dirección arriba mencionada. Gracias.

The information contained in this message and/or attached file(s), sent by Pen & Tec Consulting SLU, is confidential/privileged and is intended to be read solely by the person(s) to whom it is addressed. We hereby inform you that your data will be incorporated into the processing system owned by Pen & Tec Consulting SLU, and that provided it complies with the requirements included in the law, you may exercise the rights of access, rectification, limitation of processing, deletion, portability and opposition by sending your request to the postal address Pl. Ausias March 1, 4 floor 08195, Sant Cugat del Valles (Barcelona) or to the email address info@pentec-consulting.eu. If you read this message and you are neither the intended recipient, employee or agent in charge of delivering the message to the recipient, or if you have received this message as the result of an error, we hereby inform you that distributing, sharing or reproducing any part of this message is totally forbidden and may be illegal. As a result, we request that you immediately inform us of the error and return this message to the address mentioned above. Thank you.

From: DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>

Date: Wednesday, 28 June 2023 at 17:41

To: Nicoleta Pasecinic <nicoleta@pentec-consulting.eu>

Cc: Nikolaas Tilkin-Franssens <niko@pentec-consulting.eu>

Subject: [EXTERNAL]: GRN 1122 canola concentrate items for clarification

CAUTION: This email originated from outside of the organization. Do not click links or open attachments unless you recognize the sender and know the content is safe.

Hello Ms. Pasecinic,

After evaluating NapiFeryn's GRAS Notice No. GRN 1122 on canola concentrate we noted a few issues that should be addressed. Please respond to the following points for clarification:

1. On p. 9, NapiFeryn states that the major storage proteins in canola seed are cruciferins and napins, and that canola concentrate consists of 30-45% protein and 40-70% dietary fiber. Please provide the typical cruciferin content and napin content in canola concentrate.
2. Please confirm that all raw materials and processing aids used in the manufacturing process are used in accordance with the U.S. regulations, are GRAS for their respective uses or are the subject of an effective food contact notification. For the record, we note that the food additive regulations cited in Table 4 (p. 15) for ascorbic acid (21 CFR 182.8013), ethanol (21

CFR 184.1293), and ethyl acetate (21 CFR 173.228) do not appear to be applicable to your intended uses of these substances.

3. In Table 6 (p. 18-19), NapiFeryn provides the results from the batch analyses for heavy metals. We would like to bring to your attention a relevant FDA's ["Closer to Zero"](#) initiative that focuses on reducing the levels of heavy metals in foods and recommend that you lower the specification limits for heavy metal to better reflect the batch analyses results and to be as low as possible.
4. In Table 10 (p. 22), NapiFeryn provides batch analyses data for residual solvents and processing aids. In addition, in Table 21 (p. 50), you provided the results from the batch analyses for erucic acid in your canola concentrate ranging from 0.37% to < 0.1%.
 - a. Please include limits for residual ethanol, ethyl acetate, and sulphur dioxide as well as a limit for erucic acid in the specifications for canola concentrate and specify the analytical methods used to test for these parameters.
 - b. In addition, please provide an updated Tables 5 and 6 (p. 16-19) to include the additional specification parameters mentioned above, corresponding analytical methods, and batch analyses.
5. Please state that all analytical methods used to test batches were validated and are fit for their respective purpose.
6. Please state that canola concentrate is not intended for use in infant formula or in foods where standards of identity preclude its use.
7. In Table 15 (p.), NapiFeryn provides the results of the batch analyses for total plate count in the raw material (rapeseed press cake). Please address the significant variation in the results (from <10 to 28,000 CFU/g) and discuss whether this will impact safety of the final ingredient.
8. On p. 19, NapiFeryn states that the levels of mycotoxins in canola concentrate are below the limit of quantitation (LOQ) and provide the results from the analyses of five batches to support your statement. Please clarify whether you expect mycotoxins to be present in canola concentrate manufactured in accordance with good manufacturing practices.
9. In Part 1.4 (p. 6) and Part 3.1 (p. 33), NapiFeryn states that the intended use of canola concentrate is as a source of protein and/or fiber, thickener, or texturizer. However, we note that on p. 33 you also state the intended use of canola concentrate is as a flavoring agent or binder in various comminuted or whole muscle meat and poultry products. In addition, in Appendix 3 (p. 5) you state that canola concentrate may also be used "to create a flavored salt" or as "a flavor enhancer like monosodium glutamate". Please confirm these additional uses of canola concentrate are within the scope of GRN 001122.
10. On p. 10, the notifier describes the protein composition of canola concentrate, being primarily

cruciferins, napin, oleosin, and squalene monooxygenase. However, the pivotal safety data provided appear to only be relevant to the cruciferin and napin fractions of the canola concentrate. Please provide a brief narrative to confirm the safety of oleosin and squalene monooxygenase exposure from the intended uses.

11. On p. 31-32 of the notice, the notifier clearly establishes that canola concentrate is intended to be substitutive to protein and fiber consumption and will not contribute to additional exposure to protein or fiber in general. Please elaborate on this conclusion, and clarify if the intended uses of canola concentrate are additive or substitutive to other canola protein products currently on the market (i.e., GRNs 327, 386, and 683)?
12. On p. 37, the notifier concludes exposure to canola concentrate from the intended uses is safe since the EDI reported is “still much lower (approximately 7- to 22-fold lower) than the no-observed-adverse-effect level (NOAEL) values established” for cruciferin- and napin-rich protein isolates in male rats following a 13-week oral exposure regimen (Mejia *et al.*, 2009a & 2009b). We note that an uncertainty factor, or margin of safety (MOS), of 100 (10 for interindividual variability × 10 for interspecies variability) is normally used when assessing safety of a food ingredient by comparing estimated human exposure levels to the NOAEL from animal toxicology data. Therefore, it is not clear why MOS that is ~5-10-fold lower can be concluded as safe without proper justification. Additionally, we note that potential thyrotoxic effects were observed at the highest doses in these two rat studies, as well as for rapeseed products in general tested in other species, as cited in Table 20 of the GRAS notice. This effect was mostly attributed to the presence of glucosinolate; however, we note that since the level of glucosinolate was low or absent in both the test articles from Mejia *et al.* and the article of commerce, the rationale used by the study authors to conclude that the observed NOAEL was not in fact the LOAEL may be questionable. Regardless, it appears that the provided safety narrative lacks sufficient basis to conclude MOS of 7-22 is adequate to reach the conclusion of “reasonable certainty of no harm.” Based on generally available data and information, please provide additional narrative to explain your rationale for your GRAS conclusion.
13. We note that when discussing the absorption, distribution, metabolism, and excretion of canola concentrate (p. 49), the notifier reports unpublished data from an EU Novel Foods application for “defatted rapeseed powder” to support their conclusion. Similarly, genotoxicity conclusions are made using unpublished data from an EFSA Panel conclusion on defatted rapeseed powder. Given other data and information have been used in prior GRAS notices for canola ingredients (e.g., GRN 327), please confirm that the EFSA Panel and EU Novel Foods conclusions are only considered as corroborative, not pivotal, to the safety determination of canola concentrate at its intended use level?
14. On p. 40, the notifier discusses the allergenicity potential of canola concentrate being determined via a “bioinformatics approach” and concludes that canola concentrate “may elicit possible allergenic effects.” Additionally, on p. 59 the notifier reiterates that the bioinformatics analysis indicated “possible allergenic effects” of canola concentrate, but no further discussion is provided. While data from an allergen online database search is provided as part of Appendix 4, no discussion of these data are included in the current GRAS notice.

Please briefly detail the “possible allergenic effects” of canola concentrate similar to previous notices (e.g., GRN 683), and discuss why they would not be expected to pose a safety concern from the intended use.

15. We note that a recent study on rapeseed protein isolate was published (Xiong et al., 2022).
 - a. Please discuss if this study presents additional safety concerns for the article of commerce or contradicts the current GRAS conclusion.
 - b. Please also perform an updated literature review from 2021 to present and discuss if any additional studies relevant to the safety of canola concentrate were identified that would contradict the current GRAS conclusion.

References cited:

Xiong Z, Fu Y, Yao J, Zhang N, He R, Ju X, Wang Z. Removal of anti-nutritional factors of rapeseed protein isolate (RPI) and toxicity assessment of RPI. *Food Funct.* 2022 Jan 24;13(2):664-674. doi: 10.1039/d1fo03217h. PMID: 34933325.

Additionally, we received the following questions from USDA FSIS regarding their review of the uses of GRN 1122 concerning products within their purview. Please respond to the following and we will pass your responses along to them.

Please provide Safety Data Sheet (SDS) for the at use concentrations of the substance and include a description of how the use of this technology will not adversely affect the safety of FSIS inspectors. Workplace safety and health hazards include inhalation, direct skin contact (skin, eyes, mouth), and fire/explosion caused by exposure to the product, its working solution or dry mixture and potential by-products formed and/or off-gassed during the application process. The employee safety information should demonstrate how the New Technology will not “jeopardize the safety of Federal inspection personnel” as specified in the [FSIS Compliance Guideline Procedures for New Technology Notifications and Protocols, April 2015](#). FSIS workplace and employee safety must be specifically addressed. Please refer to Appendix A on p. 17, Workplace Safety and Health Criteria, for clarification on what to provide in the response. For additional clarity with respect to employee safety, the following are examples of information that are typically needed by FSIS’ employee safety and health group;

1. Potential workplace exposures that could result from inhalation and direct contact during use of the substance/technology. This information is required in addition to a SDS to determine accurate hazard potential and recommended exposure control measures for IPP work areas in accordance with Occupational Safety and Health Administration (OSHA) regulations: 29 CFR 1910.1200, Hazard Communication, 29 CFR 1910.132, Personal Protective Equipment, and 29 CFR 1910.1000, Air Contaminants. The information should be included as a specific section in each of the protocols.
2. If the SDS workplace hazards/precautions do not apply to the type of exposure that would be expected for the FSIS IPP, please have the submitter provide specific information (per the April 2015 FSIS Compliance Guideline Procedures) for the actual type of exposures expected.
3. If no IPP workplace exposures are expected and no control measures are required, please have the submitter state this and provide the reasons why (e.g., such as the substance “as

used” [for all concentrations] is not hazardous by inhalation or direct contact and/or IPP would not be exposed to the substance based on the system design, operation and/or control measures that will be in place).

4. Please also indicate how will FSIS IPP be informed of the above information so that it is clear that the information contained in the SDS for the concentrate does not apply to their actual workplace exposure.
5. Are there any potential hazards from chemical mixing or low pH as a result of discharges of the various solutions to floor drains? Are dedicated drain lines or any other enclosures required?
6. With respect to potential airborne exposures to FSIS IPP in the use/application areas, does the submitter have air sampling results taken during the use of the various concentrations of the technology in the listed mixture?
7. The intended use of this product in FSIS meat and poultry products is apparently as a binder/extender. The suitability support provided in Appendix 6 does sufficiently support no significant difference in yield and other organoleptic qualities when used as a partial replacement for another binder in a processed meat and poultry product, such as sausage. However, **additional suitability support is needed:**
 - a. No suitability data was provided for **whole muscle meat and poultry products at the maximum proposed use level**. We would need to see similar data as provided in Appendix 6 for:
 1. Whole muscle red meat control containing no other binders, extenders, or moisture retention agents, as compared to a whole muscle red meat product containing 15% isolated canola product.
 2. Whole muscle poultry control containing no other binders, extenders, or moisture retention agents as compared to a whole muscle poultry product containing 15% isolated canola product.

Responses may be sent in an email or in a separate document. We respectfully request a response within 10 business days. If you are unable to complete the response within that time frame, please contact me to discuss further options.

If you have any additional questions or concerns, please don't hesitate to contact me at stephen.difranco@fda.hhs.gov or by phone at 240.402.2710.

Best,

Steve

Stephen DiFranco, PhD

Regulatory Review Scientist/Chemist

Center for Food Safety and Applied Nutrition

Office of Food Additive Safety

Division of Food Ingredients

U.S. Food and Drug Administration

Tel: 240-402-2710

stephen.difranco@fda.hhs.gov



CAUTION: This email, including any attachments, is confidential. If you are not the intended recipient, please notify the sender and delete the email and any attachments from your system. In addition, you must not use, distribute or reproduce this email or any attachments. Opinions and other information in this email and any attachments which do not relate to the official business of Argenta are neither given by nor endorsed by Argenta. While Argenta uses anti-virus software, Argenta accepts no liability for any viruses in this email or any attachment, or for any effects this email or any attachment may have on your network or computer system.

CAUTION: This email, including any attachments, is confidential. If you are not the intended recipient, please notify the sender and delete the email and any attachments from your system. In addition, you must not use, distribute or reproduce this email or any attachments. Opinions and other information in this email and any attachments which do not relate to the official business of Argenta are neither given by nor endorsed by Argenta. While Argenta uses anti-virus software, Argenta accepts no liability for any viruses in this email or any attachment, or for any effects this email or any attachment may have on your network or computer system.

CAUTION: This email, including any attachments, is confidential. If you are not the intended recipient, please notify the sender and delete the email and any attachments from your system. In addition, you must not use, distribute or reproduce this email or any attachments. Opinions and other information in this email and any attachments which do not relate to the official business of Argenta are neither given by nor endorsed by Argenta. While Argenta uses anti-virus software, Argenta accepts no liability for any viruses in this email or any attachment, or for any effects this email or any attachment may have on your network or computer system.

From: [Nikolaas Tilkin-Franssens](#)
To: [DiFranco, Stephen](#)
Cc: [Justyna Pałasińska](#)
Subject: [EXTERNAL] GRN 1122 canola concentrate - update contact person
Date: Monday, December 4, 2023 4:37:35 AM
Attachments: [image001.png](#)
[image007.png](#)
[image008.png](#)

CAUTION: This email originated from outside of the organization. Do not click links or open attachments unless you recognize the sender and know the content is safe.

Hi Mr. DiFranco,

Hope this email finds you well.

Due to a change in position, I will no longer be the contact person for the GRAS Notice 1122 (Canola Protein Concentrate). Could you please update your records to ascertain that Justyna Pałasińska, in copy to this email, is informed of any relevant updates?

Could you kindly confirm receipt of this email for our records?

And if possible, let us know if there is any estimate on the timeline re. finalization of the review of this GRAS Notice.

Many thanks for your great and flexible support on this application.

Kind regards,

Niko

Nikolaas Tilkin-Franssens

Regulatory Affairs Manager | Pen & Tec Consulting

T +34 936 758 015 M +34 649 840 417 F +34 936 758 016 www.pentec-consulting.eu

Pl. Ausias March 1 | 4th floor D01 | 08195 Sant Cugat del Vallès | Barcelona | Spain

PEN + TEC
CONSULTING

PART OF THE ARGENTA GROUP

La información contenida en este mensaje y/o archivo(s) adjunto(s), enviada desde Pen & Tec Consulting SLU, es confidencial/privilegiada y está destinada a ser leída sólo por la(s) persona(s) a la(s) que va dirigida. Le recordamos que sus datos han sido incorporados en el sistema de tratamiento de Pen & Tec Consulting SLU y que siempre y cuando se cumplan los requisitos exigidos por la normativa, usted podrá ejercer sus derechos de acceso, rectificación, limitación de tratamiento, supresión, portabilidad y oposición/revocación, en los términos que establece la normativa vigente en materia de protección de datos, dirigiendo su petición a la dirección postal Pl. Ausias March 1, 4 planta 08195, Sant Cugat del Vallès (Barcelona) o bien a través de correo electrónico info@pentec-consulting.eu. Si usted lee este mensaje y no es el destinatario señalado, el empleado o el agente responsable de entregar el mensaje al destinatario, o ha recibido esta comunicación por error, le informamos que está totalmente prohibida, y puede ser ilegal, cualquier divulgación, distribución o reproducción de esta comunicación, y le rogamos que nos lo notifique inmediatamente y nos devuelva el mensaje original a la dirección arriba mencionada. Gracias.

The information contained in this message and/or attached file(s), sent by Pen & Tec Consulting SLU, is confidential/privileged and is intended to be read solely by the person(s) to whom it is addressed. We hereby inform you that your data will be incorporated into the processing system owned by Pen & Tec Consulting SLU, and that provided it complies with the requirements included in the law, you may exercise the rights of access, rectification, limitation of processing, deletion, portability and opposition by sending your request to the postal address Pl. Ausias March 1, 4 floor 08195, Sant Cugat del Valles (Barcelona) or to the email address info@pentec-consulting.eu. If you read this message and you are neither the intended recipient, employee or agent in charge of delivering the message to the recipient, or if you have received this message as the result of an error, we hereby inform you that distributing, sharing or reproducing any part of this message is totally forbidden and may be illegal. As a result, we request that you immediately inform us of the error and return this message to the address mentioned above. Thank you.

From: DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>

Date: Monday, 17 July 2023 at 17:01

To: Nikolaas Tilkin-Franssens <niko@pentec-consulting.eu>

Subject: RE: [EXTERNAL] Re: GRN 1122 canola concentrate items for clarification - Reply

Hello Niko,

No problem—I'll distribute this to the team for review.

Best,

Steve

Stephen DiFranco, PhD

Regulatory Review Scientist/Chemist

Center for Food Safety and Applied Nutrition

Office of Food Additive Safety

Division of Food Ingredients

U.S. Food and Drug Administration

Tel: 240-402-2710

stephen.difranco@fda.hhs.gov



From: Nikolaas Tilkin-Franssens <niko@pentec-consulting.eu>

Sent: Monday, July 17, 2023 10:35 AM

To: DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>

Subject: [EXTERNAL] Re: GRN 1122 canola concentrate items for clarification - Reply

CAUTION: This email originated from outside of the organization. Do not click links or open attachments unless you recognize the sender and know the content is safe.

Hi Stephen,

Apologies for this inconvenience.

We noticed that the reply to question 9 refers to Canola protein isolate (as per GRN 1103). I have updated the answer for it to be mentioning Canola protein concentrate (GRN 1122).

We hope this can be taken into consideration.

Kind regards,

Nikolaas Tilkin-Franssens

Regulatory Affairs Manager | Pen & Tec Consulting

T [+34 936 758 015](tel:+34936758015) **M** [+34 649 840 417](tel:+34649840417) **F** [+34 936 758 016](tel:+34936758016) www.pentec-consulting.eu

Pl. Ausias March 1 | 4th floor D01 | 08195 Sant Cugat del Vallès | Barcelona | Spain

PEN + TEC
CONSULTING

PART OF THE ARGENTA GROUP

La información contenida en este mensaje y/o archivo(s) adjunto(s), enviada desde Pen & Tec Consulting SLU, es confidencial/privilegiada y está destinada a ser leída sólo por la(s) persona(s) a la(s) que va dirigida. Le recordamos que sus datos han sido incorporados en el sistema de tratamiento de Pen & Tec Consulting SLU y que siempre y cuando se cumplan los requisitos exigidos por la normativa, usted podrá ejercer sus derechos de acceso, rectificación, limitación de tratamiento, supresión, portabilidad y oposición/revocación, en los términos que establece la normativa vigente en materia de protección de datos, dirigiendo su petición a la dirección postal Pl. Ausias March 1, 4 planta 08195, Sant Cugat del Vallès (Barcelona) o bien a través de correo electrónico info@pentec-consulting.eu. Si usted lee este mensaje y no es el destinatario señalado, el empleado o el agente responsable de entregar el mensaje al destinatario, o ha recibido esta comunicación por error, le informamos que está totalmente prohibida, y puede ser ilegal, cualquier divulgación, distribución o reproducción de esta comunicación, y le rogamos que nos lo notifique inmediatamente y nos devuelva el mensaje original a la dirección arriba mencionada. Gracias.

The information contained in this message and/or attached file(s), sent by Pen & Tec Consulting SLU, is confidential/privileged and is intended to be read solely by the person(s) to whom it is addressed. We hereby inform you that your data will be incorporated into the processing system owned by Pen & Tec Consulting SLU, and that provided it complies with the requirements included in the law, you may exercise the rights of access, rectification, limitation of processing, deletion, portability and opposition by sending your request to the postal address Pl. Ausias March 1, 4 floor 08195, Sant Cugat del Valles (Barcelona) or to the email address info@pentec-consulting.eu. If you read this message and you are neither the intended recipient, employee or agent in charge of delivering the message to the recipient, or if you have received this message as the result of an error, we hereby inform you that distributing, sharing or reproducing any part of this message is totally forbidden and may be illegal. As a result, we request that you immediately inform us of the error and return this message to the address mentioned above. Thank you.

From: Nikolaas Tilkin-Franssens <niko@pentec-consulting.eu>

Date: Tuesday, 11 July 2023 at 17:03

To: DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>

Cc: Justyna Pałasińska <justyna@pentec-consulting.eu>

Subject: Re: GRN 1122 canola concentrate items for clarification - Reply

Dear Stephen,

Thank you for reaching out with the questions for clarification.

We have worked closely with Napiferyn to close the doubts.

Kindly find attached a Word file including the Questions&Answers, a report on the requested literature review, a SDS sheet as requested by the USDA-FSIS, and a report on the suitability assessment.

We remain available for any further questions or updates.

Thanks for taking the application in further consideration,
best regards,

Nikolaas Tilkin-Franssens

Regulatory Affairs Manager | Pen & Tec Consulting

T [+34 936 758 015](tel:+34936758015) **M** [+34 649 840 417](tel:+34649840417) **F** [+34 936 758 016](tel:+34936758016) www.pentec-consulting.eu

Pl. Ausias March 1 | 4th floor D01 | 08195 Sant Cugat del Vallès | Barcelona | Spain

La información contenida en este mensaje y/o archivo(s) adjunto(s), enviada desde Pen & Tec Consulting SLU, es confidencial/privilegiada y está destinada a ser leída sólo por la(s) persona(s) a la(s) que va dirigida. Le recordamos que sus datos han sido incorporados en el sistema de tratamiento de Pen & Tec Consulting SLU y que siempre y cuando se cumplan los requisitos exigidos por la normativa, usted podrá ejercer sus derechos de acceso, rectificación, limitación de tratamiento, supresión, portabilidad y oposición/revocación, en los términos que establece la normativa vigente en materia de protección de datos, dirigiendo su petición a la dirección postal Pl. Ausias March 1, 4 planta 08195, Sant Cugat del Vallès (Barcelona) o bien a través de correo electrónico info@pentec-consulting.eu. Si usted lee este mensaje y no es el destinatario señalado, el empleado o el agente responsable de entregar el mensaje al destinatario, o ha recibido esta comunicación por error, le informamos que está totalmente prohibida, y puede ser ilegal, cualquier divulgación, distribución o reproducción de esta comunicación, y le rogamos que nos lo notifique inmediatamente y nos devuelva el mensaje original a la dirección arriba mencionada. Gracias.

The information contained in this message and/or attached file(s), sent by Pen & Tec Consulting SLU, is confidential/privileged and is intended to be read solely by the person(s) to whom it is addressed. We hereby inform you that your data will be incorporated into the processing system owned by Pen & Tec Consulting SLU, and that provided it complies with the requirements included in the law, you may exercise the rights of access, rectification, limitation of processing, deletion, portability and opposition by sending your request to the postal address Pl. Ausias March 1, 4 floor 08195, Sant Cugat del Valles (Barcelona) or to the email address info@pentec-consulting.eu. If you read this message and you are neither the intended recipient, employee or agent in charge of delivering the message to the recipient, or if you have received this message as the result of an error, we hereby inform you that distributing, sharing or reproducing any part of this message is totally forbidden and may be illegal. As a result, we request that you immediately inform us of the error and return this message to the address mentioned above. Thank you.

From: DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>
Date: Wednesday, 28 June 2023 at 17:41
To: Nicoleta Pasecinic <nicoleta@pentec-consulting.eu>
Cc: Nikolaas Tilkin-Franssens <niko@pentec-consulting.eu>
Subject: [EXTERNAL]: GRN 1122 canola concentrate items for clarification

CAUTION: This email originated from outside of the organization. Do not click links or open attachments unless you recognize the sender and know the content is safe.

Hello Ms. Pasecinic,

After evaluating NapiFeryn's GRAS Notice No. GRN 1122 on canola concentrate we noted a few issues that should be addressed. Please respond to the following points for clarification:

1. On p. 9, NapiFeryn states that the major storage proteins in canola seed are cruciferins and napins, and that canola concentrate consists of 30-45% protein and 40-70% dietary fiber. Please provide the typical cruciferin content and napin content in canola concentrate.
2. Please confirm that all raw materials and processing aids used in the manufacturing process are used in accordance with the U.S. regulations, are GRAS for their respective uses or are the subject of an effective food contact notification. For the record, we note that the food additive regulations cited in Table 4 (p. 15) for ascorbic acid (21 CFR 182.8013), ethanol (21 CFR 184.1293), and ethyl acetate (21 CFR 173.228) do not appear to be applicable to your intended uses of these substances.
3. In Table 6 (p. 18-19), NapiFeryn provides the results from the batch analyses for heavy metals. We would like to bring to your attention a relevant FDA's "[Closer to Zero](#)" initiative that focuses on reducing the levels of heavy metals in foods and recommend that you lower the specification limits for heavy metal to better reflect the batch analyses results and to be as low as possible.

4. In Table 10 (p. 22), NapiFeryn provides batch analyses data for residual solvents and processing aids. In addition, in Table 21 (p. 50), you provided the results from the batch analyses for erucic acid in your canola concentrate ranging from 0.37% to < 0.1%.
 - a. Please include limits for residual ethanol, ethyl acetate, and sulphur dioxide as well as a limit for erucic acid in the specifications for canola concentrate and specify the analytical methods used to test for these parameters.
 - b. In addition, please provide an updated Tables 5 and 6 (p. 16-19) to include the additional specification parameters mentioned above, corresponding analytical methods, and batch analyses.
5. Please state that all analytical methods used to test batches were validated and are fit for their respective purpose.
6. Please state that canola concentrate is not intended for use in infant formula or in foods where standards of identity preclude its use.
7. In Table 15 (p.), NapiFeryn provides the results of the batch analyses for total plate count in the raw material (rapeseed press cake). Please address the significant variation in the results (from <10 to 28,000 CFU/g) and discuss whether this will impact safety of the final ingredient.
8. On p. 19, NapiFeryn states that the levels of mycotoxins in canola concentrate are below the limit of quantitation (LOQ) and provide the results from the analyses of five batches to support your statement. Please clarify whether you expect mycotoxins to be present in canola concentrate manufactured in accordance with good manufacturing practices.
9. In Part 1.4 (p. 6) and Part 3.1 (p. 33), NapiFeryn states that the intended use of canola concentrate is as a source of protein and/or fiber, thickener, or texturizer. However, we note that on p. 33 you also state the intended use of canola concentrate is as a flavoring agent or binder in various comminuted or whole muscle meat and poultry products. In addition, in Appendix 3 (p. 5) you state that canola concentrate may also be used “to create a flavored salt” or as “a flavor enhancer like monosodium glutamate”. Please confirm these additional uses of canola concentrate are within the scope of GRN 001122.
10. On p. 10, the notifier describes the protein composition of canola concentrate, being primarily cruciferins, napin, oleosin, and squalene monoxygenase. However, the pivotal safety data provided appear to only be relevant to the cruciferin and napin fractions of the canola concentrate. Please provide a brief narrative to confirm the safety of oleosin and squalene monoxygenase exposure from the intended uses.
11. On p. 31-32 of the notice, the notifier clearly establishes that canola concentrate is intended to be substitutive to protein and fiber consumption and will not contribute to additional exposure to protein or fiber in general. Please elaborate on this conclusion, and clarify if the

intended uses of canola concentrate are additive or substitutive to other canola protein products currently on the market (i.e., GRNs 327, 386, and 683)?

12. On p. 37, the notifier concludes exposure to canola concentrate from the intended uses is safe since the EDI reported is “still much lower (approximately 7- to 22-fold lower) than the no-observed-adverse-effect level (NOAEL) values established” for cruciferin- and napin-rich protein isolates in male rats following a 13-week oral exposure regimen (Mejia *et al.*, 2009a & 2009b). We note that an uncertainty factor, or margin of safety (MOS), of 100 (10 for interindividual variability × 10 for interspecies variability) is normally used when assessing safety of a food ingredient by comparing estimated human exposure levels to the NOAEL from animal toxicology data. Therefore, it is not clear why MOS that is ~5-10-fold lower can be concluded as safe without proper justification. Additionally, we note that potential thyrotoxic effects were observed at the highest doses in these two rat studies, as well as for rapeseed products in general tested in other species, as cited in Table 20 of the GRAS notice. This effect was mostly attributed to the presence of glucosinolate; however, we note that since the level of glucosinolate was low or absent in both the test articles from Mejia *et al.* and the article of commerce, the rationale used by the study authors to conclude that the observed NOAEL was not in fact the LOAEL may be questionable. Regardless, it appears that the provided safety narrative lacks sufficient basis to conclude MOS of 7-22 is adequate to reach the conclusion of “reasonable certainty of no harm.” Based on generally available data and information, please provide additional narrative to explain your rationale for your GRAS conclusion.
13. We note that when discussing the absorption, distribution, metabolism, and excretion of canola concentrate (p. 49), the notifier reports unpublished data from an EU Novel Foods application for “defatted rapeseed powder” to support their conclusion. Similarly, genotoxicity conclusions are made using unpublished data from an EFSA Panel conclusion on defatted rapeseed powder. Given other data and information have been used in prior GRAS notices for canola ingredients (e.g., GRN 327), please confirm that the EFSA Panel and EU Novel Foods conclusions are only considered as corroborative, not pivotal, to the safety determination of canola concentrate at its intended use level?
14. On p. 40, the notifier discusses the allergenicity potential of canola concentrate being determined via a “bioinformatics approach” and concludes that canola concentrate “may elicit possible allergenic effects.” Additionally, on p. 59 the notifier reiterates that the bioinformatics analysis indicated “possible allergenic effects” of canola concentrate, but no further discussion is provided. While data from an allergen online database search is provided as part of Appendix 4, no discussion of these data are included in the current GRAS notice. Please briefly detail the “possible allergenic effects” of canola concentrate similar to previous notices (e.g., GRN 683), and discuss why they would not be expected to pose a safety concern from the intended use.
15. We note that a recent study on rapeseed protein isolate was published (Xiong *et al.*, 2022).
 - a. Please discuss if this study presents additional safety concerns for the article of commerce or contradicts the current GRAS conclusion.
 - b. Please also perform an updated literature review from 2021 to present and discuss if

any additional studies relevant to the safety of canola concentrate were identified that would contradict the current GRAS conclusion.

References cited:

Xiong Z, Fu Y, Yao J, Zhang N, He R, Ju X, Wang Z. Removal of anti-nutritional factors of rapeseed protein isolate (RPI) and toxicity assessment of RPI. *Food Funct.* 2022 Jan 24;13(2):664-674. doi: 10.1039/d1fo03217h. PMID: 34933325.

Additionally, we received the following questions from USDA FSIS regarding their review of the uses of GRN 1122 concerning products within their purview. Please respond to the following and we will pass your responses along to them.

Please provide Safety Data Sheet (SDS) for the at use concentrations of the substance and include a description of how the use of this technology will not adversely affect the safety of FSIS inspectors. Workplace safety and health hazards include inhalation, direct skin contact (skin, eyes, mouth), and fire/explosion caused by exposure to the product, its working solution or dry mixture and potential by-products formed and/or off-gassed during the application process. The employee safety information should demonstrate how the New Technology will not “jeopardize the safety of Federal inspection personnel” as specified in the [FSIS Compliance Guideline Procedures for New Technology Notifications and Protocols, April 2015](#). FSIS workplace and employee safety must be specifically addressed. Please refer to Appendix A on p. 17, Workplace Safety and Health Criteria, for clarification on what to provide in the response. For additional clarity with respect to employee safety, the following are examples of information that are typically needed by FSIS’ employee safety and health group;

1. Potential workplace exposures that could result from inhalation and direct contact during use of the substance/technology. This information is required in addition to a SDS to determine accurate hazard potential and recommended exposure control measures for IPP work areas in accordance with Occupational Safety and Health Administration (OSHA) regulations: 29 CFR 1910.1200, Hazard Communication, 29 CFR 1910.132, Personal Protective Equipment, and 29 CFR 1910.1000, Air Contaminants. The information should be included as a specific section in each of the protocols.
2. If the SDS workplace hazards/precautions do not apply to the type of exposure that would be expected for the FSIS IPP, please have the submitter provide specific information (per the April 2015 FSIS Compliance Guideline Procedures) for the actual type of exposures expected.
3. If no IPP workplace exposures are expected and no control measures are required, please have the submitter state this and provide the reasons why (e.g., such as the substance “as used” [for all concentrations] is not hazardous by inhalation or direct contact and/or IPP would not be exposed to the substance based on the system design, operation and/or control measures that will be in place).
4. Please also indicate how will FSIS IPP be informed of the above information so that it is clear that the information contained in the SDS for the concentrate does not apply to their actual workplace exposure.
5. Are there any potential hazards from chemical mixing or low pH as a result of discharges of the various solutions to floor drains? Are dedicated drain lines or any other enclosures

required?

6. With respect to potential airborne exposures to FSIS IPP in the use/application areas, does the submitter have air sampling results taken during the use of the various concentrations of the technology in the listed mixture?
7. The intended use of this product in FSIS meat and poultry products is apparently as a binder/extender. The suitability support provided in Appendix 6 does sufficiently support no significant difference in yield and other organoleptic qualities when used as a partial replacement for another binder in a processed meat and poultry product, such as sausage. However, **additional suitability support is needed:**
 - a. No suitability data was provided for **whole muscle meat and poultry products at the maximum proposed use level**. We would need to see similar data as provided in Appendix 6 for:
 1. Whole muscle red meat control containing no other binders, extenders, or moisture retention agents, as compared to a whole muscle red meat product containing 15% isolated canola product.
 2. Whole muscle poultry control containing no other binders, extenders, or moisture retention agents as compared to a whole muscle poultry product containing 15% isolated canola product.

Responses may be sent in an email or in a separate document. We respectfully request a response within 10 business days. If you are unable to complete the response within that time frame, please contact me to discuss further options.

If you have any additional questions or concerns, please don't hesitate to contact me at stephen.difranco@fda.hhs.gov or by phone at 240.402.2710.

Best,

Steve

Stephen DiFranco, PhD

Regulatory Review Scientist/Chemist

Center for Food Safety and Applied Nutrition

Office of Food Additive Safety

Division of Food Ingredients

U.S. Food and Drug Administration

Tel: 240-402-2710

stephen.difranco@fda.hhs.gov



CAUTION: This email, including any attachments, is confidential. If you are not the intended recipient, please notify the sender and delete the email and any attachments from your system.

In addition, you must not use, distribute or reproduce this email or any attachments. Opinions and other information in this email and any attachments which do not relate to the official business of Argenta are neither given by nor endorsed by Argenta. While Argenta uses anti-virus software, Argenta accepts no liability for any viruses in this email or any attachment, or for any effects this email or any attachment may have on your network or computer system.

CAUTION: This email, including any attachments, is confidential. If you are not the intended recipient, please notify the sender and delete the email and any attachments from your system. In addition, you must not use, distribute or reproduce this email or any attachments. Opinions and other information in this email and any attachments which do not relate to the official business of Argenta are neither given by nor endorsed by Argenta. While Argenta uses anti-virus software, Argenta accepts no liability for any viruses in this email or any attachment, or for any effects this email or any attachment may have on your network or computer system.

From: [Nikolaas Tilkin-Franssens](#)
To: [DiFranco, Stephen](#)
Subject: Automatic reply: [EXTERNAL] GRN 1122 canola concentrate - update contact person
Date: Tuesday, December 5, 2023 1:07:06 PM

CAUTION: This email originated from outside of the organization. Do not click links or open attachments unless you recognize the sender and know the content is safe.

Dear Sender,

I am no longer working at Pen & Tec. Please contact Justyna Palasinska (justyna@pentec-consulting.eu). Your email will not be forwarded.

Thank you.

CAUTION: This email, including any attachments, is confidential. If you are not the intended recipient, please notify the sender and delete the email and any attachments from your system. In addition, you must not use, distribute or reproduce this email or any attachments. Opinions and other information in this email and any attachments which do not relate to the official business of Argenta are neither given by nor endorsed by Argenta. While Argenta uses anti-virus software, Argenta accepts no liability for any viruses in this email or any attachment, or for any effects this email or any attachment may have on your network or computer system.

**GRN 1122 - Raptein™30 - Canola protein concentrate:
Replies to request for clarification of 5 December 2023**

USDA-FSIS is requesting a few pieces of information regarding the uses of canola concentrate under USDA jurisdiction, namely

Please provide Safety Data Sheet (SDS) for the at use concentrations of the substance and include a description of how the use of this technology will not adversely affect the safety of FSIS inspectors. Workplace safety and health hazards include inhalation, direct skin contact (skin, eyes, mouth), and fire/explosion caused by exposure to the product, its working solution or dry mixture and potential by-products formed and/or off-gassed during the application process. The employee safety information should demonstrate how the New Technology will not “jeopardize the safety of Federal inspection personnel” as specified in the [FSIS Compliance Guideline Procedures for New Technology Notifications and Protocols, April 2015](#). FSIS workplace and employee safety must be specifically addressed. Please refer to Appendix A on p. 17, Workplace Safety and Health Criteria, for clarification on what to provide in the response. For additional clarity with respect to employee safety, the following are examples of information that are typically needed by FSIS’ employee safety and health group;

Answer: A Safety Data Sheet for Canola Protein Concentrate has been included, titled ‘Canola_Protein_Concentrate_SDS_v1’.

1. Potential workplace exposures that could result from inhalation and direct contact during use of the substance/technology. This information is required in addition to a SDS to determine accurate hazard potential and recommended exposure control measures for IPP work areas in accordance with Occupational Safety and Health Administration (OSHA) regulations: 29 CFR 1910.1200, Hazard Communication, 29 CFR 1910.132, Personal Protective Equipment, and 29 CFR 1910.1000, Air Contaminants. The information should be included as a specific section in each of the protocols.

Answer:

Raptein™30 is not classified as hazardous according to OSHA Hazard Communication Standard (29 CFR 1910.1200). Nonetheless, since the product is a powder, depending on how it is used, dust can be generated, which can be both a health and a fire hazard. Also, there is a potential for allergen cross-reactivity with mustard, other members of the *Brassicaceae* family, some tree nuts and peanuts.

Therefore, the safety data sheet includes relevant precautions for safe handling, such as wearing protective gloves, protective clothing, eye and/or face protection; avoiding the formation/deposition of dust and static charges; providing for good ventilation of the room when handling the material, and, in case of inadequate ventilation, wearing respiratory protection. Breathing dust should be avoided. Also, it is advisable to prevent the powder from getting into the eyes, on skin, or on clothing as this may lead to either ingestion or adversely affect the eyes. Not eating, drinking or smoking in work areas and proper handling of contaminated clothing and protective equipment are part of normal hygiene practices.

The material is not specifically listed in 29 CFR 1910.1000. Since dust can potentially be generated, depending on how the material is used, the SDS includes 8-hour total weight average (TWA) permissible exposure limit (PEL) applicable to particulates not otherwise regulated (PNOR), which is 15 mg/m³ (measured as total dust) and 5 mg/m³ (measured as respirable fraction).

2. If the SDS workplace hazards/precautions do not apply to the type of exposure that would be expected for the FSIS IPP, please have the submitter provide specific information (per the April 2015 FSIS Compliance Guideline Procedures) for the actual type of exposures expected.

Answer: Precautions for safe handling in the SDS are relevant to the type of exposure that could be expected for the FSIS IPP.

3. If no IPP workplace exposures are expected and no control measures are required, please have the submitter state this and provide the reasons why (e.g., such as the substance “as used” [for all concentrations] is not hazardous by inhalation or direct contact and/or IPP would not be exposed to the substance based on the system design, operation and/or control measures that will be in place).

Answer: Whether IPP workplace exposures could be expected will depend on how the material is used on site. Therefore, an assessment on a case-by-case basis is recommended.

4. Please also indicate how will FSIS IPP be informed of the above information so that it is clear that the information contained in the SDS for the concentrate does not apply to their actual workplace exposure.

Answer: It is our view that the information contained in the SDS may potentially apply to the IPP’s actual workplace exposure. Therefore, an assessment on a case-by-case basis is recommended.

5. Are there any potential hazards from chemical mixing or low pH as a result of discharges of the various solutions to floor drains? Are dedicated drain lines or any other enclosures required?

Answer: Not applicable

6. With respect to potential airborne exposures to FSIS IPP in the use/application areas, does the submitter have air sampling results taken during the use of the various concentrations of the technology in the listed mixture?

Answer: Such testing has not been conducted. An assessment on a case-by-case basis is recommended.

7. The intended use of this product in FSIS meat and poultry products is apparently as a binder/extender. The suitability support provided in Appendix 6 does sufficiently support no significant difference in yield and other organoleptic qualities when used as a partial replacement for another binder in a processed meat and poultry product, such as sausage. However, additional suitability support is needed:
 - a. No suitability data was provided for whole muscle meat and poultry products at the maximum proposed use level. We would need to see similar data as provided in Appendix 6 for:
 1. Whole muscle red meat control containing no other binders, extenders, or moisture retention agents, as compared to a whole muscle red meat product containing 15% isolated canola product.
 2. Whole muscle poultry control containing no other binders, extenders, or moisture retention agents as compared to a whole muscle poultry product containing 15% isolated canola product.

Answer: Additional suitability testing has been performed, results are described in the attached report titled 'Additional_suitability_Report_meat_extensions'.

From: [Ioannis Kartanos](#)
To: [DiFranco, Stephen](#)
Cc: [Justyna Palasińska](#)
Subject: [EXTERNAL] GRN 1122 canola concentrate - request of additional information
Date: Tuesday, December 12, 2023 8:20:27 AM
Attachments: [image001.png](#)
[image007.png](#)
[image001.png](#)

CAUTION: This email originated from outside of the organization. Do not click links or open attachments unless you recognize the sender and know the content is safe.

Dear Mr. DiFranco,

I hope this finds you very well!

Thank you very much for your confirmation of the change of contact person for GRN 1122.

Regarding the requested additional information on the concentrate by the USDA-FSIS, I would like to coordinate with you since my colleague Justyna (in copy) will be away from office for few days. Please accept our apologies for any inconvenience.

I reviewed your questions and realised that we have already received and addressed these questions in the past and provided the requested SDS and suitability reports. Therefore, I would like to kindly confirm with you if our previous replies have been reviewed and further information is still needed, or if it is possible that this information was not communicated to the USDA-FSIS?

Please find below an overview of our replies:

- A Safety Data Sheet for Canola Protein Concentrate has been provided, titled
`Canola_Protein_Concentrate_SDS_v1`

1. Raptein™30 is not classified as hazardous according to OSHA Hazard Communication Standard (29 CFR 1910.1200). Nonetheless, since the product is a powder, depending on how it is used, dust can be generated, which can be both a health and a fire hazard. Also, there is a potential for allergen cross-reactivity with mustard, other members of the *Brassicaceae* family, some tree nuts and peanuts.

Therefore, the safety data sheet includes relevant precautions for safe handling, such as wearing protective gloves, protective clothing, eye and/or face protection; avoiding the formation/deposition of dust and static charges; providing for good ventilation of the room when handling the material, and, in case of inadequate ventilation, wearing respiratory protection. Breathing dust should be avoided. Also, it is advisable to prevent the powder from getting into the eyes, on skin, or on clothing as this may lead to either ingestion or adversely affect the eyes. Not eating, drinking or smoking in work areas and proper handling of contaminated clothing and protective equipment are part of normal hygiene practices.

The material is not specifically listed in 29 CFR 1910.1000. Since dust can potentially be generated, depending on how the material is used, the SDS includes 8-hour total weight average (TWA) permissible exposure limit (PEL) applicable to particulates not otherwise regulated (PNOR), which is 15 mg/m³ (measured as total dust) and 5 mg/m³ (measured as respirable fraction).

2. Precautions for safe handling in the SDS are relevant to the type of exposure that could be expected for

the FSIS IPP.

3. Whether IPP workplace exposures could be expected will depend on how the material is used on site. Therefore, an assessment on a case-by-case basis is recommended.
4. It is our view that the information contained in the SDS may potentially apply to the IPP's actual workplace exposure. Therefore, an assessment on a case-by-case basis is recommended.
5. Not applicable
6. Such testing has not been conducted. An assessment on a case-by-case basis is recommended.

- **Suitability data**

Additional suitability testing has been performed and results are described in the provided report titled 'Additional_suitability_Report_meat_extensions'.

Looking forward for your kind reply. In the meantime, please feel free to contact me if further clarification regarding our previous replies is needed.

Warm regards,

Ioannis Kartanos

Regulatory Affairs Associate | Pen & Tec Consulting

T +34936096897, +34 936 758 015 **M** +34 683 565 684, www.pentec-consulting.eu

Pl. Ausias March 1 | 4th floor D01 | 08195 Sant Cugat del Vallès | Barcelona | Spain

PEN + TEC
CONSULTING
PART OF THE ARGENTA GROUP

La información contenida en este mensaje y/o archivo(s) adjunto(s), enviada desde Pen & Tec Consulting SLU, es confidencial/privilegiada y está destinada a ser leída sólo por la(s) persona(s) a la(s) que va dirigida. Le recordamos que sus datos han sido incorporados en el sistema de tratamiento de Pen & Tec Consulting SLU y que siempre y cuando se cumplan los requisitos exigidos por la normativa, usted podrá ejercer sus derechos de acceso, rectificación, limitación de tratamiento, supresión, portabilidad y oposición/revocación, en los términos que establece la normativa vigente en materia de protección de datos, dirigiendo su petición a la dirección postal Pl. Ausias March 1, 4 planta 08195, Sant Cugat del Vallès (Barcelona) o bien a través de correo electrónico info@pentec-consulting.eu. Si usted lee este mensaje y no es el destinatario señalado, el empleado o el agente responsable de entregar el mensaje al destinatario, o ha recibido esta comunicación por error, le informamos que está totalmente prohibida, y puede ser ilegal, cualquier divulgación, distribución o reproducción de esta comunicación, y le rogamos que nos lo notifique inmediatamente y nos devuelva el mensaje original a la dirección arriba mencionada. Gracias.

The information contained in this message and/or attached file(s), sent by Pen & Tec Consulting SLU, is confidential/privileged and is intended to be read solely by the person(s) to whom it is addressed. We hereby inform you that your data will be incorporated into the processing system owned by Pen & Tec Consulting SLU, and that provided it complies with the requirements included in the law, you may exercise the rights of access, rectification, limitation of processing, deletion, portability and opposition by sending your request to the postal address Pl. Ausias March 1, 4 floor 08195, Sant Cugat del Valles (Barcelona) or to the email address info@pentec-consulting.eu. If you read this message and you are neither the intended recipient, employee or agent in charge of delivering the message to the recipient, or if you have received this message as the result of an error, we hereby inform you that distributing, sharing or reproducing any part of this message is totally forbidden and may be illegal. As a result, we request that you immediately inform us of the error and return this message to the address mentioned above. Thank you.

From: DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>

Date: Tuesday, 5 December 2023 at 19:05

To: Nikolaas Tilkin-Franssens <niko@pentec-consulting.eu>

Cc: Justyna Pałasińska <justyna@pentec-consulting.eu>

Subject: RE: [EXTERNAL] GRN 1122 canola concentrate - update contact person

You don't often get email from stephen.difranco@fda.hhs.gov. [Learn why this is important](#)

Hello Niko and Justyna,

Just confirming the change of contact person for GRN 1122.

As for timeline, FDA reviews are complete but USDA-FSIS is requesting a few pieces of information regarding the uses of canola concentrate under USDA jurisdiction, namely:

Please provide SDS for the at use concentrations of the substance and include a description of how the use of this technology will not adversely affect the safety of FSIS inspectors.

Workplace safety and health hazards include inhalation, direct skin contact (skin, eyes, mouth), and fire/explosion caused by exposure to the product, its working solution or dry mixture and potential by-products formed and/or off-gassed during the application process. The employee safety information should demonstrate how the New Technology will not “jeopardize the safety of Federal inspection personnel” as specified in the [FSIS Compliance Guideline Procedures for New Technology Notifications and Protocols, April 2015](#).

Although I’m not anticipating any issues here, FSIS workplace and employee safety must be specifically addressed. Please refer to Appendix A on page 17, Workplace Safety and Health Criteria, for clarification on what to provide in the response. For additional clarity with respect to employee safety, the following are examples of information that are typically needed by FSIS’ employee safety and health group;

1. Potential workplace exposures that could result from inhalation and direct contact during use of the substance/technology. This information is required in addition to a Safety Data Sheet (SDS) to determine accurate hazard potential and recommended exposure control measures for IPP work areas in accordance with Occupational Safety and Health Administration (OSHA) regulations: 29 CFR 1910.1200, Hazard Communication, 29 CFR 1910.132, Personal Protective Equipment, and 29 CFR 1910.1000, Air Contaminants. The information should be included as a specific section in each of the protocols.
2. If the SDS workplace hazards/precautions do not apply to the type of exposure that would be expected for the FSIS IPP, please have the submitter provide specific information (per the April 2015 FSIS Compliance Guideline Procedures) for the actual type of exposures expected.
3. If no IPP workplace exposures are expected and no control measures are required, please have the submitter state this and provide the reasons why (e.g., such as the substance “as used” [for all concentrations] is not hazardous by inhalation or direct contact and/or IPP would not be exposed to the substance based on the system design, operation and/or control measures that will be in place).
4. Please also indicate how will FSIS IPP be informed of the above information so that it is clear

that the information contained in the SDS for the concentrate does not apply to their actual workplace exposure.

5. Are there any potential hazards from chemical mixing or low pH as a result of discharges of the various solutions to floor drains? Are dedicated drain lines or any other enclosures required?

6. With respect to potential airborne exposures to FSIS IPP in the use/application areas, does the submitter have air sampling results taken during the use of the various concentrations of the technology in the listed mixture?

Suitability data;

The intended use of this product in FSIS meat and poultry products is apparently as a binder/extender. The suitability support provided in Appendix 6 does sufficiently support no significant difference in yield and other organoleptic qualities when used as a partial replacement for another binder in a processed meat and poultry product, such as sausage.

However, **additional suitability support is needed:**

- No suitability data was provided for **whole muscle meat and poultry products at the maximum proposed use level**. We would need to see similar data as provided in Appendix 6 for:
 - Whole muscle red meat control containing no other binders, extenders, or moisture retention agents, as compared to a whole muscle red meat product containing 15% isolated canola product.
 - Whole muscle poultry control containing no other binders, extenders, or moisture retention agents as compared to a whole muscle poultry product containing 15% isolated canola product.

Your responses can be emailed directly to me and I will distribute to the necessary staff inside FDA and USDA.

Thanks,

Steve

Stephen DiFranco, PhD

Regulatory Review Scientist/Chemist

Center for Food Safety and Applied Nutrition

Office of Food Additive Safety

Division of Food Ingredients

U.S. Food and Drug Administration

Tel: 240-402-2710

stephen.difranco@fda.hhs.gov





From: Nikolaas Tilkin-Franssens <niko@pentec-consulting.eu>
Sent: Monday, December 4, 2023 4:36 AM
To: DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>
Cc: Justyna Pałasińska <justyna@pentec-consulting.eu>
Subject: [EXTERNAL] GRN 1122 canola concentrate - update contact person

CAUTION: This email originated from outside of the organization. Do not click links or open attachments unless you recognize the sender and know the content is safe.

Hi Mr. DiFranco,

Hope this email finds you well.

Due to a change in position, I will no longer be the contact person for the GRAS Notice 1122 (Canola Protein Concentrate). Could you please update your records to ascertain that Justyna Pałasińska, in copy to this email, is informed of any relevant updates?

Could you kindly confirm receipt of this email for our records?

And if possible, let us know if there is any estimate on the timeline re. finalization of the review of this GRAS Notice.

Many thanks for your great and flexible support on this application.

Kind regards,

Niko

Nikolaas Tilkin-Franssens

Regulatory Affairs Manager | Pen & Tec Consulting

T [+34 936 758 015](tel:+34936758015) **M** [+34 649 840 417](tel:+34649840417) **F** [+34 936 758 016](tel:+34936758016) www.pentec-consulting.eu

Pl. Ausias March 1 | 4th floor D01 | 08195 Sant Cugat del Vallès | Barcelona | Spain

PEN + TEC
CONSULTING

PART OF THE ARGENTA GROUP

La información contenida en este mensaje y/o archivo(s) adjunto(s), enviada desde Pen & Tec Consulting SLU, es confidencial/privilegiada y está destinada a ser leída sólo por la(s) persona(s) a la(s) que va dirigida. Le recordamos que sus datos han sido incorporados en el sistema de tratamiento de Pen & Tec Consulting SLU y que siempre y cuando se cumplan los requisitos exigidos por la normativa, usted podrá ejercer sus derechos de acceso, rectificación, limitación de tratamiento, supresión, portabilidad y oposición/revocación, en los términos que establece la normativa vigente en materia de protección de datos, dirigiendo su petición a la dirección postal Pl. Ausias March 1, 4 planta 08195, Sant Cugat del Vallès (Barcelona) o bien a través de correo electrónico info@pentec-consulting.eu. Si usted lee este mensaje y no es el destinatario señalado, el empleado o el agente responsable de entregar el mensaje al destinatario, o ha recibido esta comunicación por error, le informamos que está totalmente prohibida, y puede ser ilegal, cualquier divulgación, distribución o reproducción de esta comunicación, y le rogamos que nos lo notifique inmediatamente y nos devuelva el mensaje original a la dirección arriba mencionada. Gracias.

The information contained in this message and/or attached file(s), sent by Pen & Tec Consulting SLU, is confidential/privileged and is intended to be read solely by the person(s) to whom it is addressed. We hereby inform you that your data will be incorporated into the processing system owned by Pen & Tec Consulting SLU, and that provided it complies with the requirements included in the law, you may exercise the rights of access, rectification, limitation of processing, deletion, portability and opposition by sending your request to the postal address Pl. Ausias March 1, 4 floor 08195, Sant Cugat del Valles (Barcelona) or to the email address info@pentec-consulting.eu. If you read this message and you are neither the intended recipient, employee or agent in charge of delivering the message to the recipient, or if you have received this message as the result of an error, we hereby inform you that distributing, sharing or reproducing any part of this message is totally forbidden and may be illegal. As a result, we request that you immediately inform us of the error and return this message to the address mentioned above. Thank you.

From: DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>

Date: Monday, 17 July 2023 at 17:01

To: Nikolaas Tilkin-Franssens <niko@pentec-consulting.eu>

Subject: RE: [EXTERNAL] Re: GRN 1122 canola concentrate items for clarification - Reply

Hello Niko,

No problem—I'll distribute this to the team for review.

Best,

Steve

Stephen DiFranco, PhD

Regulatory Review Scientist/Chemist

Center for Food Safety and Applied Nutrition

Office of Food Additive Safety

Division of Food Ingredients

U.S. Food and Drug Administration

Tel: 240-402-2710

stephen.difranco@fda.hhs.gov



From: Nikolaas Tilkin-Franssens <niko@pentec-consulting.eu>

Sent: Monday, July 17, 2023 10:35 AM

To: DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>

Subject: [EXTERNAL] Re: GRN 1122 canola concentrate items for clarification - Reply

CAUTION: This email originated from outside of the organization. Do not click links or open attachments unless you recognize the sender and know the content is safe.

Hi Stephen,

Apologies for this inconvenience.

We noticed that the reply to question 9 refers to Canola protein isolate (as per GRN 1103). I have updated the answer for it to be mentioning Canola protein concentrate (GRN 1122).

We hope this can be taken into consideration.

Kind regards,

Nikolaas Tilkin-Franssens

Regulatory Affairs Manager | Pen & Tec Consulting

T [+34 936 758 015](tel:+34936758015) **M** [+34 649 840 417](tel:+34649840417) **F** [+34 936 758 016](tel:+34936758016) www.pentec-consulting.eu

Pl. Ausias March 1 | 4th floor D01 | 08195 Sant Cugat del Vallès | Barcelona | Spain

PEN + TEC
CONSULTING

PART OF THE ARGENTA GROUP

La información contenida en este mensaje y/o archivo(s) adjunto(s), enviada desde Pen & Tec Consulting SLU, es confidencial/privilegiada y está destinada a ser leída sólo por la(s) persona(s) a la(s) que va dirigida. Le recordamos que sus datos han sido incorporados en el sistema de tratamiento de Pen & Tec Consulting SLU y que siempre y cuando se cumplan los requisitos exigidos por la normativa, usted podrá ejercer sus derechos de acceso, rectificación, limitación de tratamiento, supresión, portabilidad y oposición/revocación, en los términos que establece la normativa vigente en materia de protección de datos, dirigiendo su petición a la dirección postal Pl. Ausias March 1, 4 planta 08195, Sant Cugat del Vallès (Barcelona) o bien a través de correo electrónico info@pentec-consulting.eu. Si usted lee este mensaje y no es el destinatario señalado, el empleado o el agente responsable de entregar el mensaje al destinatario, o ha recibido esta comunicación por error, le informamos que está totalmente prohibida, y puede ser ilegal, cualquier divulgación, distribución o reproducción de esta comunicación, y le rogamos que nos lo notifique inmediatamente y nos devuelva el mensaje original a la dirección arriba mencionada. Gracias.

The information contained in this message and/or attached file(s), sent by Pen & Tec Consulting SLU, is confidential/privileged and is intended to be read solely by the person(s) to whom it is addressed. We hereby inform you that your data will be incorporated into the processing system owned by Pen & Tec Consulting SLU, and that provided it complies with the requirements included in the law, you may exercise the rights of access, rectification, limitation of processing, deletion, portability and opposition by sending your request to the postal address Pl. Ausias March 1, 4 floor 08195, Sant Cugat del Valles (Barcelona) or to the email address info@pentec-consulting.eu. If you read this message and you are neither the intended recipient, employee or agent in charge of delivering the message to the recipient, or if you have received this message as the result of an error, we hereby inform you that distributing, sharing or reproducing any part of this message is totally forbidden and may be illegal. As a result, we request that you immediately inform us of the error and return this message to the address mentioned above. Thank you.

From: Nikolaas Tilkin-Franssens <niko@pentec-consulting.eu>

Date: Tuesday, 11 July 2023 at 17:03

To: DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>

Cc: Justyna Pałasińska <justyna@pentec-consulting.eu>

Subject: Re: GRN 1122 canola concentrate items for clarification - Reply

Dear Stephen,

Thank you for reaching out with the questions for clarification.

We have worked closely with Napiferyn to close the doubts.

Kindly find attached a Word file including the Questions&Answers, a report on the requested literature review, a SDS sheet as requested by the USDA-FSIS, and a report on the suitability assessment.

We remain available for any further questions or updates.

Thanks for taking the application in further consideration,
best regards,

Nikolaas Tilkin-Franssens

Regulatory Affairs Manager | Pen & Tec Consulting

T [+34 936 758 015](tel:+34936758015) **M** [+34 649 840 417](tel:+34649840417) **F** [+34 936 758 016](tel:+34936758016) www.pentec-consulting.eu

Pl. Ausias March 1 | 4th floor D01 | 08195 Sant Cugat del Vallès | Barcelona | Spain

La información contenida en este mensaje y/o archivo(s) adjunto(s), enviada desde Pen & Tec Consulting SLU, es confidencial/privilegiada y está destinada a ser leída sólo por la(s) persona(s) a la(s) que va dirigida. Le recordamos que sus datos han sido incorporados en el sistema de tratamiento de Pen & Tec Consulting SLU y que siempre y cuando se cumplan los requisitos exigidos por la normativa, usted podrá ejercer sus derechos de acceso, rectificación, limitación de tratamiento, supresión, portabilidad y oposición/revocación, en los términos que establece la normativa vigente en materia de protección de datos, dirigiendo su petición a la dirección postal Pl. Ausias March 1, 4 planta 08195, Sant Cugat del Vallès (Barcelona) o bien a través de correo electrónico info@pentec-consulting.eu. Si usted lee este mensaje y no es el destinatario señalado, el empleado o el agente responsable de entregar el mensaje al destinatario, o ha recibido esta comunicación por error, le informamos que está totalmente prohibida, y puede ser ilegal, cualquier divulgación, distribución o reproducción de esta comunicación, y le rogamos que nos lo notifique inmediatamente y nos devuelva el mensaje original a la dirección arriba mencionada. Gracias.

The information contained in this message and/or attached file(s), sent by Pen & Tec Consulting SLU, is confidential/privileged and is intended to be read solely by the person(s) to whom it is addressed. We hereby inform you that your data will be incorporated into the processing system owned by Pen & Tec Consulting SLU, and that provided it complies with the requirements included in the law, you may exercise the rights of access, rectification, limitation of processing, deletion, portability and opposition by sending your request to the postal address Pl. Ausias March 1, 4 floor 08195, Sant Cugat del Valles (Barcelona) or to the email address info@pentec-consulting.eu. If you read this message and you are neither the intended recipient, employee or agent in charge of delivering the message to the recipient, or if you have received this message as the result of an error, we hereby inform you that distributing, sharing or reproducing any part of this message is totally forbidden and may be illegal. As a result, we request that you immediately inform us of the error and return this message to the address mentioned above. Thank you.

From: DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>
Date: Wednesday, 28 June 2023 at 17:41
To: Nicoleta Pasecinic <nicoleta@pentec-consulting.eu>
Cc: Nikolaas Tilkin-Franssens <niko@pentec-consulting.eu>
Subject: [EXTERNAL]: GRN 1122 canola concentrate items for clarification

CAUTION: This email originated from outside of the organization. Do not click links or open attachments unless you recognize the sender and know the content is safe.

Hello Ms. Pasecinic,

After evaluating NapiFeryn's GRAS Notice No. GRN 1122 on canola concentrate we noted a few issues that should be addressed. Please respond to the following points for clarification:

1. On p. 9, NapiFeryn states that the major storage proteins in canola seed are cruciferins and napins, and that canola concentrate consists of 30-45% protein and 40-70% dietary fiber. Please provide the typical cruciferin content and napin content in canola concentrate.
2. Please confirm that all raw materials and processing aids used in the manufacturing process are used in accordance with the U.S. regulations, are GRAS for their respective uses or are the subject of an effective food contact notification. For the record, we note that the food additive regulations cited in Table 4 (p. 15) for ascorbic acid (21 CFR 182.8013), ethanol (21 CFR 184.1293), and ethyl acetate (21 CFR 173.228) do not appear to be applicable to your intended uses of these substances.
3. In Table 6 (p. 18-19), NapiFeryn provides the results from the batch analyses for heavy metals. We would like to bring to your attention a relevant FDA's "[Closer to Zero](#)" initiative that focuses on reducing the levels of heavy metals in foods and recommend that you

lower the specification limits for heavy metal to better reflect the batch analyses results and to be as low as possible.

4. In Table 10 (p. 22), NapiFeryn provides batch analyses data for residual solvents and processing aids. In addition, in Table 21 (p. 50), you provided the results from the batch analyses for erucic acid in your canola concentrate ranging from 0.37% to < 0.1%.
Please include limits for residual ethanol, ethyl acetate, and sulphur dioxide as well as a limit for erucic acid in the specifications for canola concentrate and specify the analytical methods used to test for these parameters.
In addition, please provide an updated Tables 5 and 6 (p. 16-19) to include the additional specification parameters mentioned above, corresponding analytical methods, and batch analyses.
5. Please state that all analytical methods used to test batches were validated and are fit for their respective purpose.
6. Please state that canola concentrate is not intended for use in infant formula or in foods where standards of identity preclude its use.
7. In Table 15 (p.), NapiFeryn provides the results of the batch analyses for total plate count in the raw material (rapeseed press cake). Please address the significant variation in the results (from <10 to 28,000 CFU/g) and discuss whether this will impact safety of the final ingredient.
8. On p. 19, NapiFeryn states that the levels of mycotoxins in canola concentrate are below the limit of quantitation (LOQ) and provide the results from the analyses of five batches to support your statement. Please clarify whether you expect mycotoxins to be present in canola concentrate manufactured in accordance with good manufacturing practices.
9. In Part 1.4 (p. 6) and Part 3.1 (p. 33), NapiFeryn states that the intended use of canola concentrate is as a source of protein and/or fiber, thickener, or texturizer. However, we note that on p. 33 you also state the intended use of canola concentrate is as a flavoring agent or binder in various comminuted or whole muscle meat and poultry products. In addition, in Appendix 3 (p. 5) you state that canola concentrate may also be used “to create a flavored salt” or as “a flavor enhancer like monosodium glutamate”. Please confirm these additional uses of canola concentrate are within the scope of GRN 001122.
10. On p. 10, the notifier describes the protein composition of canola concentrate, being primarily cruciferins, napin, oleosin, and squalene monooxygenase. However, the pivotal safety data provided appear to only be relevant to the cruciferin and napin fractions of the canola concentrate. Please provide a brief narrative to confirm the safety of oleosin and

squalene monooxygenase exposure from the intended uses.

11. On p. 31-32 of the notice, the notifier clearly establishes that canola concentrate is intended to be substitutive to protein and fiber consumption and will not contribute to additional exposure to protein or fiber in general. Please elaborate on this conclusion, and clarify if the intended uses of canola concentrate are additive or substitutive to other canola protein products currently on the market (i.e., GRNs 327, 386, and 683)?
12. On p. 37, the notifier concludes exposure to canola concentrate from the intended uses is safe since the EDI reported is “still much lower (approximately 7- to 22-fold lower) than the no-observed-adverse-effect level (NOAEL) values established” for cruciferin- and napin-rich protein isolates in male rats following a 13-week oral exposure regimen (Mejia *et al.*, 2009a & 2009b). We note that an uncertainty factor, or margin of safety (MOS), of 100 (10 for interindividual variability × 10 for interspecies variability) is normally used when assessing safety of a food ingredient by comparing estimated human exposure levels to the NOAEL from animal toxicology data. Therefore, it is not clear why MOS that is ~5-10-fold lower can be concluded as safe without proper justification. Additionally, we note that potential thyrotoxic effects were observed at the highest doses in these two rat studies, as well as for rapeseed products in general tested in other species, as cited in Table 20 of the GRAS notice. This effect was mostly attributed to the presence of glucosinolate; however, we note that since the level of glucosinolate was low or absent in both the test articles from Mejia *et al.* and the article of commerce, the rationale used by the study authors to conclude that the observed NOAEL was not in fact the LOAEL may be questionable. Regardless, it appears that the provided safety narrative lacks sufficient basis to conclude MOS of 7-22 is adequate to reach the conclusion of “reasonable certainty of no harm.” Based on generally available data and information, please provide additional narrative to explain your rationale for your GRAS conclusion.
13. We note that when discussing the absorption, distribution, metabolism, and excretion of canola concentrate (p. 49), the notifier reports unpublished data from an EU Novel Foods application for “defatted rapeseed powder” to support their conclusion. Similarly, genotoxicity conclusions are made using unpublished data from an EFSA Panel conclusion on defatted rapeseed powder. Given other data and information have been used in prior GRAS notices for canola ingredients (e.g., GRN 327), please confirm that the EFSA Panel and EU Novel Foods conclusions are only considered as corroborative, not pivotal, to the safety determination of canola concentrate at its intended use level?
14. On p. 40, the notifier discusses the allergenicity potential of canola concentrate being determined via a “bioinformatics approach” and concludes that canola concentrate “may elicit possible allergenic effects.” Additionally, on p. 59 the notifier reiterates that the bioinformatics analysis indicated “possible allergenic effects” of canola concentrate, but no

further discussion is provided. While data from an allergen online database search is provided as part of Appendix 4, no discussion of these data are included in the current GRAS notice. Please briefly detail the “possible allergenic effects” of canola concentrate similar to previous notices (e.g., GRN 683), and discuss why they would not be expected to pose a safety concern from the intended use.

15. We note that a recent study on rapeseed protein isolate was published (Xiong et al., 2022).
 - a. Please discuss if this study presents additional safety concerns for the article of commerce or contradicts the current GRAS conclusion.
 - b. Please also perform an updated literature review from 2021 to present and discuss if any additional studies relevant to the safety of canola concentrate were identified that would contradict the current GRAS conclusion.

References cited:

Xiong Z, Fu Y, Yao J, Zhang N, He R, Ju X, Wang Z. Removal of anti-nutritional factors of rapeseed protein isolate (RPI) and toxicity assessment of RPI. *Food Funct.* 2022 Jan 24;13(2):664-674. doi: 10.1039/d1fo03217h. PMID: 34933325.

Additionally, we received the following questions from USDA FSIS regarding their review of the uses of GRN 1122 concerning products within their purview. Please respond to the following and we will pass your responses along to them.

Please provide Safety Data Sheet (SDS) for the at use concentrations of the substance and include a description of how the use of this technology will not adversely affect the safety of FSIS inspectors. Workplace safety and health hazards include inhalation, direct skin contact (skin, eyes, mouth), and fire/explosion caused by exposure to the product, its working solution or dry mixture and potential by-products formed and/or off-gassed during the application process. The employee safety information should demonstrate how the New Technology will not “jeopardize the safety of Federal inspection personnel” as specified in the [FSIS Compliance Guideline Procedures for New Technology Notifications and Protocols, April 2015](#). FSIS workplace and employee safety must be specifically addressed. Please refer to Appendix A on p. 17, Workplace Safety and Health Criteria, for clarification on what to provide in the response. For additional clarity with respect to employee safety, the following are examples of information that are typically needed by FSIS’ employee safety and health group;

1. Potential workplace exposures that could result from inhalation and direct contact during use of the substance/technology. This information is required in addition to a SDS to determine accurate hazard potential and recommended exposure control measures for IPP work areas in accordance with Occupational Safety and Health Administration (OSHA) regulations: 29 CFR 1910.1200, Hazard Communication, 29 CFR 1910.132, Personal Protective Equipment, and 29 CFR 1910.1000, Air Contaminants. The information should be included as a specific section in each of the protocols.
2. If the SDS workplace hazards/precautions do not apply to the type of exposure that would

- be expected for the FSIS IPP, please have the submitter provide specific information (per the April 2015 FSIS Compliance Guideline Procedures) for the actual type of exposures expected.
3. If no IPP workplace exposures are expected and no control measures are required, please have the submitter state this and provide the reasons why (e.g., such as the substance “as used” [for all concentrations] is not hazardous by inhalation or direct contact and/or IPP would not be exposed to the substance based on the system design, operation and/or control measures that will be in place).
 4. Please also indicate how will FSIS IPP be informed of the above information so that it is clear that the information contained in the SDS for the concentrate does not apply to their actual workplace exposure.
 5. Are there any potential hazards from chemical mixing or low pH as a result of discharges of the various solutions to floor drains? Are dedicated drain lines or any other enclosures required?
 6. With respect to potential airborne exposures to FSIS IPP in the use/application areas, does the submitter have air sampling results taken during the use of the various concentrations of the technology in the listed mixture?
 7. The intended use of this product in FSIS meat and poultry products is apparently as a binder/extender. The suitability support provided in Appendix 6 does sufficiently support no significant difference in yield and other organoleptic qualities when used as a partial replacement for another binder in a processed meat and poultry product, such as sausage. However, **additional suitability support is needed:**
 - a. No suitability data was provided for **whole muscle meat and poultry products at the maximum proposed use level**. We would need to see similar data as provided in Appendix 6 for:
 - Whole muscle red meat control containing no other binders, extenders, or moisture retention agents, as compared to a whole muscle red meat product containing 15% isolated canola product.
 - Whole muscle poultry control containing no other binders, extenders, or moisture retention agents as compared to a whole muscle poultry product containing 15% isolated canola product.

Responses may be sent in an email or in a separate document. We respectfully request a response within 10 business days. If you are unable to complete the response within that time frame, please contact me to discuss further options.

If you have any additional questions or concerns, please don't hesitate to contact me at stephen.difranco@fda.hhs.gov or by phone at 240.402.2710.

Best,
Steve

Stephen DiFranco, PhD

Regulatory Review Scientist/Chemist

Center for Food Safety and Applied Nutrition
Office of Food Additive Safety
Division of Food Ingredients
U.S. Food and Drug Administration
Tel: 240-402-2710
stephen.difranco@fda.hhs.gov



CAUTION: This email, including any attachments, is confidential. If you are not the intended recipient, please notify the sender and delete the email and any attachments from your system. In addition, you must not use, distribute or reproduce this email or any attachments. Opinions and other information in this email and any attachments which do not relate to the official business of Argenta are neither given by nor endorsed by Argenta. While Argenta uses anti-virus software, Argenta accepts no liability for any viruses in this email or any attachment, or for any effects this email or any attachment may have on your network or computer system.

CAUTION: This email, including any attachments, is confidential. If you are not the intended recipient, please notify the sender and delete the email and any attachments from your system. In addition, you must not use, distribute or reproduce this email or any attachments. Opinions and other information in this email and any attachments which do not relate to the official business of Argenta are neither given by nor endorsed by Argenta. While Argenta uses anti-virus software, Argenta accepts no liability for any viruses in this email or any attachment, or for any effects this email or any attachment may have on your network or computer system.

CAUTION: This email, including any attachments, is confidential. If you are not the intended recipient, please notify the sender and delete the email and any attachments from your system. In addition, you must not use, distribute or reproduce this email or any attachments. Opinions and other information in this email and any attachments which do not relate to the official business of Argenta are neither given by nor endorsed by Argenta. While Argenta uses anti-virus software, Argenta accepts no liability for any viruses in this email or any attachment, or for any effects this email or any attachment may have on your network or computer system.

CAUTION: This email, including any attachments, is confidential. If you are not the intended recipient, please notify the sender and delete the email and any attachments from your system. In addition, you must not use, distribute or reproduce this email or any attachments. Opinions and other information in this email and any attachments which do not relate to the official business of Argenta are neither given by nor endorsed by Argenta. While Argenta uses anti-virus software, Argenta accepts no liability for any viruses in this email or any attachment, or for any effects this email or any attachment may have on your network or computer system.

From: [Justyna Pałasińska](#)
To: [Justyna Pałasińska](#); [DiFranco, Stephen](#)
Cc: [Ioannis Kartanos](#)
Subject: Re: [EXTERNAL] GRN 1122 canola concentrate - update contact person
Date: Wednesday, January 31, 2024 11:54:14 AM
Attachments: [image001.png](#)
[image007.png](#)
[image008.png](#)
[image009.png](#)
[image010.png](#)

CAUTION: This email originated from outside of the organization. Do not click links or open attachments unless you recognize the sender and know the content is safe.

Dear Steve,

I hope this e-mail finds you well. I was wondering if there are any updates on the finalization of this notification?

Is there any additional information that needs to be provided?

Kind regards,

Justyna Pałasińska

Regulatory Affairs Director – Human Nutrition, Argenta Barcelona



M [+34 682 894 653](tel:+34682894653) T [+34 936 758 015](tel:+34936758015)

www.argentaglobal.com

La información contenida en este mensaje y/o archivo(s) adjunto(s), enviada desde Pen & Tec Consulting SLU cotiza como Argenta, es confidencial/privilegiada y está destinada a ser leída sólo por la(s) persona(s) a la(s) que va dirigida. Le recordamos que sus datos han sido incorporados en el sistema de tratamiento de Pen & Tec Consulting SLU cotiza como Argenta, y que siempre y cuando se cumplan los requisitos exigidos por la normativa, usted podrá ejercer sus derechos de acceso, rectificación, limitación de tratamiento, supresión, portabilidad y oposición/revocación, en los términos que establece la normativa vigente en materia de protección de datos, dirigiendo su petición a la dirección postal Pl. Ausias March 1, 4 planta 08195, Sant Cugat del Vallès (Barcelona) o bien a través de correo electrónico info@pentec-consulting.eu. Si usted lee este mensaje y no es el destinatario señalado, el empleado o el agente responsable de entregar el mensaje al destinatario, o ha recibido esta comunicación por error, le informamos que está totalmente prohibida, y puede ser ilegal, cualquier divulgación, distribución o reproducción de esta comunicación, y le rogamos que nos lo notifique inmediatamente y nos devuelva el mensaje original a la dirección arriba mencionada. Gracias.

The information contained in this message and/or attached file(s), sent by Pen & Tec Consulting SLU trading as Argenta, is confidential/privileged and is intended to be read solely by the person(s) to whom it is addressed. We hereby inform you that your data will be incorporated into the processing system owned by Pen & Tec Consulting SLU, and that provided it complies with the requirements included in the law, you may exercise the rights of access, rectification, limitation of processing, deletion, portability and opposition by sending your request to the postal address Pl. Ausias March 1, 4 floor 08195, Sant Cugat del Valles (Barcelona) or to the email address info@pentec-consulting.eu. If you read this message and you are neither the intended recipient, employee or agent in charge of delivering the message to the recipient, or if you have received this message as the result of an error, we hereby inform you that distributing, sharing or reproducing any part of this message is totally forbidden and may be illegal. As a result, we request that you immediately inform us of the error and return this message to the address mentioned above. Thank you.

From: Justyna Pałasińska <justyna@pentec-consulting.eu>

Date: Friday, 22 December 2023 at 13:31

To: DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>

Cc: Ioannis Kartanos <ioannis@pentec-consulting.eu>

Subject: Re: [EXTERNAL] GRN 1122 canola concentrate - update contact person

Dear Stephen,

Many thanks for confirming the change of contact person.

I'm following up on my colleague Ioannis e-mail from 12/12/2023. As he mentioned, we have already provided the answers to the questions to USDA-FSIS. Nevertheless, I have included them in a separate document.

Please let us know in case any additional information is required.

In the meantime, we wish you a Happy Holiday Season & all the best in 2024!

Kind regards,

Ing. Justyna Pałasińska

Regulatory Affairs Director – Human Nutrition | Pen & Tec Consulting

T +34 936 758 015 M +34 682 894 653 F +34 936 758 016 www.pentec-consulting.eu

Pl. Ausias March 1 | 4th floor D01 | 08195 Sant Cugat del Vallès | Barcelona | Spain

PEN + TEC
CONSULTING
PART OF THE ARGENTA GROUP

La información contenida en este mensaje y/o archivo(s) adjunto(s), enviada desde Pen & Tec Consulting SLU, es confidencial/privilegiada y está destinada a ser leída sólo por la(s) persona(s) a la(s) que va dirigida. Le recordamos que sus datos han sido incorporados en el sistema de tratamiento de Pen & Tec Consulting SLU y que siempre y cuando se cumplan los requisitos exigidos por la normativa, usted podrá ejercer sus derechos de acceso, rectificación, limitación de tratamiento, supresión, portabilidad y oposición/revocación, en los términos que establece la normativa vigente en materia de protección de datos, dirigiendo su petición a la dirección postal Pl. Ausias March 1, 4 planta 08195, Sant Cugat del Vallès (Barcelona) o bien a través de correo electrónico info@pentec-consulting.eu. Si usted lee este mensaje y no es el destinatario señalado, el empleado o el agente responsable de entregar el mensaje al destinatario, o ha recibido esta comunicación por error, le informamos que está totalmente prohibida, y puede ser ilegal, cualquier divulgación, distribución o reproducción de esta comunicación, y le rogamos que nos lo notifique inmediatamente y nos devuelva el mensaje original a la dirección arriba mencionada. Gracias.

The information contained in this message and/or attached file(s), sent by Pen & Tec Consulting SLU, is confidential/privileged and is intended to be read solely by the person(s) to whom it is addressed. We hereby inform you that your data will be incorporated into the processing system owned by Pen & Tec Consulting SLU, and that provided it complies with the requirements included in the law, you may exercise the rights of access, rectification, limitation of processing, deletion, portability and opposition by sending your request to the postal address Pl. Ausias March 1, 4 floor 08195, Sant Cugat del Valles (Barcelona) or to the email address info@pentec-consulting.eu. If you read this message and you are neither the intended recipient, employee or agent in charge of delivering the message to the recipient, or if you have received this message as the result of an error, we hereby inform you that distributing, sharing or reproducing any part of this message is totally forbidden and may be illegal. As a result, we request that you immediately inform us of the error and return this message to the address mentioned above. Thank you.

From: DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>

Date: Tuesday, 5 December 2023 at 19:05

To: Nikolaas Tilkin-Franssens <niko@pentec-consulting.eu>

Cc: Justyna Pałasińska <justyna@pentec-consulting.eu>

Subject: RE: [EXTERNAL] GRN 1122 canola concentrate - update contact person

You don't often get email from stephen.difranco@fda.hhs.gov. [Learn why this is important](#)

Hello Niko and Justyna,

Just confirming the change of contact person for GRN 1122.

As for timeline, FDA reviews are complete but USDA-FSIS is requesting a few pieces of information regarding the uses of canola concentrate under USDA jurisdiction, namely:

Please provide SDS for the at use concentrations of the substance and include a description of how the use of this technology will not adversely affect the safety of FSIS inspectors. Workplace safety and health hazards include inhalation, direct skin contact (skin, eyes, mouth), and fire/explosion caused by exposure to the product, its working solution or dry mixture and potential by-products formed and/or off-gassed during the application process. The employee safety information should demonstrate how the New Technology will not “jeopardize the safety of Federal inspection personnel” as specified in the [FSIS Compliance Guideline Procedures for New Technology Notifications and Protocols, April 2015](#).

Although I’m not anticipating any issues here, FSIS workplace and employee safety must be specifically addressed. Please refer to Appendix A on page 17, Workplace Safety and Health Criteria, for clarification on what to provide in the response. For additional clarity with respect to employee safety, the following are examples of information that are typically needed by FSIS’ employee safety and health group;

1. Potential workplace exposures that could result from inhalation and direct contact during use of the substance/technology. This information is required in addition to a Safety Data Sheet (SDS) to determine accurate hazard potential and recommended exposure control measures for IPP work areas in accordance with Occupational Safety and Health Administration (OSHA) regulations: 29 CFR 1910.1200, Hazard Communication, 29 CFR 1910.132, Personal Protective Equipment, and 29 CFR 1910.1000, Air Contaminants. The information should be included as a specific section in each of the protocols.
2. If the SDS workplace hazards/precautions do not apply to the type of exposure that would be expected for the FSIS IPP, please have the submitter provide specific information (per the April 2015 FSIS Compliance Guideline Procedures) for the actual type of exposures expected.
3. If no IPP workplace exposures are expected and no control measures are required, please have the submitter state this and provide the reasons why (e.g., such as the substance “as used” [for all concentrations] is not hazardous by inhalation or direct contact and/or IPP would not be exposed to the substance based on the system design, operation and/or control measures that will be in place).
4. Please also indicate how will FSIS IPP be informed of the above information so that it is clear that the information contained in the SDS for the concentrate does not apply to their actual workplace exposure.
5. Are there any potential hazards from chemical mixing or low pH as a result of discharges of the various solutions to floor drains? Are dedicated drain lines or any other enclosures required?
6. With respect to potential airborne exposures to FSIS IPP in the use/application areas, does the submitter have air sampling results taken during the use of the various concentrations of the technology in the listed mixture?

Suitability data;

The intended use of this product in FSIS meat and poultry products is apparently as a binder/extender. The suitability support provided in Appendix 6 does sufficiently support no significant difference in yield and other organoleptic qualities when used as a partial replacement for another binder in a processed meat and poultry product, such as sausage.

However, **additional suitability support is needed:**

- No suitability data was provided for **whole muscle meat and poultry products at the maximum proposed use level**. We would need to see similar data as provided in Appendix 6 for:
 - Whole muscle red meat control containing no other binders, extenders, or moisture retention agents, as compared to a whole muscle red meat product containing 15% isolated canola product.
 - Whole muscle poultry control containing no other binders, extenders, or moisture

retention agents as compared to a whole muscle poultry product containing 15% isolated canola product.

You responses can be emailed directly to me and I will distribute to the necessary staff inside FDA and USDA.

Thanks,

Steve

Stephen DiFranco, PhD

Regulatory Review Scientist/Chemist

Center for Food Safety and Applied Nutrition

Office of Food Additive Safety

Division of Food Ingredients

U.S. Food and Drug Administration

Tel: 240-402-2710

stephen.difranco@fda.hhs.gov



From: Nikolaas Tilkin-Franssens <niko@pentec-consulting.eu>

Sent: Monday, December 4, 2023 4:36 AM

To: DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>

Cc: Justyna Pałasińska <justyna@pentec-consulting.eu>

Subject: [EXTERNAL] GRN 1122 canola concentrate - update contact person

CAUTION: This email originated from outside of the organization. Do not click links or open attachments unless you recognize the sender and know the content is safe.

Hi Mr. DiFranco,

Hope this email finds you well.

Due to a change in position, I will no longer be the contact person for the GRAS Notice 1122 (Canola Protein Concentrate). Could you please update your records to ascertain that Justyna Pałasińska, in copy to this email, is informed of any relevant updates?

Could you kindly confirm receipt of this email for our records?

And if possible, let us know if there is any estimate on the timeline re. finalization of the review of this GRAS Notice.

Many thanks for your great and flexible support on this application.

Kind regards,

Niko

Nikolaas Tilkin-Franssens

Regulatory Affairs Manager | Pen & Tec Consulting

T [+34 936 758 015](tel:+34936758015) **M** [+34 649 840 417](tel:+34649840417) **F** [+34 936 758 016](tel:+34936758016) www.pentec-consulting.eu

Pl. Ausias March 1 | 4th floor D01 | 08195 Sant Cugat del Vallès | Barcelona | Spain

PEN + TEC
CONSULTING

PART OF THE ARGENTA GROUP

La información contenida en este mensaje y/o archivo(s) adjunto(s), enviada desde Pen & Tec Consulting SLU, es confidencial/privilegiada y está destinada a ser leída sólo por la(s) persona(s) a la(s) que va dirigida. Le recordamos que sus datos han sido incorporados en el sistema de tratamiento de Pen & Tec Consulting SLU y que siempre y cuando se cumplan los requisitos exigidos por la normativa, usted podrá ejercer sus derechos de acceso, rectificación, limitación de tratamiento, supresión, portabilidad y oposición/revocación, en los términos que establece la normativa vigente en materia de protección de datos, dirigiendo su petición a la dirección postal Pl. Ausias March 1, 4 planta 08195, Sant Cugat del Vallès (Barcelona) o bien a través de correo electrónico info@pentec-consulting.eu. Si usted lee este mensaje y no es el destinatario señalado, el empleado o el agente responsable de entregar el mensaje al destinatario, o ha recibido esta comunicación por error, le informamos que está totalmente prohibida, y puede ser ilegal, cualquier divulgación, distribución o reproducción de esta comunicación, y le rogamos que nos lo notifique inmediatamente y nos devuelva el mensaje original a la dirección arriba mencionada. Gracias.

The information contained in this message and/or attached file(s), sent by Pen & Tec Consulting SLU, is confidential/privileged and is intended to be read solely by the person(s) to whom it is addressed. We hereby inform you that your data will be incorporated into the processing system owned by Pen & Tec Consulting SLU, and that provided it complies with the requirements included in the law, you may exercise the rights of access, rectification, limitation of processing, deletion, portability and opposition by sending your request to the postal address Pl. Ausias March 1, 4 floor 08195, Sant Cugat del Valles (Barcelona) or to the email address info@pentec-consulting.eu. If you read this message and you are neither the intended recipient, employee or agent in charge of delivering the message to the recipient, or if you have received this message as the result of an error, we hereby inform you that distributing, sharing or reproducing any part of this message is totally forbidden and may be illegal. As a result, we request that you immediately inform us of the error and return this message to the address mentioned above. Thank you.

From: DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>

Date: Monday, 17 July 2023 at 17:01

To: Nikolaas Tilkin-Franssens <niko@pentec-consulting.eu>

Subject: RE: [EXTERNAL] Re: GRN 1122 canola concentrate items for clarification -
Reply

Hello Niko,

No problem—Ill distribute this to the team for review.

Best,

Steve

Stephen DiFranco, PhD

Regulatory Review Scientist/Chemist

Center for Food Safety and Applied Nutrition

Office of Food Additive Safety

Division of Food Ingredients

U.S. Food and Drug Administration

Tel: 240-402-2710

stephen.difranco@fda.hhs.gov



From: Nikolaas Tilkin-Franssens <niko@pentec-consulting.eu>
Sent: Monday, July 17, 2023 10:35 AM
To: DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>
Subject: [EXTERNAL] Re: GRN 1122 canola concentrate items for clarification - Reply

CAUTION: This email originated from outside of the organization. Do not click links or open attachments unless you recognize the sender and know the content is safe.

Hi Stephen,

Apologies for this inconvenience.

We noticed that the reply to question 9 refers to Canola protein isolate (as per GRN 1103). I have updated the answer for it to be mentioning Canola protein concentrate (GRN 1122).

We hope this can be taken into consideration.

Kind regards,

Nikolaas Tilkin-Franssens

Regulatory Affairs Manager | Pen & Tec Consulting

T +34 936 758 015 M +34 649 840 417 F +34 936 758 016 www.pentec-consulting.eu

Pl. Ausias March 1 | 4th floor D01 | 08195 Sant Cugat del Vallès | Barcelona | Spain

PEN + TEC
CONSULTING

PART OF THE ARGENTA GROUP

La información contenida en este mensaje y/o archivo(s) adjunto(s), enviada desde Pen & Tec Consulting SLU, es confidencial/privilegiada y está destinada a ser leída sólo por la(s) persona(s) a la(s) que va dirigida. Le recordamos que sus datos han sido incorporados en el sistema de tratamiento de Pen & Tec Consulting SLU y que siempre y cuando se cumplan los requisitos exigidos por la normativa, usted podrá ejercer sus derechos de acceso, rectificación, limitación de tratamiento, supresión, portabilidad y oposición/revocación, en los términos que establece la normativa vigente en materia de protección de datos, dirigiendo su petición a la dirección postal Pl. Ausias March 1, 4 planta 08195, Sant Cugat del Vallès (Barcelona) o bien a través de correo electrónico info@pentec-consulting.eu. Si usted lee este mensaje y no es el destinatario señalado, el empleado o el agente responsable de entregar el mensaje al destinatario, o ha recibido esta comunicación por error, le informamos que está totalmente prohibida, y puede ser ilegal, cualquier divulgación, distribución o reproducción de esta comunicación, y le rogamos que nos lo notifique inmediatamente y nos devuelva el mensaje original a la dirección arriba mencionada. Gracias.

The information contained in this message and/or attached file(s), sent by Pen & Tec Consulting SLU, is confidential/privileged and is intended to be read solely by the person(s) to whom it is addressed. We hereby inform you that your data will be incorporated into the processing system owned by Pen & Tec Consulting SLU, and that provided it complies with the requirements included in the law, you may exercise the rights of access, rectification, limitation of processing, deletion, portability and opposition by sending your request to the postal address Pl. Ausias March 1, 4 floor 08195, Sant Cugat del Valles (Barcelona) or to the email address info@pentec-consulting.eu. If you read this message and you are neither the intended recipient, employee or agent in charge of delivering the message to the recipient, or if you have received this message as the result of an error, we hereby inform you that distributing, sharing or reproducing any part of this message is totally forbidden and may be illegal. As a result, we request that you immediately inform us of the error and return this message to the address mentioned above. Thank you.

From: Nikolaas Tilkin-Franssens <niko@pentec-consulting.eu>
Date: Tuesday, 11 July 2023 at 17:03
To: DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>
Cc: Justyna Pałasińska <justyna@pentec-consulting.eu>
Subject: Re: GRN 1122 canola concentrate items for clarification - Reply

Dear Stephen,

Thank you for reaching out with the questions for clarification.
We have worked closely with Napiferyn to close the doubts.

Kindly find attached a Word file including the Questions&Answers, a report on the requested literature review, a SDS sheet as requested by the USDA-FSIS, and a report on the suitability assessment.

We remain available for any further questions or updates.

Thanks for taking the application in further consideration,
best regards,

Nikolaas Tilkin-Franssens

Regulatory Affairs Manager | Pen & Tec Consulting

T +34 936 758 015 **M** +34 649 840 417 **F** +34 936 758 016 www.pentec-consulting.eu

Pl. Ausias March 1 | 4th floor D01 | 08195 Sant Cugat del Vallès | Barcelona | Spain

PEN + TEC
CONSULTING

PART OF THE ARGENTA GROUP

La información contenida en este mensaje y/o archivo(s) adjunto(s), enviada desde Pen & Tec Consulting SLU, es confidencial/privilegiada y está destinada a ser leída sólo por la(s) persona(s) a la(s) que va dirigida. Le recordamos que sus datos han sido incorporados en el sistema de tratamiento de Pen & Tec Consulting SLU y que siempre y cuando se cumplan los requisitos exigidos por la normativa, usted podrá ejercer sus derechos de acceso, rectificación, limitación de tratamiento, supresión, portabilidad y oposición/revocación, en los términos que establece la normativa vigente en materia de protección de datos, dirigiendo su petición a la dirección postal Pl. Ausias March 1, 4 planta 08195, Sant Cugat del Vallès (Barcelona) o bien a través de correo electrónico info@pentec-consulting.eu. Si usted lee este mensaje y no es el destinatario señalado, el empleado o el agente responsable de entregar el mensaje al destinatario, o ha recibido esta comunicación por error, le informamos que está totalmente prohibida, y puede ser ilegal, cualquier divulgación, distribución o reproducción de esta comunicación, y le rogamos que nos lo notifique inmediatamente y nos devuelva el mensaje original a la dirección arriba mencionada. Gracias.

The information contained in this message and/or attached file(s), sent by Pen & Tec Consulting SLU, is confidential/privileged and is intended to be read solely by the person(s) to whom it is addressed. We hereby inform you that your data will be incorporated into the processing system owned by Pen & Tec Consulting SLU, and that provided it complies with the requirements included in the law, you may exercise the rights of access, rectification, limitation of processing, deletion, portability and opposition by sending your request to the postal address Pl. Ausias March 1, 4 floor 08195, Sant Cugat del Valles (Barcelona) or to the email address info@pentec-consulting.eu. If you read this message and you are neither the intended recipient, employee or agent in charge of delivering the message to the recipient, or if you have received this message as the result of an error, we hereby inform you that distributing, sharing or reproducing any part of this message is totally forbidden and may be illegal. As a result, we request that you immediately inform us of the error and return this message to the address mentioned above. Thank you.

From: DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>
Date: Wednesday, 28 June 2023 at 17:41
To: Nicoleta Pasecinic <nicoleta@pentec-consulting.eu>
Cc: Nikolaas Tilkin-Franssens <niko@pentec-consulting.eu>

Subject: [EXTERNAL]: GRN 1122 canola concentrate items for clarification

CAUTION: This email originated from outside of the organization. Do not click links or open attachments unless you recognize the sender and know the content is safe.

Hello Ms. Pasecinic,

After evaluating NapiFeryn's GRAS Notice No. GRN 1122 on canola concentrate we noted a few issues that should be addressed. Please respond to the following points for clarification:

1. On p. 9, NapiFeryn states that the major storage proteins in canola seed are cruciferins and napins, and that canola concentrate consists of 30-45% protein and 40-70% dietary fiber. Please provide the typical cruciferin content and napin content in canola concentrate.
2. Please confirm that all raw materials and processing aids used in the manufacturing process are used in accordance with the U.S. regulations, are GRAS for their respective uses or are the subject of an effective food contact notification. For the record, we note that the food additive regulations cited in Table 4 (p. 15) for ascorbic acid (21 CFR 182.8013), ethanol (21 CFR 184.1293), and ethyl acetate (21 CFR 173.228) do not appear to be applicable to your intended uses of these substances.
3. In Table 6 (p. 18-19), NapiFeryn provides the results from the batch analyses for heavy metals. We would like to bring to your attention a relevant FDA's "[Closer to Zero](#)" initiative that focuses on reducing the levels of heavy metals in foods and recommend that you lower the specification limits for heavy metal to better reflect the batch analyses results and to be as low as possible.
4. In Table 10 (p. 22), NapiFeryn provides batch analyses data for residual solvents and processing aids. In addition, in Table 21 (p. 50), you provided the results from the batch analyses for erucic acid in your canola concentrate ranging from 0.37% to < 0.1%.
 - a. Please include limits for residual ethanol, ethyl acetate, and sulphur dioxide as well as a limit for erucic acid in the specifications for canola concentrate and specify the analytical methods used to test for these parameters.
 - b. In addition, please provide an updated Tables 5 and 6 (p. 16-19) to include the additional specification parameters mentioned above, corresponding analytical methods, and batch analyses.
5. Please state that all analytical methods used to test batches were validated and are fit for their respective purpose.
6. Please state that canola concentrate is not intended for use in infant formula or in foods where standards of identity preclude its use.
7. In Table 15 (p.), NapiFeryn provides the results of the batch analyses for total plate count in the raw material (rapeseed press cake). Please address the significant variation in the results (from <10 to 28,000 CFU/g) and discuss whether this will impact safety of the final ingredient.

8. On p. 19, NapiFeryn states that the levels of mycotoxins in canola concentrate are below the limit of quantitation (LOQ) and provide the results from the analyses of five batches to support your statement. Please clarify whether you expect mycotoxins to be present in canola concentrate manufactured in accordance with good manufacturing practices.
9. In Part 1.4 (p. 6) and Part 3.1 (p. 33), NapiFeryn states that the intended use of canola concentrate is as a source of protein and/or fiber, thickener, or texturizer. However, we note that on p. 33 you also state the intended use of canola concentrate is as a flavoring agent or binder in various comminuted or whole muscle meat and poultry products. In addition, in Appendix 3 (p. 5) you state that canola concentrate may also be used “to create a flavored salt” or as “a flavor enhancer like monosodium glutamate”. Please confirm these additional uses of canola concentrate are within the scope of GRN 001122.
10. On p. 10, the notifier describes the protein composition of canola concentrate, being primarily cruciferins, napin, oleosin, and squalene monooxygenase. However, the pivotal safety data provided appear to only be relevant to the cruciferin and napin fractions of the canola concentrate. Please provide a brief narrative to confirm the safety of oleosin and squalene monooxygenase exposure from the intended uses.
11. On p. 31-32 of the notice, the notifier clearly establishes that canola concentrate is intended to be substitutive to protein and fiber consumption and will not contribute to additional exposure to protein or fiber in general. Please elaborate on this conclusion, and clarify if the intended uses of canola concentrate are additive or substitutive to other canola protein products currently on the market (i.e., GRNs 327, 386, and 683)?
12. On p. 37, the notifier concludes exposure to canola concentrate from the intended uses is safe since the EDI reported is “still much lower (approximately 7- to 22-fold lower) than the no-observed-adverse-effect level (NOAEL) values established” for cruciferin- and napin-rich protein isolates in male rats following a 13-week oral exposure regimen (Mejia *et al.*, 2009a & 2009b). We note that an uncertainty factor, or margin of safety (MOS), of 100 (10 for interindividual variability × 10 for interspecies variability) is normally used when assessing safety of a food ingredient by comparing estimated human exposure levels to the NOAEL from animal toxicology data. Therefore, it is not clear why MOS that is ~5-10-fold lower can be concluded as safe without proper justification. Additionally, we note that potential thyrotoxic effects were observed at the highest doses in these two rat studies, as well as for rapeseed products in general tested in other species, as cited in Table 20 of the GRAS notice. This effect was mostly attributed to the presence of glucosinolate; however, we note that since the level of glucosinolate was low or absent in both the test articles from Mejia *et al.* and the article of commerce, the rationale used by the study authors to conclude that the observed NOAEL was not in fact the LOAEL may be questionable. Regardless, it appears that the provided safety narrative lacks sufficient basis to conclude MOS of 7-22 is adequate to reach the conclusion of “reasonable certainty of no harm.” Based on generally available data and information, please provide additional narrative to explain your rationale for your GRAS conclusion.

13. We note that when discussing the absorption, distribution, metabolism, and excretion of canola concentrate (p. 49), the notifier reports unpublished data from an EU Novel Foods application for “defatted rapeseed powder” to support their conclusion. Similarly, genotoxicity conclusions are made using unpublished data from an EFSA Panel conclusion on defatted rapeseed powder. Given other data and information have been used in prior GRAS notices for canola ingredients (e.g., GRN 327), please confirm that the EFSA Panel and EU Novel Foods conclusions are only considered as corroborative, not pivotal, to the safety determination of canola concentrate at its intended use level?
14. On p. 40, the notifier discusses the allergenicity potential of canola concentrate being determined via a “bioinformatics approach” and concludes that canola concentrate “may elicit possible allergenic effects.” Additionally, on p. 59 the notifier reiterates that the bioinformatics analysis indicated “possible allergenic effects” of canola concentrate, but no further discussion is provided. While data from an allergen online database search is provided as part of Appendix 4, no discussion of these data are included in the current GRAS notice. Please briefly detail the “possible allergenic effects” of canola concentrate similar to previous notices (e.g., GRN 683), and discuss why they would not be expected to pose a safety concern from the intended use.
15. We note that a recent study on rapeseed protein isolate was published (Xiong et al., 2022).
 - a. Please discuss if this study presents additional safety concerns for the article of commerce or contradicts the current GRAS conclusion.
 - b. Please also perform an updated literature review from 2021 to present and discuss if any additional studies relevant to the safety of canola concentrate were identified that would contradict the current GRAS conclusion.

References cited:

Xiong Z, Fu Y, Yao J, Zhang N, He R, Ju X, Wang Z. Removal of anti-nutritional factors of rapeseed protein isolate (RPI) and toxicity assessment of RPI. *Food Funct.* 2022 Jan 24;13(2):664-674. doi: 10.1039/d1fo03217h. PMID: 34933325.

Additionally, we received the following questions from USDA FSIS regarding their review of the uses of GRN 1122 concerning products within their purview. Please respond to the following and we will pass your responses along to them.

Please provide Safety Data Sheet (SDS) for the at use concentrations of the substance and include a description of how the use of this technology will not adversely affect the safety of FSIS inspectors. Workplace safety and health hazards include inhalation, direct skin contact (skin, eyes, mouth), and fire/explosion caused by exposure to the product, its working solution or dry mixture and potential by-products formed and/or off-gassed during the application process. The employee safety information should demonstrate how the New Technology will not “jeopardize the safety of Federal inspection personnel” as specified in the [FSIS Compliance Guideline Procedures for New Technology Notifications and Protocols, April 2015](#). FSIS workplace and employee safety must be specifically addressed. Please refer to Appendix A on p. 17, Workplace Safety and Health Criteria, for clarification on what to provide in the response. For additional clarity with respect to employee safety, the following

are examples of information that are typically needed by FSIS' employee safety and health group;

1. Potential workplace exposures that could result from inhalation and direct contact during use of the substance/technology. This information is required in addition to a SDS to determine accurate hazard potential and recommended exposure control measures for IPP work areas in accordance with Occupational Safety and Health Administration (OSHA) regulations: 29 CFR 1910.1200, Hazard Communication, 29 CFR 1910.132, Personal Protective Equipment, and 29 CFR 1910.1000, Air Contaminants. The information should be included as a specific section in each of the protocols.
2. If the SDS workplace hazards/precautions do not apply to the type of exposure that would be expected for the FSIS IPP, please have the submitter provide specific information (per the April 2015 FSIS Compliance Guideline Procedures) for the actual type of exposures expected.
3. If no IPP workplace exposures are expected and no control measures are required, please have the submitter state this and provide the reasons why (e.g., such as the substance "as used" [for all concentrations] is not hazardous by inhalation or direct contact and/or IPP would not be exposed to the substance based on the system design, operation and/or control measures that will be in place).
4. Please also indicate how will FSIS IPP be informed of the above information so that it is clear that the information contained in the SDS for the concentrate does not apply to their actual workplace exposure.
5. Are there any potential hazards from chemical mixing or low pH as a result of discharges of the various solutions to floor drains? Are dedicated drain lines or any other enclosures required?
6. With respect to potential airborne exposures to FSIS IPP in the use/application areas, does the submitter have air sampling results taken during the use of the various concentrations of the technology in the listed mixture?
7. The intended use of this product in FSIS meat and poultry products is apparently as a binder/extender. The suitability support provided in Appendix 6 does sufficiently support no significant difference in yield and other organoleptic qualities when used as a partial replacement for another binder in a processed meat and poultry product, such as sausage. However, **additional suitability support is needed:**
 - a. No suitability data was provided for **whole muscle meat and poultry products at the maximum proposed use level**. We would need to see similar data as provided in Appendix 6 for:
 1. Whole muscle red meat control containing no other binders, extenders, or moisture retention agents, as compared to a whole muscle red meat product containing 15% isolated canola product.
 2. Whole muscle poultry control containing no other binders, extenders, or moisture retention agents as compared to a whole muscle poultry product containing 15% isolated canola product.

Responses may be sent in an email or in a separate document. We respectfully request a response within 10 business days. If you are unable to complete the response within that time frame, please contact me to discuss further options.

If you have any additional questions or concerns, please don't hesitate to contact me at stephen.difranco@fda.hhs.gov or by phone at 240.402.2710.

Best,

Steve

Stephen DiFranco, PhD

Regulatory Review Scientist/Chemist

Center for Food Safety and Applied Nutrition

Office of Food Additive Safety

Division of Food Ingredients

U.S. Food and Drug Administration

Tel: 240-402-2710

stephen.difranco@fda.hhs.gov



CAUTION: This email, including any attachments, is confidential. If you are not the intended recipient, please notify the sender and delete the email and any attachments from your system. In addition, you must not use, distribute or reproduce this email or any attachments. Opinions and other information in this email and any attachments which do not relate to the official business of Argenta are neither given by nor endorsed by Argenta. While Argenta uses anti-virus software, Argenta accepts no liability for any viruses in this email or any attachment, or for any effects this email or any attachment may have on your network or computer system.

CAUTION: This email, including any attachments, is confidential. If you are not the intended recipient, please notify the sender and delete the email and any attachments from your system. In addition, you must not use, distribute or reproduce this email or any attachments. Opinions and other information in this email and any attachments which do not relate to the official business of Argenta are neither given by nor endorsed by Argenta. While Argenta uses anti-virus software, Argenta accepts no liability for any viruses in this email or any attachment, or for any effects this email or any attachment may have on your network or computer system.

Este correo electrónico y los archivos adjuntos, enviados por Pen & Tec Consulting SLU, que opera bajo el nombre comercial de Argenta® (Argenta), son confidenciales y pueden estar protegidos por ley. Si usted no es el destinatario, cualquier divulgación, reproducción, copia, distribución u otro tipo de difusión o uso de esta comunicación está estrictamente prohibido. Si ha recibido esta transmisión por error, notifíquelo al remitente y elimine inmediatamente el correo electrónico y cualquier archivo adjunto de su sistema. Argenta no emite ni respalda las opiniones y demás información contenida en este correo electrónico y en sus anexos que no estén relacionadas con las actividades oficiales de Argenta. Aunque Argenta utiliza software antivirus, Argenta no acepta ninguna responsabilidad por cualquier virus en este correo electrónico o cualquier archivo adjunto, o por cualquier efecto que este correo

electrónico o cualquier archivo adjunto pueda tener en su red o sistema informático. Argenta registra y almacena los correos electrónicos enviados a nosotros o a nuestros afiliados de acuerdo con nuestras políticas y procedimientos internos. Consulte www.pentec-consulting.eu para obtener información sobre Argenta y/o nuestra política de privacidad.

This email and any attached file(s), sent by Pen & Tec Consulting SLU trading as Argenta® (Argenta), are confidential and may be legally privileged. If you are not the intended recipient, any disclosure, reproduction, copying, distribution, or other dissemination or use of this communication is strictly prohibited. If you have received this transmission in error, please notify the sender and delete the email and any attachments from your system immediately. Opinions and other information in this email and any attachments which do not relate to the official business of Argenta are neither given by nor endorsed by Argenta. While Argenta uses anti-virus software, Argenta accepts no liability for any viruses in this email or any attachment, or for any effects this email or any attachment may have on your network or computer system. Argenta records and stores emails sent to us or our affiliates in keeping with our internal policies and procedures. Please see www.pentec-consulting.eu for information regarding Argenta and/or our privacy policy.

From: [Justyna Pałasińska](#)
To: [DiFranco, Stephen](#)
Subject: Re: [EXTERNAL] GRN 1122 canola concentrate status
Date: Monday, March 4, 2024 5:05:08 AM
Attachments: [image001.png](#)
[image009.png](#)
[image010.png](#)
[image011.png](#)
[image012.png](#)
[image007.png](#)
[image008.png](#)

CAUTION: This email originated from outside of the organization. Do not click links or open attachments unless you recognize the sender and know the content is safe.

Many thanks for the update, Stephen. We look forward to hearing an update, hopefully soon!

Kind regards,

Justyna Pałasińska

Regulatory Affairs Director – Human Nutrition, Argenta Barcelona



M [+34 682 894 653](tel:+34682894653) T [+34 936 758 015](tel:+34936758015)

www.argentaglobal.com

La información contenida en este mensaje y/o archivo(s) adjunto(s), enviada desde Pen & Tec Consulting SLU cotiza como Argenta, es confidencial/privilegiada y está destinada a ser leída sólo por la(s) persona(s) a la(s) que va dirigida. Le recordamos que sus datos han sido incorporados en el sistema de tratamiento de Pen & Tec Consulting SLU cotiza como Argenta, y que siempre y cuando se cumplan los requisitos exigidos por la normativa, usted podrá ejercer sus derechos de acceso, rectificación, limitación de tratamiento, supresión, portabilidad y oposición/revocación, en los términos que establece la normativa vigente en materia de protección de datos, dirigiendo su petición a la dirección postal Pl. Ausias March 1, 4 planta 08195, Sant Cugat del Vallès (Barcelona) o bien a través de correo electrónico info@pentec-consulting.eu. Si usted lee este mensaje y no es el destinatario señalado, el empleado o el agente responsable de entregar el mensaje al destinatario, o ha recibido esta comunicación por error, le informamos que está totalmente prohibida, y puede ser ilegal, cualquier divulgación, distribución o reproducción de esta comunicación, y le rogamos que nos lo notifique inmediatamente y nos devuelva el mensaje original a la dirección arriba mencionada. Gracias.

The information contained in this message and/or attached file(s), sent by Pen & Tec Consulting SLU trading as Argenta, is confidential/privileged and is intended to be read solely by the person(s) to whom it is addressed. We hereby inform you that your data will be incorporated into the processing system owned by Pen & Tec Consulting SLU, and that provided it complies with the requirements included in the law, you may exercise the rights of access, rectification, limitation of processing, deletion, portability and opposition by sending your request to the postal address Pl. Ausias March 1, 4 floor 08195, Sant Cugat del Valles (Barcelona) or to the email address info@pentec-consulting.eu. If you read this message and you are neither the intended recipient, employee or agent in charge of delivering the message to the recipient, or if you have received this message as the result of an error, we hereby inform you that distributing, sharing or reproducing any part of this message is totally forbidden and may be illegal. As a result, we request that you immediately inform us of the error and return this message to the address mentioned above. Thank you.

From: DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>

Date: Monday, 26 February 2024 at 17:20

To: Justyna Pałasińska <justyna.palasinaska@argentaglobal.com>

Subject: RE: [EXTERNAL] GRN 1122 canola concentrate status

You don't often get email from stephen.difranco@fda.hhs.gov. [Learn why this is important](#)

Hello Justyna,

Regarding GRN 1122; FDA has completed its review and has drafted a response letter. Unfortunately, we cannot move forward before USDA-FSIS completes their review of the uses under their jurisdiction. I have been periodically inquiring with FSIS as to the status and will get this to you as soon as possible.

We appreciate your continued patience.

Best,

Steve

Stephen DiFranco, PhD

Regulatory Review Scientist/Chemist

**Center for Food Safety and Applied Nutrition
Office of Food Additive Safety
Division of Food Ingredients
U.S. Food and Drug Administration**
Tel: 240-402-2710
stephen.difranco@fda.hhs.gov



From: Justyna Pałasińska <justyna.palasinska@argentaglobal.com>
Sent: Wednesday, February 14, 2024 12:07 PM
To: Premarkt <Premarkt@fda.hhs.gov>
Cc: DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>; Ioannis Kartanos <ioannis.kartanos@argentaglobal.com>
Subject: [EXTERNAL] GRN 1122 canola concentrate status

CAUTION: This email originated from outside of the organization. Do not click links or open attachments unless you recognize the sender and know the content is safe.

Dear HHS team,

I am writing to enquire about a GRAS notice that was submitted to the FDA & filed April 19, 2023 (GRN 1122). We have been in touch with Mr Stephen DiFranco & at the beginning of December he has informed us that the FDA reviews are complete & the notice is now with USDA-FSIS.

Mr DiFranco has been very helpful through the whole process. However, we have tried to contact him several times since December without success. We were wondering if there is someone else we can get in touch with for an update on this application. We would be happy to provide any information that would help finalize the process.

I look forward to hearing from you.

Kind regards,

Justyna Pałasińska

Regulatory Affairs Director – Human Nutrition, Argenta Barcelona



M [+34 682 894 653](tel:+34682894653) T [+34 936 758 015](tel:+34936758015)

www.argentaglobal.com

La información contenida en este mensaje y/o archivo(s) adjunto(s), enviada desde Pen & Tec Consulting SLU cotiza como Argenta, es confidencial/privilegiada y está destinada a ser leída sólo por la(s) persona(s) a la(s) que va dirigida. Le recordamos que sus datos han sido incorporados en el sistema de tratamiento de Pen & Tec Consulting SLU cotiza como Argenta, y que siempre y cuando se cumplan los requisitos exigidos por la normativa, usted podrá ejercer sus derechos de acceso, rectificación, limitación de tratamiento, supresión, portabilidad y oposición/revocación, en los términos que establece la normativa vigente en materia de protección de datos, dirigiendo su petición a la dirección postal Pl. Ausias March 1, 4 planta 08195, Sant Cugat del Vallès (Barcelona) o bien a través de correo electrónico info@pentec-consulting.eu. Si usted lee este mensaje y no es el destinatario señalado, el empleado o el agente responsable de entregar el mensaje al destinatario, o ha recibido esta comunicación por error, le informamos que está totalmente prohibida, y puede ser ilegal, cualquier divulgación, distribución o reproducción de esta comunicación, y le rogamos que nos lo notifique inmediatamente y nos devuelva el mensaje original a la dirección arriba mencionada. Gracias.

The information contained in this message and/or attached file(s), sent by Pen & Tec Consulting SLU trading as Argenta, is confidential/privileged and is intended to be read solely by the person(s) to whom it is addressed. We hereby inform you that your data will be incorporated into the processing system owned by Pen & Tec Consulting SLU, and that provided it complies with the requirements included in the law, you may exercise the rights of access, rectification, limitation of processing, deletion, portability and opposition by sending your request to the postal address Pl. Ausias March 1, 4 floor 08195, Sant Cugat del Valles (Barcelona) or to the email address info@pentec-consulting.eu. If you read this message and you are neither the intended recipient, employee or agent in charge of delivering the message to the recipient, or if you have received this message as the result of an error, we hereby inform you that distributing, sharing or reproducing any part of this message is totally forbidden and may be illegal. As a result, we request that you immediately inform us of the error and return this message to the address mentioned above. Thank you.

From: Justyna Pałasińska <justyna.palasinaska@argentaglobal.com>

Date: Wednesday, 31 January 2024 at 17:53

To: Justyna Pałasińska <justyna.palasinaska@argentaglobal.com>, DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>

Cc: Ioannis Kartanos <ioannis.kartanos@argentaglobal.com>

Subject: Re: [EXTERNAL] GRN 1122 canola concentrate - update contact person

Dear Steve,

I hope this e-mail finds you well. I was wondering if there are any updates on the finalization of this notification?

Is there any additional information that needs to be provided?

Kind regards,

Justyna Pałasińska

Regulatory Affairs Director – Human Nutrition, Argenta Barcelona



M [+34 682 894 653](tel:+34682894653) T [+34 936 758 015](tel:+34936758015)

www.argentaglobal.com



La información contenida en este mensaje y/o archivo(s) adjunto(s), enviada desde Pen & Tec Consulting SLU cotiza como Argenta, es confidencial/privilegiada y está destinada a ser leída sólo por la(s) persona(s) a la(s) que va dirigida. Le recordamos que sus datos han sido incorporados en el sistema de tratamiento de Pen & Tec Consulting SLU cotiza como Argenta, y que siempre y cuando se cumplan los requisitos exigidos por la normativa, usted podrá ejercer sus derechos de acceso, rectificación, limitación de tratamiento, supresión, portabilidad y oposición/revocación, en los términos que establece la normativa vigente en materia de protección de datos, dirigiendo su petición a la dirección postal Pl. Ausias March 1, 4 planta 08195, Sant Cugat del Vallès (Barcelona) o bien a través de correo electrónico info@pentec-consulting.eu. Si usted lee este mensaje y no es el destinatario señalado, el empleado o el agente responsable de entregar el mensaje al destinatario, o ha recibido esta comunicación por error, le informamos que está totalmente prohibida, y puede ser ilegal, cualquier divulgación, distribución o reproducción de esta comunicación, y le rogamos que nos lo notifique inmediatamente y nos devuelva el mensaje original a la dirección arriba mencionada. Gracias.

The information contained in this message and/or attached file(s), sent by Pen & Tec Consulting SLU trading as Argenta, is confidential/privileged and is intended to be read solely by the person(s) to whom it is addressed. We hereby inform you that your data will be incorporated into the processing system owned by Pen & Tec Consulting SLU, and that provided it complies with the requirements included in the law, you may exercise the rights of access, rectification, limitation of processing, deletion, portability and opposition by sending your request to the postal address Pl. Ausias March 1, 4 floor 08195, Sant Cugat del Valles (Barcelona) or to the email address info@pentec-consulting.eu. If you read this message and you are neither the intended recipient, employee or agent in charge of delivering the message to the recipient, or if you have received this message as the result of an error, we hereby inform you that distributing, sharing or reproducing any part of this message is totally forbidden and may be illegal. As a result, we request that you immediately inform us of the error and return this message to the address mentioned above. Thank you.

From: Justyna Pałasińska <justyna@pentec-consulting.eu>

Date: Friday, 22 December 2023 at 13:31

To: DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>

Cc: Ioannis Kartanos <ioannis@pentec-consulting.eu>

Subject: Re: [EXTERNAL] GRN 1122 canola concentrate - update contact person

Dear Stephen,

Many thanks for confirming the change of contact person.

I'm following up on my colleague Ioannis e-mail from 12/12/2023. As he mentioned, we have already provided the answers to the questions to USDA-FSIS. Nevertheless, I have included them in a separate document.

Please let us know in case any additional information is required.

In the meantime, we wish you a Happy Holiday Season & all the best in 2024!

Kind regards,

Ing. Justyna Pałasińska

Regulatory Affairs Director – Human Nutrition | Pen & Tec Consulting

T +34 936 758 015 M +34 682 894 653 F +34 936 758 016 www.pentec-consulting.eu

Pl. Ausias March 1 | 4th floor D01 | 08195 Sant Cugat del Vallès | Barcelona | Spain

PEN + TEC
CONSULTING
PART OF THE ARGENTA GROUP

La información contenida en este mensaje y/o archivo(s) adjunto(s), enviada desde Pen & Tec Consulting SLU, es confidencial/privilegiada y está destinada a ser leída sólo por la(s) persona(s) a la(s) que va dirigida. Le recordamos que sus datos han

sido incorporados en el sistema de tratamiento de Pen & Tec Consulting SLU y que siempre y cuando se cumplan los requisitos exigidos por la normativa, usted podrá ejercer sus derechos de acceso, rectificación, limitación de tratamiento, supresión, portabilidad y oposición/revocación, en los términos que establece la normativa vigente en materia de protección de datos, dirigiendo su petición a la dirección postal Pl. Ausias March 1, 4 planta 08195, Sant Cugat del Vallès (Barcelona) o bien a través de correo electrónico info@pentec-consulting.eu. Si usted lee este mensaje y no es el destinatario señalado, el empleado o el agente responsable de entregar el mensaje al destinatario, o ha recibido esta comunicación por error, le informamos que está totalmente prohibida, y puede ser ilegal, cualquier divulgación, distribución o reproducción de esta comunicación, y le rogamos que nos lo notifique inmediatamente y nos devuelva el mensaje original a la dirección arriba mencionada. Gracias.

The information contained in this message and/or attached file(s), sent by Pen & Tec Consulting SLU, is confidential/privileged and is intended to be read solely by the person(s) to whom it is addressed. We hereby inform you that your data will be incorporated into the processing system owned by Pen & Tec Consulting SLU, and that provided it complies with the requirements included in the law, you may exercise the rights of access, rectification, limitation of processing, deletion, portability and opposition by sending your request to the postal address Pl. Ausias March 1, 4 floor 08195, Sant Cugat del Valles (Barcelona) or to the email address info@pentec-consulting.eu. If you read this message and you are neither the intended recipient, employee or agent in charge of delivering the message to the recipient, or if you have received this message as the result of an error, we hereby inform you that distributing, sharing or reproducing any part of this message is totally forbidden and may be illegal. As a result, we request that you immediately inform us of the error and return this message to the address mentioned above. Thank you.

From: DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>

Date: Tuesday, 5 December 2023 at 19:05

To: Nikolaas Tilkin-Franssens <niko@pentec-consulting.eu>

Cc: Justyna Pałasińska <justyna@pentec-consulting.eu>

Subject: RE: [EXTERNAL] GRN 1122 canola concentrate - update contact person

You don't often get email from stephen.difranco@fda.hhs.gov. [Learn why this is important](#)

Hello Niko and Justyna,

Just confirming the change of contact person for GRN 1122.

As for timeline, FDA reviews are complete but USDA-FSIS is requesting a few pieces of information regarding the uses of canola concentrate under USDA jurisdiction, namely:

Please provide SDS for the at use concentrations of the substance and include a description of how the use of this technology will not adversely affect the safety of FSIS inspectors. Workplace safety and health hazards include inhalation, direct skin contact (skin, eyes, mouth), and fire/explosion caused by exposure to the product, its working solution or dry mixture and potential by-products formed and/or off-gassed during the application process. The employee safety information should demonstrate how the New Technology will not “jeopardize the safety of Federal inspection personnel” as specified in the [FSIS Compliance Guideline Procedures for New Technology Notifications and Protocols, April 2015](#).

Although I'm not anticipating any issues here, FSIS workplace and employee safety must be specifically addressed. Please refer to Appendix A on page 17, Workplace Safety and Health Criteria, for clarification on what to provide in the response. For additional clarity with respect to employee safety, the following are examples of information that are typically needed by FSIS' employee safety and health group;

1. Potential workplace exposures that could result from inhalation and direct contact during use of the substance/technology. This information is required in addition to a Safety Data Sheet (SDS) to determine accurate hazard potential and recommended exposure control measures for IPP work areas in accordance with Occupational Safety and Health Administration (OSHA) regulations: 29 CFR 1910.1200, Hazard Communication, 29 CFR 1910.132, Personal Protective Equipment, and 29 CFR 1910.1000, Air Contaminants. The information should be included as a specific section in each of the protocols.
2. If the SDS workplace hazards/precautions do not apply to the type of exposure that would be expected for the FSIS IPP, please have the submitter provide specific information (per the April 2015 FSIS Compliance Guideline Procedures) for the actual type of exposures expected.

3. If no IPP workplace exposures are expected and no control measures are required, please have the submitter state this and provide the reasons why (e.g., such as the substance “as used” [for all concentrations] is not hazardous by inhalation or direct contact and/or IPP would not be exposed to the substance based on the system design, operation and/or control measures that will be in place).
4. Please also indicate how will FSIS IPP be informed of the above information so that it is clear that the information contained in the SDS for the concentrate does not apply to their actual workplace exposure.
5. Are there any potential hazards from chemical mixing or low pH as a result of discharges of the various solutions to floor drains? Are dedicated drain lines or any other enclosures required?
6. With respect to potential airborne exposures to FSIS IPP in the use/application areas, does the submitter have air sampling results taken during the use of the various concentrations of the technology in the listed mixture?

Suitability data;

The intended use of this product in FSIS meat and poultry products is apparently as a binder/extender. The suitability support provided in Appendix 6 does sufficiently support no significant difference in yield and other organoleptic qualities when used as a partial replacement for another binder in a processed meat and poultry product, such as sausage.

However, **additional suitability support is needed:**

- No suitability data was provided for **whole muscle meat and poultry products at the maximum proposed use level**. We would need to see similar data as provided in Appendix 6 for:
 - Whole muscle red meat control containing no other binders, extenders, or moisture retention agents, as compared to a whole muscle red meat product containing 15% isolated canola product.
 - Whole muscle poultry control containing no other binders, extenders, or moisture retention agents as compared to a whole muscle poultry product containing 15% isolated canola product.

You responses can be emailed directly to me and I will distribute to the necessary staff inside FDA and USDA.

Thanks,

Steve

Stephen DiFranco, PhD

Regulatory Review Scientist/Chemist

**Center for Food Safety and Applied Nutrition
Office of Food Additive Safety
Division of Food Ingredients
U.S. Food and Drug Administration**
Tel: 240-402-2710
stephen.difranco@fda.hhs.gov



From: Nikolaas Tilkin-Franssens <niko@pentec-consulting.eu>
Sent: Monday, December 4, 2023 4:36 AM
To: DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>
Cc: Justyna Pałasińska <justyna@pentec-consulting.eu>
Subject: [EXTERNAL] GRN 1122 canola concentrate - update contact person

CAUTION: This email originated from outside of the organization. Do not click links or open attachments unless you recognize the sender and know the content is safe.

Hi Mr. DiFranco,

Hope this email finds you well.

Due to a change in position, I will no longer be the contact person for the GRAS Notice 1122 (Canola Protein Concentrate). Could you please update your records to ascertain that Justyna Pałasińska, in copy to this email, is informed of any relevant updates?

Could you kindly confirm receipt of this email for our records?
And if possible, let us know if there is any estimate on the timeline re. finalization of the review of this GRAS Notice.

Many thanks for your great and flexible support on this application.

Kind regards,

Niko

Nikolaas Tilkin-Franssens

Regulatory Affairs Manager | Pen & Tec Consulting

T +34 936 758 015 M +34 649 840 417 F +34 936 758 016 www.pentec-consulting.eu

Pl. Ausias March 1 | 4th floor D01 | 08195 Sant Cugat del Vallès | Barcelona | Spain

PEN + TEC
CONSULTING
PART OF THE ARGENTA GROUP

La información contenida en este mensaje y/o archivo(s) adjunto(s), enviada desde Pen & Tec Consulting SLU, es confidencial/privilegiada y está destinada a ser leída sólo por la(s) persona(s) a la(s) que va dirigida. Le recordamos que sus datos han sido incorporados en el sistema de tratamiento de Pen & Tec Consulting SLU y que siempre y cuando se cumplan los requisitos exigidos por la normativa, usted podrá ejercer sus derechos de acceso, rectificación, limitación de tratamiento, supresión, portabilidad y oposición/revocación, en los términos que establece la normativa vigente en materia de protección de datos, dirigiendo su petición a la dirección postal Pl. Ausias March 1, 4 planta 08195, Sant Cugat del Vallès (Barcelona) o bien a través de correo electrónico info@pentec-consulting.eu. Si usted lee este mensaje y no es el destinatario señalado, el empleado o el agente responsable de entregar el mensaje al destinatario, o ha recibido esta comunicación por error, le informamos que está totalmente prohibida, y puede ser ilegal, cualquier divulgación, distribución o reproducción de esta comunicación, y le rogamos que nos lo notifique inmediatamente y nos devuelva el mensaje original a la dirección arriba mencionada. Gracias.

The information contained in this message and/or attached file(s), sent by Pen & Tec Consulting SLU, is confidential/privileged and is intended to be read solely by the person(s) to whom it is addressed. We hereby inform you that your data will be incorporated into the processing system owned by Pen & Tec Consulting SLU, and that provided it complies with the requirements included in the law, you may exercise the rights of access, rectification, limitation of processing, deletion, portability and opposition by sending your request to the postal address Pl. Ausias March 1, 4 floor 08195, Sant Cugat del Valles (Barcelona) or to the email address info@pentec-consulting.eu. If you read this message and you are neither the intended recipient, employee or agent in charge of delivering the message to the recipient, or if you have received this message as the result of an error, we hereby inform you that distributing, sharing or reproducing any part of this message is totally forbidden and may be illegal. As a result, we request that you immediately inform us of the error and return this message to the address mentioned above. Thank you.

From: DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>

Date: Monday, 17 July 2023 at 17:01

To: Nikolaas Tilkin-Franssens <niko@pentec-consulting.eu>

Subject: RE: [EXTERNAL] Re: GRN 1122 canola concentrate items for clarification - Reply

Hello Niko,

No problem—I'll distribute this to the team for review.

Best,

Steve

Stephen DiFranco, PhD

Regulatory Review Scientist/Chemist

Center for Food Safety and Applied Nutrition

Office of Food Additive Safety

Division of Food Ingredients

U.S. Food and Drug Administration

Tel: 240-402-2710

stephen.difranco@fda.hhs.gov



From: Nikolaas Tilkin-Franssens <niko@pentec-consulting.eu>

Sent: Monday, July 17, 2023 10:35 AM

To: DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>

Subject: [EXTERNAL] Re: GRN 1122 canola concentrate items for clarification - Reply

CAUTION: This email originated from outside of the organization. Do not click links or open attachments unless you recognize the sender and know the content is safe.

Hi Stephen,

Apologies for this inconvenience.

We noticed that the reply to question 9 refers to Canola protein isolate (as per GRN 1103). I have updated the answer for it to be mentioning Canola protein concentrate (GRN 1122).

We hope this can be taken into consideration.

Kind regards,

Nikolaas Tilkin-Franssens

Regulatory Affairs Manager | Pen & Tec Consulting

T [+34 936 758 015](tel:+34936758015) **M** [+34 649 840 417](tel:+34649840417) **F** [+34 936 758 016](tel:+34936758016) www.pentec-consulting.eu

Pl. Ausias March 1 | 4th floor D01 | 08195 Sant Cugat del Vallès | Barcelona | Spain

PEN + TEC
CONSULTING

PART OF THE ARGENTA GROUP

La información contenida en este mensaje y/o archivo(s) adjunto(s), enviada desde Pen & Tec Consulting SLU, es confidencial/privilegiada y está destinada a ser leída sólo por la(s) persona(s) a la(s) que va dirigida. Le recordamos que sus datos han sido incorporados en el sistema de tratamiento de Pen & Tec Consulting SLU y que siempre y cuando se cumplan los requisitos exigidos por la normativa, usted podrá ejercer sus derechos de acceso, rectificación, limitación de tratamiento, supresión, portabilidad y oposición/revocación, en los términos que establece la normativa vigente en materia de protección de datos, dirigiendo su petición a la dirección postal Pl. Ausias March 1, 4 planta 08195, Sant Cugat del Vallès (Barcelona) o bien a través de correo electrónico info@pentec-consulting.eu. Si usted lee este mensaje y no es el destinatario señalado, el empleado o el agente responsable de entregar el mensaje al destinatario, o ha recibido esta comunicación por error, le informamos que está totalmente prohibida, y puede ser ilegal, cualquier divulgación, distribución o reproducción de esta comunicación, y le rogamos que nos lo notifique inmediatamente y nos devuelva el mensaje original a la dirección arriba mencionada. Gracias.

The information contained in this message and/or attached file(s), sent by Pen & Tec Consulting SLU, is confidential/privileged and is intended to be read solely by the person(s) to whom it is addressed. We hereby inform you that your data will be incorporated into the processing system owned by Pen & Tec Consulting SLU, and that provided it complies with the requirements included in the law, you may exercise the rights of access, rectification, limitation of processing, deletion, portability and opposition by sending your request to the postal address Pl. Ausias March 1, 4 floor 08195, Sant Cugat del Valles (Barcelona) or to the email address info@pentec-consulting.eu. If you read this message and you are neither the intended recipient, employee or agent in charge of delivering the message to the recipient, or if you have received this message as the result of an error, we hereby inform you that distributing, sharing or reproducing any part of this message is totally forbidden and may be illegal. As a result, we request that you immediately inform us of the error and return this message to the address mentioned above. Thank you.

From: Nikolaas Tilkin-Franssens <niko@pentec-consulting.eu>

Date: Tuesday, 11 July 2023 at 17:03

To: DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>

Cc: Justyna Pałasińska <justyna@pentec-consulting.eu>

Subject: Re: GRN 1122 canola concentrate items for clarification - Reply

Dear Stephen,

Thank you for reaching out with the questions for clarification.
We have worked closely with Napiferyn to close the doubts.

Kindly find attached a Word file including the Questions&Answers, a report on the requested literature review, a SDS sheet as requested by the USDA-FSIS, and a report on the suitability assessment.

We remain available for any further questions or updates.

Thanks for taking the application in further consideration,
best regards,

Nikolaas Tilkin-Franssens

Regulatory Affairs Manager | Pen & Tec Consulting

T [+34 936 758 015](tel:+34936758015) **M** [+34 649 840 417](tel:+34649840417) **F** [+34 936 758 016](tel:+34936758016) www.pentec-consulting.eu

Pl. Ausias March 1 | 4th floor D01 | 08195 Sant Cugat del Vallès | Barcelona | Spain

La información contenida en este mensaje y/o archivo(s) adjunto(s), enviada desde Pen & Tec Consulting SLU, es confidencial/privilegiada y está destinada a ser leída sólo por la(s) persona(s) a la(s) que va dirigida. Le recordamos que sus datos han sido incorporados en el sistema de tratamiento de Pen & Tec Consulting SLU y que siempre y cuando se cumplan los requisitos exigidos por la normativa, usted podrá ejercer sus derechos de acceso, rectificación, limitación de tratamiento, supresión, portabilidad y oposición/revocación, en los términos que establece la normativa vigente en materia de protección de datos, dirigiendo su petición a la dirección postal Pl. Ausias March 1, 4 planta 08195, Sant Cugat del Vallès (Barcelona) o bien a través de correo electrónico info@pentec-consulting.eu. Si usted lee este mensaje y no es el destinatario señalado, el empleado o el agente responsable de entregar el mensaje al destinatario, o ha recibido esta comunicación por error, le informamos que está totalmente prohibida, y puede ser ilegal, cualquier divulgación, distribución o reproducción de esta comunicación, y le rogamos que nos lo notifique inmediatamente y nos devuelva el mensaje original a la dirección arriba mencionada. Gracias.

The information contained in this message and/or attached file(s), sent by Pen & Tec Consulting SLU, is confidential/privileged and is intended to be read solely by the person(s) to whom it is addressed. We hereby inform you that your data will be incorporated into the processing system owned by Pen & Tec Consulting SLU, and that provided it complies with the requirements included in the law, you may exercise the rights of access, rectification, limitation of processing, deletion, portability and opposition by sending your request to the postal address Pl. Ausias March 1, 4 floor 08195, Sant Cugat del Valles (Barcelona) or to the email address info@pentec-consulting.eu. If you read this message and you are neither the intended recipient, employee or agent in charge of delivering the message to the recipient, or if you have received this message as the result of an error, we hereby inform you that distributing, sharing or reproducing any part of this message is totally forbidden and may be illegal. As a result, we request that you immediately inform us of the error and return this message to the address mentioned above. Thank you.

From: DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>
Date: Wednesday, 28 June 2023 at 17:41
To: Nicoleta Pasecinic <nicoleta@pentec-consulting.eu>
Cc: Nikolaas Tilkin-Franssens <niko@pentec-consulting.eu>
Subject: [EXTERNAL]: GRN 1122 canola concentrate items for clarification

CAUTION: This email originated from outside of the organization. Do not click links or open attachments unless you recognize the sender and know the content is safe.

Hello Ms. Pasecinic,

After evaluating NapiFeryn's GRAS Notice No. GRN 1122 on canola concentrate we noted a few issues that should be addressed. Please respond to the following points for clarification:

1. On p. 9, NapiFeryn states that the major storage proteins in canola seed are cruciferins and napins, and that canola concentrate consists of 30-45% protein and 40-70% dietary fiber. Please provide the typical cruciferin content and napin content in canola concentrate.
2. Please confirm that all raw materials and processing aids used in the manufacturing process are used in accordance with the U.S. regulations, are GRAS for their respective uses or are the subject of an effective food contact notification. For the record, we note that the food additive regulations cited in Table 4 (p. 15) for ascorbic acid (21 CFR 182.8013), ethanol (21 CFR 184.1293), and ethyl acetate (21 CFR 173.228) do not appear to be applicable to your intended uses of these substances.
3. In Table 6 (p. 18-19), NapiFeryn provides the results from the batch analyses for heavy metals. We would like to bring to your attention a relevant FDA's "[Closer to Zero](#)" initiative that focuses on reducing the levels of heavy metals in foods and recommend that you lower the specification limits for heavy metal to better reflect the batch analyses results and to be as low as possible.

4. In Table 10 (p. 22), NapiFeryn provides batch analyses data for residual solvents and processing aids. In addition, in Table 21 (p. 50), you provided the results from the batch analyses for erucic acid in your canola concentrate ranging from 0.37% to < 0.1%.

Please include limits for residual ethanol, ethyl acetate, and sulphur dioxide as well as a limit for erucic acid in the specifications for canola concentrate and specify the analytical methods used to test for these parameters.

In addition, please provide an updated Tables 5 and 6 (p. 16-19) to include the additional specification parameters mentioned above, corresponding analytical methods, and batch analyses.
5. Please state that all analytical methods used to test batches were validated and are fit for their respective purpose.
6. Please state that canola concentrate is not intended for use in infant formula or in foods where standards of identity preclude its use.
7. In Table 15 (p.), NapiFeryn provides the results of the batch analyses for total plate count in the raw material (rapeseed press cake). Please address the significant variation in the results (from <10 to 28,000 CFU/g) and discuss whether this will impact safety of the final ingredient.
8. On p. 19, NapiFeryn states that the levels of mycotoxins in canola concentrate are below the limit of quantitation (LOQ) and provide the results from the analyses of five batches to support your statement. Please clarify whether you expect mycotoxins to be present in canola concentrate manufactured in accordance with good manufacturing practices.
9. In Part 1.4 (p. 6) and Part 3.1 (p. 33), NapiFeryn states that the intended use of canola concentrate is as a source of protein and/or fiber, thickener, or texturizer. However, we note that on p. 33 you also state the intended use of canola concentrate is as a flavoring agent or binder in various comminuted or whole muscle meat and poultry products. In addition, in Appendix 3 (p. 5) you state that canola concentrate may also be used “to create a flavored salt” or as “a flavor enhancer like monosodium glutamate”. Please confirm these additional uses of canola concentrate are within the scope of GRN 001122.
10. On p. 10, the notifier describes the protein composition of canola concentrate, being primarily cruciferins, napin, oleosin, and squalene monooxygenase. However, the pivotal safety data provided appear to only be relevant to the cruciferin and napin fractions of the canola concentrate. Please provide a brief narrative to confirm the safety of oleosin and squalene monooxygenase exposure from the intended uses.
11. On p. 31-32 of the notice, the notifier clearly establishes that canola concentrate is intended to be substitutive to protein and fiber consumption and will not contribute to additional exposure to protein or fiber in general. Please elaborate on this conclusion, and clarify if the

intended uses of canola concentrate are additive or substitutive to other canola protein products currently on the market (i.e., GRNs 327, 386, and 683)?

12. On p. 37, the notifier concludes exposure to canola concentrate from the intended uses is safe since the EDI reported is “still much lower (approximately 7- to 22-fold lower) than the no-observed-adverse-effect level (NOAEL) values established” for cruciferin- and napin-rich protein isolates in male rats following a 13-week oral exposure regimen (Mejia *et al.*, 2009a & 2009b). We note that an uncertainty factor, or margin of safety (MOS), of 100 (10 for interindividual variability × 10 for interspecies variability) is normally used when assessing safety of a food ingredient by comparing estimated human exposure levels to the NOAEL from animal toxicology data. Therefore, it is not clear why MOS that is ~5-10-fold lower can be concluded as safe without proper justification. Additionally, we note that potential thyrotoxic effects were observed at the highest doses in these two rat studies, as well as for rapeseed products in general tested in other species, as cited in Table 20 of the GRAS notice. This effect was mostly attributed to the presence of glucosinolate; however, we note that since the level of glucosinolate was low or absent in both the test articles from Mejia *et al.* and the article of commerce, the rationale used by the study authors to conclude that the observed NOAEL was not in fact the LOAEL may be questionable. Regardless, it appears that the provided safety narrative lacks sufficient basis to conclude MOS of 7-22 is adequate to reach the conclusion of “reasonable certainty of no harm.” Based on generally available data and information, please provide additional narrative to explain your rationale for your GRAS conclusion.
13. We note that when discussing the absorption, distribution, metabolism, and excretion of canola concentrate (p. 49), the notifier reports unpublished data from an EU Novel Foods application for “defatted rapeseed powder” to support their conclusion. Similarly, genotoxicity conclusions are made using unpublished data from an EFSA Panel conclusion on defatted rapeseed powder. Given other data and information have been used in prior GRAS notices for canola ingredients (e.g., GRN 327), please confirm that the EFSA Panel and EU Novel Foods conclusions are only considered as corroborative, not pivotal, to the safety determination of canola concentrate at its intended use level?
14. On p. 40, the notifier discusses the allergenicity potential of canola concentrate being determined via a “bioinformatics approach” and concludes that canola concentrate “may elicit possible allergenic effects.” Additionally, on p. 59 the notifier reiterates that the bioinformatics analysis indicated “possible allergenic effects” of canola concentrate, but no further discussion is provided. While data from an allergen online database search is provided as part of Appendix 4, no discussion of these data are included in the current GRAS notice. Please briefly detail the “possible allergenic effects” of canola concentrate similar to previous notices (e.g., GRN 683), and discuss why they would not be expected to pose a safety concern from the intended use.
15. We note that a recent study on rapeseed protein isolate was published (Xiong *et al.*, 2022).
 - a. Please discuss if this study presents additional safety concerns for the article of commerce or contradicts the current GRAS conclusion.
 - b. Please also perform an updated literature review from 2021 to present and discuss if

any additional studies relevant to the safety of canola concentrate were identified that would contradict the current GRAS conclusion.

References cited:

Xiong Z, Fu Y, Yao J, Zhang N, He R, Ju X, Wang Z. Removal of anti-nutritional factors of rapeseed protein isolate (RPI) and toxicity assessment of RPI. *Food Funct.* 2022 Jan 24;13(2):664-674. doi: 10.1039/d1fo03217h. PMID: 34933325.

Additionally, we received the following questions from USDA FSIS regarding their review of the uses of GRN 1122 concerning products within their purview. Please respond to the following and we will pass your responses along to them.

Please provide Safety Data Sheet (SDS) for the at use concentrations of the substance and include a description of how the use of this technology will not adversely affect the safety of FSIS inspectors. Workplace safety and health hazards include inhalation, direct skin contact (skin, eyes, mouth), and fire/explosion caused by exposure to the product, its working solution or dry mixture and potential by-products formed and/or off-gassed during the application process. The employee safety information should demonstrate how the New Technology will not “jeopardize the safety of Federal inspection personnel” as specified in the [FSIS Compliance Guideline Procedures for New Technology Notifications and Protocols, April 2015](#). FSIS workplace and employee safety must be specifically addressed. Please refer to Appendix A on p. 17, Workplace Safety and Health Criteria, for clarification on what to provide in the response. For additional clarity with respect to employee safety, the following are examples of information that are typically needed by FSIS’ employee safety and health group;

1. Potential workplace exposures that could result from inhalation and direct contact during use of the substance/technology. This information is required in addition to a SDS to determine accurate hazard potential and recommended exposure control measures for IPP work areas in accordance with Occupational Safety and Health Administration (OSHA) regulations: 29 CFR 1910.1200, Hazard Communication, 29 CFR 1910.132, Personal Protective Equipment, and 29 CFR 1910.1000, Air Contaminants. The information should be included as a specific section in each of the protocols.
2. If the SDS workplace hazards/precautions do not apply to the type of exposure that would be expected for the FSIS IPP, please have the submitter provide specific information (per the April 2015 FSIS Compliance Guideline Procedures) for the actual type of exposures expected.
3. If no IPP workplace exposures are expected and no control measures are required, please have the submitter state this and provide the reasons why (e.g., such as the substance “as used” [for all concentrations] is not hazardous by inhalation or direct contact and/or IPP would not be exposed to the substance based on the system design, operation and/or control measures that will be in place).
4. Please also indicate how will FSIS IPP be informed of the above information so that it is clear that the information contained in the SDS for the concentrate does not apply to their actual workplace exposure.
5. Are there any potential hazards from chemical mixing or low pH as a result of discharges of the various solutions to floor drains? Are dedicated drain lines or any other enclosures

required?

6. With respect to potential airborne exposures to FSIS IPP in the use/application areas, does the submitter have air sampling results taken during the use of the various concentrations of the technology in the listed mixture?
7. The intended use of this product in FSIS meat and poultry products is apparently as a binder/extender. The suitability support provided in Appendix 6 does sufficiently support no significant difference in yield and other organoleptic qualities when used as a partial replacement for another binder in a processed meat and poultry product, such as sausage. However, **additional suitability support is needed:**

- a. No suitability data was provided for **whole muscle meat and poultry products at the maximum proposed use level**. We would need to see similar data as provided in Appendix 6 for:

Whole muscle red meat control containing no other binders, extenders, or moisture retention agents, as compared to a whole muscle red meat product containing 15% isolated canola product.

Whole muscle poultry control containing no other binders, extenders, or moisture retention agents as compared to a whole muscle poultry product containing 15% isolated canola product.

Responses may be sent in an email or in a separate document. We respectfully request a response within 10 business days. If you are unable to complete the response within that time frame, please contact me to discuss further options.

If you have any additional questions or concerns, please don't hesitate to contact me at stephen.difranco@fda.hhs.gov or by phone at 240.402.2710.

Best,

Steve

Stephen DiFranco, PhD

Regulatory Review Scientist/Chemist

Center for Food Safety and Applied Nutrition

Office of Food Additive Safety

Division of Food Ingredients

U.S. Food and Drug Administration

Tel: 240-402-2710

stephen.difranco@fda.hhs.gov



CAUTION: This email, including any attachments, is confidential. If you are not the intended recipient, please notify the sender and delete the email and any attachments from your system.

In addition, you must not use, distribute or reproduce this email or any attachments. Opinions and other information in this email and any attachments which do not relate to the official business of Argenta are neither given by nor endorsed by Argenta. While Argenta uses anti-virus software, Argenta accepts no liability for any viruses in this email or any attachment, or for any effects this email or any attachment may have on your network or computer system.

CAUTION: This email, including any attachments, is confidential. If you are not the intended recipient, please notify the sender and delete the email and any attachments from your system. In addition, you must not use, distribute or reproduce this email or any attachments. Opinions and other information in this email and any attachments which do not relate to the official business of Argenta are neither given by nor endorsed by Argenta. While Argenta uses anti-virus software, Argenta accepts no liability for any viruses in this email or any attachment, or for any effects this email or any attachment may have on your network or computer system.

Este correo electrónico y los archivos adjuntos, enviados por Pen & Tec Consulting SLU, que opera bajo el nombre comercial de Argenta® (Argenta), son confidenciales y pueden estar protegidos por ley. Si usted no es el destinatario, cualquier divulgación, reproducción, copia, distribución u otro tipo de difusión o uso de esta comunicación está estrictamente prohibido. Si ha recibido esta transmisión por error, notifíquelo al remitente y elimine inmediatamente el correo electrónico y cualquier archivo adjunto de su sistema. Argenta no emite ni respalda las opiniones y demás información contenida en este correo electrónico y en sus anexos que no estén relacionadas con las actividades oficiales de Argenta. Aunque Argenta utiliza software antivirus, Argenta no acepta ninguna responsabilidad por cualquier virus en este correo electrónico o cualquier archivo adjunto, o por cualquier efecto que este correo electrónico o cualquier archivo adjunto pueda tener en su red o sistema informático. Argenta registra y almacena los correos electrónicos enviados a nosotros o a nuestros afiliados de acuerdo con nuestras políticas y procedimientos internos. Consulte www.pentec-consulting.eu para obtener información sobre Argenta y/o nuestra política de privacidad.

This email and any attached file(s), sent by Pen & Tec Consulting SLU trading as Argenta® (Argenta), are confidential and may be legally privileged. If you are not the intended recipient, any disclosure, reproduction, copying, distribution, or other dissemination or use of this communication is strictly prohibited. If you have received this transmission in error, please notify the sender and delete the email and any attachments from your system immediately. Opinions and other information in this email and any attachments which do not relate to the official business of Argenta are neither given by nor endorsed by Argenta. While Argenta uses anti-virus software, Argenta accepts no liability for any viruses in this email or any attachment, or for any effects this email or any attachment may have on your network or computer system. Argenta records and stores emails sent to us or our affiliates in keeping with our internal policies and procedures. Please see www.pentec-consulting.eu for information regarding Argenta and/or our privacy policy.

Este correo electrónico y los archivos adjuntos, enviados por Pen & Tec Consulting SLU, que opera bajo el nombre comercial de Argenta® (Argenta), son confidenciales y pueden estar protegidos por ley. Si usted no es el destinatario, cualquier divulgación, reproducción, copia, distribución u otro tipo de difusión o uso de esta comunicación está estrictamente prohibido. Si ha recibido esta transmisión por error, notifíquelo al remitente y elimine inmediatamente el correo electrónico y cualquier archivo adjunto de su sistema. Argenta no emite ni respalda las opiniones y demás información contenida en este correo electrónico y en sus anexos que no estén relacionadas con las actividades oficiales de Argenta. Aunque Argenta utiliza software antivirus, Argenta no acepta ninguna responsabilidad por cualquier virus en este correo electrónico o cualquier archivo adjunto, o por cualquier efecto que este correo electrónico o cualquier archivo adjunto pueda tener en su red o sistema informático. Argenta registra y almacena los correos electrónicos enviados a nosotros o a nuestros afiliados de acuerdo con nuestras políticas y procedimientos internos. Consulte www.pentec-consulting.eu para obtener información sobre Argenta y/o nuestra política de privacidad.

This email and any attached file(s), sent by Pen & Tec Consulting SLU trading as Argenta® (Argenta), are confidential and may be legally privileged. If you are not the intended recipient, any disclosure, reproduction, copying, distribution, or other dissemination or use of this communication is strictly prohibited. If you have received this transmission in error, please notify the sender and delete the email and any attachments from your system immediately. Opinions and other information in this email and any attachments which do not relate to the official business of Argenta are neither given by nor endorsed by Argenta. While Argenta uses anti-virus software, Argenta accepts no liability for any viruses in this email or any attachment, or for any effects this email or any attachment may have on your

network or computer system. Argenta records and stores emails sent to us or our affiliates in keeping with our internal policies and procedures. Please see www.pentec-consulting.eu for information regarding Argenta and/or our privacy policy.

From: [Justyna Pałasińska](#)
To: [DiFranco, Stephen](#)
Subject: Re: [EXTERNAL] GRN 1122 canola concentrate status
Date: Friday, March 29, 2024 6:10:18 AM
Attachments: [image001.png](#)
[image007.png](#)
[image008.png](#)
[image009.png](#)
[image010.png](#)
[image011.png](#)
[image012.png](#)

CAUTION: This email originated from outside of the organization. Do not click links or open attachments unless you recognize the sender and know the content is safe.

Many thanks for sharing this information, Stephen.

I will get back to you on this as soon as possible, hopefully next week.

Kind regards,

Justyna Pałasińska

Regulatory Affairs Director – Human Nutrition, Argenta Barcelona



M [+34 682 894 653](tel:+34682894653) T [+34 936 758 015](tel:+34936758015)

www.argentaglobal.com

La información contenida en este mensaje y/o archivo(s) adjunto(s), enviada desde Pen & Tec Consulting SLU cotiza como Argenta, es confidencial/privilegiada y está destinada a ser leída sólo por la(s) persona(s) a la(s) que va dirigida. Le recordamos que sus datos han sido incorporados en el sistema de tratamiento de Pen & Tec Consulting SLU cotiza como Argenta, y que siempre y cuando se cumplan los requisitos exigidos por la normativa, usted podrá ejercer sus derechos de acceso, rectificación, limitación de tratamiento, supresión, portabilidad y oposición/revocación, en los términos que establece la normativa vigente en materia de protección de datos, dirigiendo su petición a la dirección postal OneCoWork, Portal de l'Àngel 40, 08002, Barcelona o bien a través de correo electrónico info@pentec-consulting.eu. Si usted lee este mensaje y no es el destinatario señalado, el empleado o el agente responsable de entregar el mensaje al destinatario, o ha recibido esta comunicación por error, le informamos que está totalmente prohibida, y puede ser ilegal, cualquier divulgación, distribución o reproducción de esta comunicación, y le rogamos que nos lo notifique inmediatamente y nos devuelva el mensaje original a la dirección arriba mencionada. Gracias.

The information contained in this message and/or attached file(s), sent by Pen & Tec Consulting SLU trading as Argenta, is confidential/privileged and is intended to be read solely by the person(s) to whom it is addressed. We hereby inform you that your data will be incorporated into the processing system owned by Pen & Tec Consulting SLU, and that provided it complies with the requirements included in the law, you may exercise the rights of access, rectification, limitation of processing, deletion, portability and opposition by sending your request to the postal address OneCoWork, Portal de l'Àngel 40, 08002, Barcelona or to the email address info@pentec-consulting.eu. If you read this message and you are neither the intended recipient, employee or agent in charge of delivering the message to the recipient, or if you have received this message as the result of an error, we hereby inform you that distributing, sharing or reproducing any part of this message is totally forbidden and may be illegal. As a result, we request that you immediately inform us of the error and return this message to the address mentioned above. Thank you.

From: DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>

Date: Thursday, 28 March 2024 at 20:47

To: Justyna Pałasińska <justyna.palasinaska@argentaglobal.com>

Subject: RE: [EXTERNAL] GRN 1122 canola concentrate status

Hello Justyna,

I got feedback from FSIS about their review of GRN 1122. They send the following:

I have now completed the review of the documentation submitted for the approval of the above-referenced compound. I noted that it contains Lead (≤ 0.5 mg/kg), Arsenic (≤ 0.2 mg/kg), Cadmium (≤ 0.2 mg/kg), and Mercury (≤ 0.1 mg/kg). OSHA has established OEL for these substances at 0.05 mg/m³, 0.01 mg/m³, 0.01 mg/m³, 0.025 mg/m³ (depending on presentation) respectively.

To finalize my analysis, I require the composition in mg/m³ of each of these elements or the density so I may calculate their composition accurately and evaluate them against their OSHA standards.

Are you able to provide the density of the canola concentrate? I believe this is the easiest way to answer their questions. From the density and the specified ppm levels, the reviewer should be able to calculate the maximum amount by weight of each heavy metal contaminate for a given volume of canola concentrate.

Best,

Steve

Stephen DiFranco, PhD

Regulatory Review Scientist/Chemist

Center for Food Safety and Applied Nutrition
Office of Food Additive Safety
Division of Food Ingredients
U.S. Food and Drug Administration
Tel: 240-402-2710
stephen.difranco@fda.hhs.gov



From: Justyna Pałasińska <justyna.palasinska@argentaglobal.com>

Sent: Monday, March 4, 2024 5:04 AM

To: DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>

Subject: Re: [EXTERNAL] GRN 1122 canola concentrate status

CAUTION: This email originated from outside of the organization. Do not click links or open attachments unless you recognize the sender and know the content is safe.

Many thanks for the update, Stephen. We look forward to hearing an update, hopefully soon!

Kind regards,

Justyna Pałasińska

Regulatory Affairs Director – Human Nutrition, Argenta Barcelona



M [+34 682 894 653](tel:+34682894653) T [+34 936 758 015](tel:+34936758015)

www.argentaglobal.com

La información contenida en este mensaje y/o archivo(s) adjunto(s), enviada desde Pen & Tec Consulting SLU cotiza como Argenta, es confidencial/privilegiada y está destinada a ser leída sólo por la(s) persona(s) a la(s) que va dirigida. Le recordamos que sus datos han sido incorporados en el sistema de tratamiento de Pen & Tec Consulting SLU cotiza como Argenta, y que siempre y cuando se cumplan los requisitos exigidos por la normativa, usted podrá ejercer sus derechos de acceso, rectificación, limitación de tratamiento, supresión, portabilidad y oposición/revocación, en los términos que establece la normativa vigente en materia de protección de datos, dirigiendo su petición a la dirección postal Pl. Ausias March 1, 4 planta 08195, Sant Cugat del Vallès (Barcelona) o bien a través de correo electrónico info@pentec-consulting.eu. Si usted lee este mensaje y no es el destinatario señalado, el empleado o el agente responsable de entregar el mensaje al destinatario, o ha recibido esta comunicación por error, le informamos que está totalmente prohibida, y puede ser ilegal, cualquier divulgación, distribución o reproducción de esta comunicación, y le rogamos que nos lo notifique inmediatamente y nos devuelva el mensaje original a la dirección arriba mencionada. Gracias.

The information contained in this message and/or attached file(s), sent by Pen & Tec Consulting SLU trading as Argenta, is confidential/privileged and is intended to be read solely by the person(s) to whom it is addressed. We hereby inform you that your data will be incorporated into the processing system owned by Pen & Tec Consulting SLU, and that provided it complies with the requirements included in the law, you may exercise the rights of access, rectification, limitation of processing, deletion, portability and opposition by sending your request to the postal address Pl. Ausias March 1, 4 floor 08195, Sant Cugat del Valles (Barcelona) or to the email address info@pentec-consulting.eu. If you read this message and you are neither the intended recipient, employee or agent in charge of delivering the message to the recipient, or if you have received this message as the result of an error, we hereby inform you that distributing, sharing or reproducing any part of this message is totally forbidden and may be illegal. As a result, we request that you immediately inform us of the error and return this message to the address mentioned above. Thank you.

From: DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>

Date: Monday, 26 February 2024 at 17:20

To: Justyna Pałasińska <justyna.palasinaska@argentaglobal.com>

Subject: RE: [EXTERNAL] GRN 1122 canola concentrate status

Hello Justyna,

Regarding GRN 1122; FDA has completed its review and has drafted a response letter. Unfortunately, we cannot move forward before USDA-FSIS completes their review of the uses under their jurisdiction. I have been periodically inquiring with FSIS as to the status and will get this to you as soon as possible.

We appreciate your continued patience.

Best,

Steve

Stephen DiFranco, PhD

Regulatory Review Scientist/Chemist

**Center for Food Safety and Applied Nutrition
Office of Food Additive Safety
Division of Food Ingredients**

U.S. Food and Drug Administration

Tel: 240-402-2710

stephen.difranco@fda.hhs.gov



From: Justyna Pałasińska <justyna.palasinaska@argentaglobal.com>
Sent: Wednesday, February 14, 2024 12:07 PM
To: Premarkt <Premarkt@fda.hhs.gov>
Cc: DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>; Ioannis Kartanos <ioannis.kartanos@argentaglobal.com>
Subject: [EXTERNAL] GRN 1122 canola concentrate status

CAUTION: This email originated from outside of the organization. Do not click links or open attachments unless you recognize the sender and know the content is safe.

Dear HHS team,

I am writing to enquire about a GRAS notice that was submitted to the FDA & filed April 19, 2023 (GRN 1122). We have been in touch with Mr Stephen DiFranco & at the beginning of December he has informed us that the FDA reviews are complete & the notice is now with USDA-FSIS.

Mr DiFranco has been very helpful through the whole process. However, we have tried to contact him several times since December without success. We were wondering if there is someone else we can get in touch with for an update on this application. We would be happy to provide any information that would help finalize the process.

I look forward to hearing from you.

Kind regards,

Justyna Pałasińska

Regulatory Affairs Director – Human Nutrition, Argenta Barcelona



M +34 682 894 653 T +34 936 758 015

www.argentaglobal.com

La información contenida en este mensaje y/o archivo(s) adjunto(s), enviada desde Pen & Tec Consulting SLU cotiza como Argenta, es confidencial/privilegiada y está destinada a ser leída sólo por la(s) persona(s) a la(s) que va dirigida. Le recordamos que sus datos han sido incorporados en el sistema de tratamiento de Pen & Tec Consulting SLU cotiza como Argenta, y que siempre y cuando se cumplan los requisitos exigidos por la normativa, usted podrá ejercer sus derechos de acceso, rectificación, limitación de tratamiento, supresión, portabilidad y oposición/revocación, en los términos que establece la normativa vigente en materia de protección de datos, dirigiendo su petición a la dirección postal Pl. Ausias March 1, 4 planta 08195, Sant Cugat del Vallès (Barcelona) o bien a través de correo electrónico info@pentec-consulting.eu. Si usted lee este mensaje y no es el destinatario señalado, el empleado o el agente responsable de entregar el mensaje al destinatario, o ha recibido esta comunicación por error, le informamos que está totalmente prohibida, y puede ser ilegal, cualquier divulgación, distribución o reproducción de esta comunicación, y le rogamos que nos lo notifique inmediatamente y nos devuelva el mensaje original a la dirección arriba mencionada. Gracias.

The information contained in this message and/or attached file(s), sent by Pen & Tec Consulting SLU trading as Argenta, is confidential/privileged and is intended to be read solely by the person(s) to whom it is addressed. We hereby inform you that your data will be incorporated into the processing system owned by Pen & Tec Consulting SLU, and that provided it complies with the requirements

included in the law, you may exercise the rights of access, rectification, limitation of processing, deletion, portability and opposition by sending your request to the postal address Pl. Ausias March 1, 4 floor 08195, Sant Cugat del Valles (Barcelona) or to the email address info@pentec-consulting.eu. If you read this message and you are neither the intended recipient, employee or agent in charge of delivering the message to the recipient, or if you have received this message as the result of an error, we hereby inform you that distributing, sharing or reproducing any part of this message is totally forbidden and may be illegal. As a result, we request that you immediately inform us of the error and return this message to the address mentioned above. Thank you.

From: Justyna Pałasińska <justyna.palasinaska@argentaglobal.com>

Date: Wednesday, 31 January 2024 at 17:53

To: Justyna Pałasińska <justyna.palasinaska@argentaglobal.com>, DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>

Cc: Ioannis Kartanos <ioannis.kartanos@argentaglobal.com>

Subject: Re: [EXTERNAL] GRN 1122 canola concentrate - update contact person

Dear Steve,

I hope this e-mail finds you well. I was wondering if there are any updates on the finalization of this notification?

Is there any additional information that needs to be provided?

Kind regards,

Justyna Pałasińska

Regulatory Affairs Director – Human Nutrition, Argenta Barcelona



M [+34 682 894 653](tel:+34682894653) T [+34 936 758 015](tel:+34936758015)

www.argentaglobal.com

La información contenida en este mensaje y/o archivo(s) adjunto(s), enviada desde Pen & Tec Consulting SLU cotiza como Argenta, es confidencial/privilegiada y está destinada a ser leída sólo por la(s) persona(s) a la(s) que va dirigida. Le recordamos que sus datos han sido incorporados en el sistema de tratamiento de Pen & Tec Consulting SLU cotiza como Argenta, y que siempre y cuando se cumplan los requisitos exigidos por la normativa, usted podrá ejercer sus derechos de acceso, rectificación, limitación de tratamiento, supresión, portabilidad y oposición/revocación, en los términos que establece la normativa vigente en materia de protección de datos, dirigiendo su petición a la dirección postal Pl. Ausias March 1, 4 planta 08195, Sant Cugat del Vallès (Barcelona) o bien a través de correo electrónico info@pentec-consulting.eu. Si usted lee este mensaje y no es el destinatario señalado, el empleado o el agente responsable de entregar el mensaje al destinatario, o ha recibido esta comunicación por error, le informamos que está totalmente prohibida, y puede ser ilegal, cualquier divulgación, distribución o reproducción de esta comunicación, y le rogamos que nos lo notifique inmediatamente y nos devuelva el mensaje original a la dirección arriba mencionada. Gracias.

The information contained in this message and/or attached file(s), sent by Pen & Tec Consulting SLU trading as Argenta, is confidential/privileged and is intended to be read solely by the person(s) to whom it is addressed. We hereby inform you that your data will be incorporated into the processing system owned by Pen & Tec Consulting SLU, and that provided it complies with the requirements included in the law, you may exercise the rights of access, rectification, limitation of processing, deletion, portability and opposition by sending your request to the postal address Pl. Ausias March 1, 4 floor 08195, Sant Cugat del Valles (Barcelona) or to the email address info@pentec-consulting.eu. If you read this message and you are neither the intended recipient, employee or agent in charge of delivering the message to the recipient, or if you have received this message as the result of an error, we hereby inform you that distributing, sharing or reproducing any part of this message is totally forbidden and may be illegal. As a result, we request that you immediately inform us of the error and return this message to the address mentioned above. Thank you.

From: Justyna Pałasińska <justyna@pentec-consulting.eu>

Date: Friday, 22 December 2023 at 13:31

To: DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>

Cc: Ioannis Kartanos <ioannis@pentec-consulting.eu>

Subject: Re: [EXTERNAL] GRN 1122 canola concentrate - update contact person

Dear Stephen,

Many thanks for confirming the change of contact person.

I'm following up on my colleague Ioannis e-mail from 12/12/2023. As he mentioned, we have already provided the answers to the questions to USDA-FSIS. Nevertheless, I have included them in a separate document.

Please let us know in case any additional information is required.

In the meantime, we wish you a Happy Holiday Season & all the best in 2024!

Kind regards,

Ing. Justyna Pałasińska

Regulatory Affairs Director – Human Nutrition | Pen & Tec Consulting

T +34 936 758 015 M +34 682 894 653 F +34 936 758 016 www.pentec-consulting.eu

Pl. Ausias March 1 | 4th floor D01 | 08195 Sant Cugat del Vallès | Barcelona | Spain

PEN + TEC
CONSULTING
PART OF THE ARGENTA GROUP

La información contenida en este mensaje y/o archivo(s) adjunto(s), enviada desde Pen & Tec Consulting SLU, es confidencial/privilegiada y está destinada a ser leída sólo por la(s) persona(s) a la(s) que va dirigida. Le recordamos que sus datos han sido incorporados en el sistema de tratamiento de Pen & Tec Consulting SLU y que siempre y cuando se cumplan los requisitos exigidos por la normativa, usted podrá ejercer sus derechos de acceso, rectificación, limitación de tratamiento, supresión, portabilidad y oposición/revocación, en los términos que establece la normativa vigente en materia de protección de datos, dirigiendo su petición a la dirección postal Pl. Ausias March 1, 4 planta 08195, Sant Cugat del Vallès (Barcelona) o bien a través de correo electrónico info@pentec-consulting.eu. Si usted lee este mensaje y no es el destinatario señalado, el empleado o el agente responsable de entregar el mensaje al destinatario, o ha recibido esta comunicación por error, le informamos que está totalmente prohibida, y puede ser ilegal, cualquier divulgación, distribución o reproducción de esta comunicación, y le rogamos que nos lo notifique inmediatamente y nos devuelva el mensaje original a la dirección arriba mencionada. Gracias.

The information contained in this message and/or attached file(s), sent by Pen & Tec Consulting SLU, is confidential/privileged and is intended to be read solely by the person(s) to whom it is addressed. We hereby inform you that your data will be incorporated into the processing system owned by Pen & Tec Consulting SLU, and that provided it complies with the requirements included in the law, you may exercise the rights of access, rectification, limitation of processing, deletion, portability and opposition by sending your request to the postal address Pl. Ausias March 1, 4 floor 08195, Sant Cugat del Valles (Barcelona) or to the email address info@pentec-consulting.eu. If you read this message and you are neither the intended recipient, employee or agent in charge of delivering the message to the recipient, or if you have received this message as the result of an error, we hereby inform you that distributing, sharing or reproducing any part of this message is totally forbidden and may be illegal. As a result, we request that you immediately inform us of the error and return this message to the address mentioned above. Thank you.

From: DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>

Date: Tuesday, 5 December 2023 at 19:05

To: Nikolaas Tilkin-Franssens <niko@pentec-consulting.eu>

Cc: Justyna Pałasińska <justyna@pentec-consulting.eu>

Subject: RE: [EXTERNAL] GRN 1122 canola concentrate - update contact person

Hello Niko and Justyna,

Just confirming the change of contact person for GRN 1122.

As for timeline, FDA reviews are complete but USDA-FSIS is requesting a few pieces of information regarding the uses of canola concentrate under USDA jurisdiction, namely:

Please provide SDS for the at use concentrations of the substance and include a description of how the use of this technology will not adversely affect the safety of FSIS inspectors. Workplace safety and health hazards include inhalation, direct skin contact (skin, eyes, mouth), and fire/explosion caused by exposure to the product, its working solution or dry mixture and potential by-products formed and/or off-gassed during the application process. The employee safety information should demonstrate how the New Technology will not “jeopardize the safety of Federal inspection personnel” as specified in the [FSIS Compliance Guideline Procedures for New Technology Notifications and Protocols, April 2015](#).

Although I'm not anticipating any issues here, FSIS workplace and employee safety must be specifically addressed. Please refer to Appendix A on page 17, Workplace Safety and Health Criteria, for clarification on what to provide in the response. For additional clarity with respect to employee safety, the following are examples of information that are typically needed by FSIS' employee safety and health group;

1. Potential workplace exposures that could result from inhalation and direct contact during use of the substance/technology. This information is required in addition to a Safety Data Sheet (SDS) to determine accurate hazard potential and recommended exposure control measures for IPP work areas in accordance with Occupational Safety and Health Administration (OSHA) regulations: 29 CFR 1910.1200, Hazard Communication, 29 CFR 1910.132, Personal Protective Equipment, and 29 CFR 1910.1000, Air Contaminants. The information should be included as a specific section in each of the protocols.
2. If the SDS workplace hazards/precautions do not apply to the type of exposure that would be expected for the FSIS IPP, please have the submitter provide specific information (per the April 2015 FSIS Compliance Guideline Procedures) for the actual type of exposures expected.
3. If no IPP workplace exposures are expected and no control measures are required, please have the submitter state this and provide the reasons why (e.g., such as the substance “as used” [for all concentrations] is not hazardous by inhalation or direct contact and/or IPP would not be exposed to the substance based on the system design, operation and/or control measures that will be in place).
4. Please also indicate how will FSIS IPP be informed of the above information so that it is clear that the information contained in the SDS for the concentrate does not apply to their actual workplace exposure.
5. Are there any potential hazards from chemical mixing or low pH as a result of discharges of the various solutions to floor drains? Are dedicated drain lines or any other enclosures required?
6. With respect to potential airborne exposures to FSIS IPP in the use/application areas, does the submitter have air sampling results taken during the use of the various concentrations of the technology in the listed mixture?

Suitability data;

The intended use of this product in FSIS meat and poultry products is apparently as a binder/extender. The suitability support provided in Appendix 6 does sufficiently support no significant difference in yield and other organoleptic qualities when used as a partial replacement for another binder in a processed meat and poultry product, such as sausage.

However, **additional suitability support is needed:**

- No suitability data was provided for **whole muscle meat and poultry products at the maximum proposed use level**. We would need to see similar data as provided in Appendix 6 for:
 - Whole muscle red meat control containing no other binders, extenders, or moisture

- retention agents, as compared to a whole muscle red meat product containing 15% isolated canola product.
- Whole muscle poultry control containing no other binders, extenders, or moisture retention agents as compared to a whole muscle poultry product containing 15% isolated canola product.

You responses can be emailed directly to me and I will distribute to the necessary staff inside FDA and USDA.

Thanks,

Steve

Stephen DiFranco, PhD

Regulatory Review Scientist/Chemist

Center for Food Safety and Applied Nutrition
Office of Food Additive Safety
Division of Food Ingredients
U.S. Food and Drug Administration
Tel: 240-402-2710
stephen.difranco@fda.hhs.gov



From: Nikolaas Tilkin-Franssens <niko@pentec-consulting.eu>
Sent: Monday, December 4, 2023 4:36 AM
To: DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>
Cc: Justyna Pałasińska <justyna@pentec-consulting.eu>
Subject: [EXTERNAL] GRN 1122 canola concentrate - update contact person

CAUTION: This email originated from outside of the organization. Do not click links or open attachments unless you recognize the sender and know the content is safe.

Hi Mr. DiFranco,

Hope this email finds you well.

Due to a change in position, I will no longer be the contact person for the GRAS Notice 1122 (Canola Protein Concentrate). Could you please update your records to ascertain that Justyna Pałasińska, in copy to this email, is informed of any relevant updates?

Could you kindly confirm receipt of this email for our records?

And if possible, let us know if there is any estimate on the timeline re. finalization of the review of this GRAS Notice.

Many thanks for your great and flexible support on this application.

Kind regards,

Niko

Nikolaas Tilkin-Franssens

Regulatory Affairs Manager | Pen & Tec Consulting

T +34 936 758 015 M +34 649 840 417 F +34 936 758 016 www.pentec-consulting.eu

Pl. Ausias March 1 | 4th floor D01 | 08195 Sant Cugat del Vallès | Barcelona | Spain

PEN + TEC
CONSULTING
PART OF THE ARGENTA GROUP

La información contenida en este mensaje y/o archivo(s) adjunto(s), enviada desde Pen & Tec Consulting SLU, es confidencial/privilegiada y está destinada a ser leída sólo por la(s) persona(s) a la(s) que va dirigida. Le recordamos que sus datos han sido incorporados en el sistema de tratamiento de Pen & Tec Consulting SLU y que siempre y cuando se cumplan los requisitos exigidos por la normativa, usted podrá ejercer sus derechos de acceso, rectificación, limitación de tratamiento, supresión, portabilidad y oposición/revocación, en los términos que establece la normativa vigente en materia de protección de datos, dirigiendo su petición a la dirección postal Pl. Ausias March 1, 4 planta 08195, Sant Cugat del Vallès (Barcelona) o bien a través de correo electrónico info@pentec-consulting.eu. Si usted lee este mensaje y no es el destinatario señalado, el empleado o el agente responsable de entregar el mensaje al destinatario, o ha recibido esta comunicación por error, le informamos que está totalmente prohibida, y puede ser ilegal, cualquier divulgación, distribución o reproducción de esta comunicación, y le rogamos que nos lo notifique inmediatamente y nos devuelva el mensaje original a la dirección arriba mencionada. Gracias.

The information contained in this message and/or attached file(s), sent by Pen & Tec Consulting SLU, is confidential/privileged and is intended to be read solely by the person(s) to whom it is addressed. We hereby inform you that your data will be incorporated into the processing system owned by Pen & Tec Consulting SLU, and that provided it complies with the requirements included in the law, you may exercise the rights of access, rectification, limitation of processing, deletion, portability and opposition by sending your request to the postal address Pl. Ausias March 1, 4 floor 08195, Sant Cugat del Valles (Barcelona) or to the email address info@pentec-consulting.eu. If you read this message and you are neither the intended recipient, employee or agent in charge of delivering the message to the recipient, or if you have received this message as the result of an error, we hereby inform you that distributing, sharing or reproducing any part of this message is totally forbidden and may be illegal. As a result, we request that you immediately inform us of the error and return this message to the address mentioned above. Thank you.

From: DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>

Date: Monday, 17 July 2023 at 17:01

To: Nikolaas Tilkin-Franssens <niko@pentec-consulting.eu>

Subject: RE: [EXTERNAL] Re: GRN 1122 canola concentrate items for clarification -
Reply

Hello Niko,

No problem—Ill distribute this to the team for review.

Best,

Steve

Stephen DiFranco, PhD

Regulatory Review Scientist/Chemist

**Center for Food Safety and Applied Nutrition
Office of Food Additive Safety**

Division of Food Ingredients
U.S. Food and Drug Administration
Tel: 240-402-2710
stephen.difranco@fda.hhs.gov



From: Nikolaas Tilkin-Franssens <niko@pentec-consulting.eu>
Sent: Monday, July 17, 2023 10:35 AM
To: DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>
Subject: [EXTERNAL] Re: GRN 1122 canola concentrate items for clarification - Reply

CAUTION: This email originated from outside of the organization. Do not click links or open attachments unless you recognize the sender and know the content is safe.

Hi Stephen,

Apologies for this inconvenience.

We noticed that the reply to question 9 refers to Canola protein isolate (as per GRN 1103). I have updated the answer for it to be mentioning Canola protein concentrate (GRN 1122).

We hope this can be taken into consideration.

Kind regards,

Nikolaas Tilkin-Franssens

Regulatory Affairs Manager | Pen & Tec Consulting

T +34 936 758 015 **M** +34 649 840 417 **F** +34 936 758 016 www.pentec-consulting.eu

Pl. Ausias March 1 | 4th floor D01 | 08195 Sant Cugat del Vallès | Barcelona | Spain



La información contenida en este mensaje y/o archivo(s) adjunto(s), enviada desde Pen & Tec Consulting SLU, es confidencial/privilegiada y está destinada a ser leída sólo por la(s) persona(s) a la(s) que va dirigida. Le recordamos que sus datos han sido incorporados en el sistema de tratamiento de Pen & Tec Consulting SLU y que siempre y cuando se cumplan los requisitos exigidos por la normativa, usted podrá ejercer sus derechos de acceso, rectificación, limitación de tratamiento, supresión, portabilidad y oposición/revocación, en los términos que establece la normativa vigente en materia de protección de datos, dirigiendo su petición a la dirección postal Pl. Ausias March 1, 4 planta 08195, Sant Cugat del Vallès (Barcelona) o bien a través de correo electrónico info@pentec-consulting.eu. Si usted lee este mensaje y no es el destinatario señalado, el empleado o el agente responsable de entregar el mensaje al destinatario, o ha recibido esta comunicación por error, le informamos que está totalmente prohibida, y puede ser ilegal, cualquier divulgación, distribución o reproducción de esta comunicación, y le rogamos que nos lo notifique inmediatamente y nos devuelva el mensaje original a la dirección arriba mencionada. Gracias.

The information contained in this message and/or attached file(s), sent by Pen & Tec Consulting SLU, is confidential/privileged and is intended to be read solely by the person(s) to whom it is addressed. We hereby inform you that your data will be incorporated into the processing system owned by Pen & Tec Consulting SLU, and that provided it complies with the requirements included in the law, you may exercise the rights of access, rectification, limitation of processing, deletion, portability and opposition by sending your request to the postal address Pl. Ausias March 1, 4 floor 08195, Sant Cugat del Valles (Barcelona) or to the email address info@pentec-consulting.eu. If you read this message and you are neither the intended recipient, employee or agent in charge of delivering the message to the recipient, or if you have received this message as the result of an error, we hereby inform you that distributing, sharing or reproducing

any part of this message is totally forbidden and may be illegal. As a result, we request that you immediately inform us of the error and return this message to the address mentioned above. Thank you.

From: Nikolaas Tilkin-Franssens <niko@pentec-consulting.eu>
Date: Tuesday, 11 July 2023 at 17:03
To: DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>
Cc: Justyna Pałasińska <justyna@pentec-consulting.eu>
Subject: Re: GRN 1122 canola concentrate items for clarification - Reply

Dear Stephen,

Thank you for reaching out with the questions for clarification.
We have worked closely with Napiferyn to close the doubts.

Kindly find attached a Word file including the Questions&Answers, a report on the requested literature review, a SDS sheet as requested by the USDA-FSIS, and a report on the suitability assessment.

We remain available for any further questions or updates.

Thanks for taking the application in further consideration,
best regards,

Nikolaas Tilkin-Franssens

Regulatory Affairs Manager | Pen & Tec Consulting

T +34 936 758 015 **M** +34 649 840 417 **F** +34 936 758 016 www.pentec-consulting.eu

Pl. Ausias March 1 | 4th floor D01 | 08195 Sant Cugat del Vallès | Barcelona | Spain

PEN + TEC
CONSULTING

PART OF THE ARGENTA GROUP

La información contenida en este mensaje y/o archivo(s) adjunto(s), enviada desde Pen & Tec Consulting SLU, es confidencial/privilegiada y está destinada a ser leída sólo por la(s) persona(s) a la(s) que va dirigida. Le recordamos que sus datos han sido incorporados en el sistema de tratamiento de Pen & Tec Consulting SLU y que siempre y cuando se cumplan los requisitos exigidos por la normativa, usted podrá ejercer sus derechos de acceso, rectificación, limitación de tratamiento, supresión, portabilidad y oposición/revocación, en los términos que establece la normativa vigente en materia de protección de datos, dirigiendo su petición a la dirección postal Pl. Ausias March 1, 4 planta 08195, Sant Cugat del Vallès (Barcelona) o bien a través de correo electrónico info@pentec-consulting.eu. Si usted lee este mensaje y no es el destinatario señalado, el empleado o el agente responsable de entregar el mensaje al destinatario, o ha recibido esta comunicación por error, le informamos que está totalmente prohibida, y puede ser ilegal, cualquier divulgación, distribución o reproducción de esta comunicación, y le rogamos que nos lo notifique inmediatamente y nos devuelva el mensaje original a la dirección arriba mencionada. Gracias.

The information contained in this message and/or attached file(s), sent by Pen & Tec Consulting SLU, is confidential/privileged and is intended to be read solely by the person(s) to whom it is addressed. We hereby inform you that your data will be incorporated into the processing system owned by Pen & Tec Consulting SLU, and that provided it complies with the requirements included in the law, you may exercise the rights of access, rectification, limitation of processing, deletion, portability and opposition by sending your request to the postal address Pl. Ausias March 1, 4 floor 08195, Sant Cugat del Valles (Barcelona) or to the email address info@pentec-consulting.eu. If you read this message and you are neither the intended recipient, employee or agent in charge of delivering the message to the recipient, or if you have received this message as the result of an error, we hereby inform you that distributing, sharing or reproducing any part of this message is totally forbidden and may be illegal. As a result, we request that you immediately inform us of the error and return this message to the address mentioned above. Thank you.

From: DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>
Date: Wednesday, 28 June 2023 at 17:41
To: Nicoleta Pasecinic <nicoleta@pentec-consulting.eu>

Cc: Nikolaas Tilkin-Franssens <niko@pentec-consulting.eu>

Subject: [EXTERNAL]: GRN 1122 canola concentrate items for clarification

CAUTION: This email originated from outside of the organization. Do not click links or open attachments unless you recognize the sender and know the content is safe.

Hello Ms. Pasecinic,

After evaluating NapiFeryn's GRAS Notice No. GRN 1122 on canola concentrate we noted a few issues that should be addressed. Please respond to the following points for clarification:

1. On p. 9, NapiFeryn states that the major storage proteins in canola seed are cruciferins and napins, and that canola concentrate consists of 30-45% protein and 40-70% dietary fiber. Please provide the typical cruciferin content and napin content in canola concentrate.
2. Please confirm that all raw materials and processing aids used in the manufacturing process are used in accordance with the U.S. regulations, are GRAS for their respective uses or are the subject of an effective food contact notification. For the record, we note that the food additive regulations cited in Table 4 (p. 15) for ascorbic acid (21 CFR 182.8013), ethanol (21 CFR 184.1293), and ethyl acetate (21 CFR 173.228) do not appear to be applicable to your intended uses of these substances.
3. In Table 6 (p. 18-19), NapiFeryn provides the results from the batch analyses for heavy metals. We would like to bring to your attention a relevant FDA's "[Closer to Zero](#)" initiative that focuses on reducing the levels of heavy metals in foods and recommend that you lower the specification limits for heavy metal to better reflect the batch analyses results and to be as low as possible.
4. In Table 10 (p. 22), NapiFeryn provides batch analyses data for residual solvents and processing aids. In addition, in Table 21 (p. 50), you provided the results from the batch analyses for erucic acid in your canola concentrate ranging from 0.37% to < 0.1%.
Please include limits for residual ethanol, ethyl acetate, and sulphur dioxide as well as a limit for erucic acid in the specifications for canola concentrate and specify the analytical methods used to test for these parameters.
In addition, please provide an updated Tables 5 and 6 (p. 16-19) to include the additional specification parameters mentioned above, corresponding analytical methods, and batch analyses.
5. Please state that all analytical methods used to test batches were validated and are fit for their respective purpose.
6. Please state that canola concentrate is not intended for use in infant formula or in foods where standards of identity preclude its use.
7. In Table 15 (p.), NapiFeryn provides the results of the batch analyses for total plate count in

the raw material (rapeseed press cake). Please address the significant variation in the results (from <10 to 28,000 CFU/g) and discuss whether this will impact safety of the final ingredient.

8. On p. 19, NapiFeryn states that the levels of mycotoxins in canola concentrate are below the limit of quantitation (LOQ) and provide the results from the analyses of five batches to support your statement. Please clarify whether you expect mycotoxins to be present in canola concentrate manufactured in accordance with good manufacturing practices.
9. In Part 1.4 (p. 6) and Part 3.1 (p. 33), NapiFeryn states that the intended use of canola concentrate is as a source of protein and/or fiber, thickener, or texturizer. However, we note that on p. 33 you also state the intended use of canola concentrate is as a flavoring agent or binder in various comminuted or whole muscle meat and poultry products. In addition, in Appendix 3 (p. 5) you state that canola concentrate may also be used “to create a flavored salt” or as “a flavor enhancer like monosodium glutamate”. Please confirm these additional uses of canola concentrate are within the scope of GRN 001122.
10. On p. 10, the notifier describes the protein composition of canola concentrate, being primarily cruciferins, napin, oleosin, and squalene monooxygenase. However, the pivotal safety data provided appear to only be relevant to the cruciferin and napin fractions of the canola concentrate. Please provide a brief narrative to confirm the safety of oleosin and squalene monooxygenase exposure from the intended uses.
11. On p. 31-32 of the notice, the notifier clearly establishes that canola concentrate is intended to be substitutive to protein and fiber consumption and will not contribute to additional exposure to protein or fiber in general. Please elaborate on this conclusion, and clarify if the intended uses of canola concentrate are additive or substitutive to other canola protein products currently on the market (i.e., GRNs 327, 386, and 683)?
12. On p. 37, the notifier concludes exposure to canola concentrate from the intended uses is safe since the EDI reported is “still much lower (approximately 7- to 22-fold lower) than the no-observed-adverse-effect level (NOAEL) values established” for cruciferin- and napin-rich protein isolates in male rats following a 13-week oral exposure regimen (Mejia *et al.*, 2009a & 2009b). We note that an uncertainty factor, or margin of safety (MOS), of 100 (10 for interindividual variability × 10 for interspecies variability) is normally used when assessing safety of a food ingredient by comparing estimated human exposure levels to the NOAEL from animal toxicology data. Therefore, it is not clear why MOS that is ~5-10-fold lower can be concluded as safe without proper justification. Additionally, we note that potential thyrotoxic effects were observed at the highest doses in these two rat studies, as well as for rapeseed products in general tested in other species, as cited in Table 20 of the GRAS notice. This effect was mostly attributed to the presence of glucosinolate; however, we note that since the level of glucosinolate was low or absent in both the test articles from Mejia *et al.* and the article of commerce, the rationale used by the study authors to conclude that the observed NOAEL was not in fact the LOAEL may be questionable. Regardless, it appears that the provided safety narrative lacks sufficient basis to conclude MOS of 7-22 is adequate to reach the conclusion of “reasonable certainty of no harm.” Based on generally available data and information, please

provide additional narrative to explain your rationale for your GRAS conclusion.

13. We note that when discussing the absorption, distribution, metabolism, and excretion of canola concentrate (p. 49), the notifier reports unpublished data from an EU Novel Foods application for “defatted rapeseed powder” to support their conclusion. Similarly, genotoxicity conclusions are made using unpublished data from an EFSA Panel conclusion on defatted rapeseed powder. Given other data and information have been used in prior GRAS notices for canola ingredients (e.g., GRN 327), please confirm that the EFSA Panel and EU Novel Foods conclusions are only considered as corroborative, not pivotal, to the safety determination of canola concentrate at its intended use level?
14. On p. 40, the notifier discusses the allergenicity potential of canola concentrate being determined via a “bioinformatics approach” and concludes that canola concentrate “may elicit possible allergenic effects.” Additionally, on p. 59 the notifier reiterates that the bioinformatics analysis indicated “possible allergenic effects” of canola concentrate, but no further discussion is provided. While data from an allergen online database search is provided as part of Appendix 4, no discussion of these data are included in the current GRAS notice. Please briefly detail the “possible allergenic effects” of canola concentrate similar to previous notices (e.g., GRN 683), and discuss why they would not be expected to pose a safety concern from the intended use.
15. We note that a recent study on rapeseed protein isolate was published (Xiong et al., 2022).
 - a. Please discuss if this study presents additional safety concerns for the article of commerce or contradicts the current GRAS conclusion.
 - b. Please also perform an updated literature review from 2021 to present and discuss if any additional studies relevant to the safety of canola concentrate were identified that would contradict the current GRAS conclusion.

References cited:

Xiong Z, Fu Y, Yao J, Zhang N, He R, Ju X, Wang Z. Removal of anti-nutritional factors of rapeseed protein isolate (RPI) and toxicity assessment of RPI. *Food Funct.* 2022 Jan 24;13(2):664-674. doi: 10.1039/d1fo03217h. PMID: 34933325.

Additionally, we received the following questions from USDA FSIS regarding their review of the uses of GRN 1122 concerning products within their purview. Please respond to the following and we will pass your responses along to them.

Please provide Safety Data Sheet (SDS) for the at use concentrations of the substance and include a description of how the use of this technology will not adversely affect the safety of FSIS inspectors. Workplace safety and health hazards include inhalation, direct skin contact (skin, eyes, mouth), and fire/explosion caused by exposure to the product, its working solution or dry mixture and potential by-products formed and/or off-gassed during the application process. The employee safety information should demonstrate how the New Technology will not “jeopardize the safety of Federal inspection personnel” as specified in the [FSIS Compliance Guideline Procedures for New Technology Notifications and Protocols, April 2015](#). FSIS workplace and employee safety must be specifically addressed. Please refer

to Appendix A on p. 17, Workplace Safety and Health Criteria, for clarification on what to provide in the response. For additional clarity with respect to employee safety, the following are examples of information that are typically needed by FSIS' employee safety and health group;

1. Potential workplace exposures that could result from inhalation and direct contact during use of the substance/technology. This information is required in addition to a SDS to determine accurate hazard potential and recommended exposure control measures for IPP work areas in accordance with Occupational Safety and Health Administration (OSHA) regulations: 29 CFR 1910.1200, Hazard Communication, 29 CFR 1910.132, Personal Protective Equipment, and 29 CFR 1910.1000, Air Contaminants. The information should be included as a specific section in each of the protocols.
2. If the SDS workplace hazards/precautions do not apply to the type of exposure that would be expected for the FSIS IPP, please have the submitter provide specific information (per the April 2015 FSIS Compliance Guideline Procedures) for the actual type of exposures expected.
3. If no IPP workplace exposures are expected and no control measures are required, please have the submitter state this and provide the reasons why (e.g., such as the substance "as used" [for all concentrations] is not hazardous by inhalation or direct contact and/or IPP would not be exposed to the substance based on the system design, operation and/or control measures that will be in place).
4. Please also indicate how will FSIS IPP be informed of the above information so that it is clear that the information contained in the SDS for the concentrate does not apply to their actual workplace exposure.
5. Are there any potential hazards from chemical mixing or low pH as a result of discharges of the various solutions to floor drains? Are dedicated drain lines or any other enclosures required?
6. With respect to potential airborne exposures to FSIS IPP in the use/application areas, does the submitter have air sampling results taken during the use of the various concentrations of the technology in the listed mixture?
7. The intended use of this product in FSIS meat and poultry products is apparently as a binder/extender. The suitability support provided in Appendix 6 does sufficiently support no significant difference in yield and other organoleptic qualities when used as a partial replacement for another binder in a processed meat and poultry product, such as sausage. However, **additional suitability support is needed:**
 - a. No suitability data was provided for **whole muscle meat and poultry products at the maximum proposed use level**. We would need to see similar data as provided in Appendix 6 for:
 - Whole muscle red meat control containing no other binders, extenders, or moisture retention agents, as compared to a whole muscle red meat product containing 15% isolated canola product.
 - Whole muscle poultry control containing no other binders, extenders, or moisture retention agents as compared to a whole muscle poultry product containing 15% isolated canola product.

Responses may be sent in an email or in a separate document. We respectfully request a response

within 10 business days. If you are unable to complete the response within that time frame, please contact me to discuss further options.

If you have any additional questions or concerns, please don't hesitate to contact me at stephen.difranco@fda.hhs.gov or by phone at 240.402.2710.

Best,

Steve

Stephen DiFranco, PhD

Regulatory Review Scientist/Chemist

Center for Food Safety and Applied Nutrition

Office of Food Additive Safety

Division of Food Ingredients

U.S. Food and Drug Administration

Tel: 240-402-2710

stephen.difranco@fda.hhs.gov



CAUTION: This email, including any attachments, is confidential. If you are not the intended recipient, please notify the sender and delete the email and any attachments from your system. In addition, you must not use, distribute or reproduce this email or any attachments. Opinions and other information in this email and any attachments which do not relate to the official business of Argenta are neither given by nor endorsed by Argenta. While Argenta uses anti-virus software, Argenta accepts no liability for any viruses in this email or any attachment, or for any effects this email or any attachment may have on your network or computer system.

CAUTION: This email, including any attachments, is confidential. If you are not the intended recipient, please notify the sender and delete the email and any attachments from your system. In addition, you must not use, distribute or reproduce this email or any attachments. Opinions and other information in this email and any attachments which do not relate to the official business of Argenta are neither given by nor endorsed by Argenta. While Argenta uses anti-virus software, Argenta accepts no liability for any viruses in this email or any attachment, or for any effects this email or any attachment may have on your network or computer system.

Este correo electrónico y los archivos adjuntos, enviados por Pen & Tec Consulting SLU, que opera bajo el nombre comercial de Argenta® (Argenta), son confidenciales y pueden estar protegidos por ley. Si usted no es el destinatario, cualquier divulgación, reproducción, copia, distribución u otro tipo de difusión o uso de esta comunicación está estrictamente prohibido. Si ha recibido esta

transmisión por error, notifíquelo al remitente y elimine inmediatamente el correo electrónico y cualquier archivo adjunto de su sistema. Argenta no emite ni respalda las opiniones y demás información contenida en este correo electrónico y en sus anexos que no estén relacionadas con las actividades oficiales de Argenta. Aunque Argenta utiliza software antivirus, Argenta no acepta ninguna responsabilidad por cualquier virus en este correo electrónico o cualquier archivo adjunto, o por cualquier efecto que este correo electrónico o cualquier archivo adjunto pueda tener en su red o sistema informático. Argenta registra y almacena los correos electrónicos enviados a nosotros o a nuestros afiliados de acuerdo con nuestras políticas y procedimientos internos. Consulte www.pentec-consulting.eu para obtener información sobre Argenta y/o nuestra política de privacidad.

This email and any attached file(s), sent by Pen & Tec Consulting SLU trading as Argenta® (Argenta), are confidential and may be legally privileged. If you are not the intended recipient, any disclosure, reproduction, copying, distribution, or other dissemination or use of this communication is strictly prohibited. If you have received this transmission in error, please notify the sender and delete the email and any attachments from your system immediately. Opinions and other information in this email and any attachments which do not relate to the official business of Argenta are neither given by nor endorsed by Argenta. While Argenta uses anti-virus software, Argenta accepts no liability for any viruses in this email or any attachment, or for any effects this email or any attachment may have on your network or computer system. Argenta records and stores emails sent to us or our affiliates in keeping with our internal policies and procedures. Please see www.pentec-consulting.eu for information regarding Argenta and/or our privacy policy.

Este correo electrónico y los archivos adjuntos, enviados por Pen & Tec Consulting SLU, que opera bajo el nombre comercial de Argenta® (Argenta), son confidenciales y pueden estar protegidos por ley. Si usted no es el destinatario, cualquier divulgación, reproducción, copia, distribución u otro tipo de difusión o uso de esta comunicación está estrictamente prohibido. Si ha recibido esta transmisión por error, notifíquelo al remitente y elimine inmediatamente el correo electrónico y cualquier archivo adjunto de su sistema. Argenta no emite ni respalda las opiniones y demás información contenida en este correo electrónico y en sus anexos que no estén relacionadas con las actividades oficiales de Argenta. Aunque Argenta utiliza software antivirus, Argenta no acepta ninguna responsabilidad por cualquier virus en este correo electrónico o cualquier archivo adjunto, o por cualquier efecto que este correo electrónico o cualquier archivo adjunto pueda tener en su red o sistema informático. Argenta registra y almacena los correos electrónicos enviados a nosotros o a nuestros afiliados de acuerdo con nuestras políticas y procedimientos internos. Consulte www.pentec-consulting.eu para obtener información sobre Argenta y/o nuestra política de privacidad.

This email and any attached file(s), sent by Pen & Tec Consulting SLU trading as Argenta® (Argenta), are confidential and may be legally privileged. If you are not the intended recipient, any disclosure, reproduction, copying, distribution, or other dissemination or use of this communication is strictly prohibited. If you have received this transmission in error, please notify the sender and delete the email and any attachments from your system immediately. Opinions and other information in this email and any attachments which do not relate to the official business of Argenta are neither given by nor endorsed by Argenta. While Argenta uses anti-virus software, Argenta accepts no liability for any viruses in this email or any attachment, or for any effects this email or any attachment may have on your network or computer system. Argenta records and stores emails sent to us or our affiliates in keeping with our internal policies and procedures. Please see www.pentec-consulting.eu for information regarding Argenta and/or our privacy policy.

Este correo electrónico y los archivos adjuntos, enviados por Pen & Tec Consulting SLU, que opera bajo el nombre comercial de Argenta® (Argenta), son confidenciales y pueden estar protegidos por ley. Si usted no es el destinatario, cualquier divulgación, reproducción, copia, distribución u otro tipo de difusión o uso de esta comunicación está estrictamente prohibido. Si ha recibido esta transmisión por error, notifíquelo al remitente y elimine inmediatamente el correo electrónico y cualquier archivo adjunto de su sistema. Argenta no emite ni respalda las opiniones y demás información contenida en este correo electrónico y en sus anexos que no estén relacionadas con las actividades oficiales de Argenta. Aunque Argenta utiliza software antivirus, Argenta no acepta ninguna responsabilidad por cualquier virus en este correo electrónico o cualquier archivo adjunto, o por cualquier efecto que este correo electrónico o cualquier archivo adjunto pueda tener en su red o sistema informático. Argenta registra y almacena los correos electrónicos enviados a nosotros o a nuestros afiliados de acuerdo con nuestras políticas y procedimientos internos. Consulte www.pentec-consulting.eu para obtener información sobre Argenta y/o nuestra política de privacidad.

This email and any attached file(s), sent by Pen & Tec Consulting SLU trading as Argenta® (Argenta), are confidential and may be legally privileged. If you are not the intended recipient, any disclosure, reproduction, copying, distribution, or other dissemination or use of this communication is strictly prohibited. If you have received this transmission in error, please notify the sender and delete the email and any attachments from your system immediately. Opinions and other information in this email and any attachments which do not relate to the official business of Argenta are neither given by nor endorsed by Argenta. While Argenta uses anti-virus software, Argenta accepts no liability for any viruses in this email or any attachment, or for any effects this email or any attachment may have on your network or computer system. Argenta records and stores emails sent to us or our affiliates in keeping with our internal policies and procedures. Please see www.pentec-consulting.eu for information regarding Argenta and/or our privacy policy.

From: [Justyna Pałasińska](#)
To: [DiFranco, Stephen](#)
Subject: Re: [EXTERNAL] GRN 1122 canola concentrate status
Date: Thursday, April 4, 2024 7:38:34 AM
Attachments: [image001.png](#)
[image007.png](#)
[image008.png](#)
[image009.png](#)
[image010.png](#)
[image011.png](#)
[image012.png](#)
[Canola Protein Concentrate SDS v1 \(2\)\[40\].pdf](#)

CAUTION: This email originated from outside of the organization. Do not click links or open attachments unless you recognize the sender and know the content is safe.

Dear Stephen,

Please find our reply below:

It is the applicant's understanding that OSHA OELs for heavy metals indicated by FSIS relate to the risk of exposure to heavy metals in the material under assessment via inhalation route only. The material indeed may create dust hazard if handled improperly. We note that the safety data sheet provided for the material (attached for reference) not only informs about the potential to form dust if handled improperly but also includes information on precautionary measures and personal protection and engineering controls aimed at eliminating or greatly reducing the risk of exposure to airborne particles. Proper handling of the material / adherence to these measures and controls by extension would eliminate or greatly reduce the risk of exposure to heavy metals that may be present in the material.

In case the above does not sufficiently address the potential risk of exposure to heavy metals present in the material via inhalation route, the applicant would like to inform that the bulk density of the material ranges between 0.1 and 0.3 g/cm³. A confirmation whether this information is sufficient to proceed with the calculations would be much appreciated. It would also be helpful to understand the assumptions being made by FSIS (e.g. concentration of airborne particles) when assessing whether the levels of heavy metals in the product may exceed OSHA OELs.

Kind regards,

Justyna Pałasińska

Regulatory Affairs Director – Human Nutrition, Argenta Barcelona



M [+34 682 894 653](tel:+34682894653) T [+34 936 758 015](tel:+34936758015)

www.argentaglobal.com

La información contenida en este mensaje y/o archivo(s) adjunto(s), enviada desde Pen & Tec Consulting SLU cotiza como Argenta, es confidencial/privilegiada y está destinada a ser leída sólo por la(s) persona(s) a la(s) que va dirigida. Le recordamos que sus datos han sido incorporados en el sistema de tratamiento de Pen & Tec Consulting SLU cotiza como Argenta, y que siempre y cuando se cumplan los requisitos exigidos por la normativa, usted podrá ejercer sus derechos de acceso, rectificación, limitación de tratamiento, supresión, portabilidad y oposición/revocación, en los términos que establece la normativa vigente en materia de protección de datos, dirigiendo su petición a la dirección postal OneCoWork, Portal de l'Àngel 40, 08002, Barcelona o bien a través de correo electrónico info@pentec-consulting.eu. Si usted lee este mensaje y no es el destinatario señalado, el empleado o el agente responsable de entregar el mensaje al destinatario, o ha recibido esta comunicación por error, le informamos que está totalmente prohibida, y puede ser ilegal, cualquier divulgación, distribución o reproducción de esta comunicación, y le rogamos que nos lo notifique inmediatamente y nos devuelva el mensaje original a la dirección arriba mencionada. Gracias.

The information contained in this message and/or attached file(s), sent by Pen & Tec Consulting SLU trading as Argenta, is

confidential/privileged and is intended to be read solely by the person(s) to whom it is addressed. We hereby inform you that your data will be incorporated into the processing system owned by Pen & Tec Consulting SLU, and that provided it complies with the requirements included in the law, you may exercise the rights of access, rectification, limitation of processing, deletion, portability and opposition by sending your request to the postal address OneCoWork, Portal de l'Àngel 40, 08002, Barcelona or to the email address info@pentec-consulting.eu. If you read this message and you are neither the intended recipient, employee or agent in charge of delivering the message to the recipient, or if you have received this message as the result of an error, we hereby inform you that distributing, sharing or reproducing any part of this message is totally forbidden and may be illegal. As a result, we request that you immediately inform us of the error and return this message to the address mentioned above. Thank you.

From: DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>

Date: Thursday, 28 March 2024 at 20:47

To: Justyna Pałasińska <justyna.palasinaska@argentaglobal.com>

Subject: RE: [EXTERNAL] GRN 1122 canola concentrate status

Hello Justyna,

I got feedback from FSIS about their review of GRN 1122. They send the following:

I have now completed the review of the documentation submitted for the approval of the above-referenced compound. I noted that it contains Lead (≤ 0.5 mg/kg), Arsenic (≤ 0.2 mg/kg), Cadmium (≤ 0.2 mg/kg), and Mercury (≤ 0.1 mg/kg). OSHA has established OEL for these substances at 0.05 mg/m³, 0.01 mg/m³, 0.01 mg/m³, 0.025 mg/m³ (depending on presentation) respectively.

To finalize my analysis, I require the composition in mg/m³ of each of these elements or the density so I may calculate their composition accurately and evaluate them against their OSHA standards.

Are you able to provide the density of the canola concentrate? I believe this is the easiest way to answer their questions. From the density and the specified ppm levels, the reviewer should be able to calculate the maximum amount by weight of each heavy metal contaminate for a given volume of canola concentrate.

Best,

Steve

Stephen DiFranco, PhD

Regulatory Review Scientist/Chemist

Center for Food Safety and Applied Nutrition

Office of Food Additive Safety

Division of Food Ingredients

U.S. Food and Drug Administration

Tel: 240-402-2710

stephen.difranco@fda.hhs.gov



From: Justyna Pałasińska <justyna.palasincka@argentaglobal.com>
Sent: Monday, March 4, 2024 5:04 AM
To: DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>
Subject: Re: [EXTERNAL] GRN 1122 canola concentrate status

CAUTION: This email originated from outside of the organization. Do not click links or open attachments unless you recognize the sender and know the content is safe.

Many thanks for the update, Stephen. We look forward to hearing an update, hopefully soon!

Kind regards,

Justyna Pałasińska

Regulatory Affairs Director – Human Nutrition, Argenta Barcelona



M [+34 682 894 653](tel:+34682894653) T [+34 936 758 015](tel:+34936758015)

www.argentaglobal.com

La información contenida en este mensaje y/o archivo(s) adjunto(s), enviada desde Pen & Tec Consulting SLU cotiza como Argenta, es confidencial/privilegiada y está destinada a ser leída sólo por la(s) persona(s) a la(s) que va dirigida. Le recordamos que sus datos han sido incorporados en el sistema de tratamiento de Pen & Tec Consulting SLU cotiza como Argenta, y que siempre y cuando se cumplan los requisitos exigidos por la normativa, usted podrá ejercer sus derechos de acceso, rectificación, limitación de tratamiento, supresión, portabilidad y oposición/revocación, en los términos que establece la normativa vigente en materia de protección de datos, dirigiendo su petición a la dirección postal Pl. Ausias March 1, 4 planta 08195, Sant Cugat del Vallès (Barcelona) o bien a través de correo electrónico info@pentec-consulting.eu. Si usted lee este mensaje y no es el destinatario señalado, el empleado o el agente responsable de entregar el mensaje al destinatario, o ha recibido esta comunicación por error, le informamos que está totalmente prohibida, y puede ser ilegal, cualquier divulgación, distribución o reproducción de esta comunicación, y le rogamos que nos lo notifique inmediatamente y nos devuelva el mensaje original a la dirección arriba mencionada. Gracias.

The information contained in this message and/or attached file(s), sent by Pen & Tec Consulting SLU trading as Argenta, is confidential/privileged and is intended to be read solely by the person(s) to whom it is addressed. We hereby inform you that your data will be incorporated into the processing system owned by Pen & Tec Consulting SLU, and that provided it complies with the requirements included in the law, you may exercise the rights of access, rectification, limitation of processing, deletion, portability and opposition by sending your request to the postal address Pl. Ausias March 1, 4 floor 08195, Sant Cugat del Valles (Barcelona) or to the email address info@pentec-consulting.eu. If you read this message and you are neither the intended recipient, employee or agent in charge of delivering the message to the recipient, or if you have received this message as the result of an error, we hereby inform you that distributing, sharing or reproducing any part of this message is totally forbidden and may be illegal. As a result, we request that you immediately inform us of the error and return this message to the address mentioned above. Thank you.

From: DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>

Date: Monday, 26 February 2024 at 17:20

To: Justyna Pałasińska <justyna.palasincka@argentaglobal.com>

Subject: RE: [EXTERNAL] GRN 1122 canola concentrate status

Hello Justyna,

Regarding GRN 1122; FDA has completed its review and has drafted a response letter.

Unfortunately, we cannot move forward before USDA-FSIS completes their review of the uses under their jurisdiction. I have been periodically inquiring with FSIS as to the status and will get this to you

as soon as possible.

We appreciate your continued patience.

Best,

Steve

Stephen DiFranco, PhD

Regulatory Review Scientist/Chemist

**Center for Food Safety and Applied Nutrition
Office of Food Additive Safety
Division of Food Ingredients
U.S. Food and Drug Administration**
Tel: 240-402-2710
stephen.difranco@fda.hhs.gov



From: Justyna Pałasińska <justyna.palasinska@argentaglobal.com>

Sent: Wednesday, February 14, 2024 12:07 PM

To: Premarkt <Premarkt@fda.hhs.gov>

Cc: DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>; Ioannis Kartanos <ioannis.kartanos@argentaglobal.com>

Subject: [EXTERNAL] GRN 1122 canola concentrate status

CAUTION: This email originated from outside of the organization. Do not click links or open attachments unless you recognize the sender and know the content is safe.

Dear HHS team,

I am writing to enquire about a GRAS notice that was submitted to the FDA & filed April 19, 2023 (GRN 1122). We have been in touch with Mr Stephen DiFranco & at the beginning of December he has informed us that the FDA reviews are complete & the notice is now with USDA-FSIS.

Mr DiFranco has been very helpful through the whole process. However, we have tried to contact him several times since December without success. We were wondering if there is someone else we can get in touch with for an update on this application. We would be happy to provide any information that would help finalize the process.

I look forward to hearing from you.

Kind regards,

Justyna Pałasińska

Regulatory Affairs Director – Human Nutrition, Argenta Barcelona



M +34 682 894 653 T +34 936 758 015

www.argentaglobal.com

La información contenida en este mensaje y/o archivo(s) adjunto(s), enviada desde Pen & Tec Consulting SLU cotiza como Argenta, es confidencial/privilegiada y está destinada a ser leída sólo por la(s) persona(s) a la(s) que va dirigida. Le recordamos que sus datos han sido incorporados en el sistema de tratamiento de Pen & Tec Consulting SLU cotiza como Argenta, y que siempre y cuando se cumplan los requisitos exigidos por la normativa, usted podrá ejercer sus derechos de acceso, rectificación, limitación de tratamiento, supresión, portabilidad y oposición/revocación, en los términos que establece la normativa vigente en materia de protección de datos, dirigiendo su petición a la dirección postal Pl. Ausias March 1, 4 planta 08195, Sant Cugat del Vallès (Barcelona) o bien a través de correo electrónico info@pentec-consulting.eu. Si usted lee este mensaje y no es el destinatario señalado, el empleado o el agente responsable de entregar el mensaje al destinatario, o ha recibido esta comunicación por error, le informamos que está totalmente prohibida, y puede ser ilegal, cualquier divulgación, distribución o reproducción de esta comunicación, y le rogamos que nos lo notifique inmediatamente y nos devuelva el mensaje original a la dirección arriba mencionada. Gracias.

The information contained in this message and/or attached file(s), sent by Pen & Tec Consulting SLU trading as Argenta, is confidential/privileged and is intended to be read solely by the person(s) to whom it is addressed. We hereby inform you that your data will be incorporated into the processing system owned by Pen & Tec Consulting SLU, and that provided it complies with the requirements included in the law, you may exercise the rights of access, rectification, limitation of processing, deletion, portability and opposition by sending your request to the postal address Pl. Ausias March 1, 4 floor 08195, Sant Cugat del Valles (Barcelona) or to the email address info@pentec-consulting.eu. If you read this message and you are neither the intended recipient, employee or agent in charge of delivering the message to the recipient, or if you have received this message as the result of an error, we hereby inform you that distributing, sharing or reproducing any part of this message is totally forbidden and may be illegal. As a result, we request that you immediately inform us of the error and return this message to the address mentioned above. Thank you.

From: Justyna Pałasińska <justyna.palasinaska@argentaglobal.com>

Date: Wednesday, 31 January 2024 at 17:53

To: Justyna Pałasińska <justyna.palasinaska@argentaglobal.com>, DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>

Cc: Ioannis Kartanos <ioannis.kartanos@argentaglobal.com>

Subject: Re: [EXTERNAL] GRN 1122 canola concentrate - update contact person

Dear Steve,

I hope this e-mail finds you well. I was wondering if there are any updates on the finalization of this notification?

Is there any additional information that needs to be provided?

Kind regards,

Justyna Pałasińska

Regulatory Affairs Director – Human Nutrition, Argenta Barcelona

The logo for Argenta, featuring the word "argenta" in a lowercase, sans-serif font. Above the letter "a" is a stylized blue graphic consisting of two overlapping shapes that resemble a drop or a leaf.

M +34 682 894 653 T +34 936 758 015

www.argentaglobal.com

La información contenida en este mensaje y/o archivo(s) adjunto(s), enviada desde Pen & Tec Consulting SLU cotiza como Argenta, es confidencial/privilegiada y está destinada a ser leída sólo por la(s) persona(s) a la(s) que va dirigida. Le recordamos que sus datos han sido incorporados en el sistema de tratamiento de Pen & Tec Consulting SLU cotiza como Argenta, y que siempre y cuando se cumplan los requisitos exigidos por la normativa, usted podrá ejercer sus derechos de acceso, rectificación, limitación de tratamiento, supresión, portabilidad y oposición/revocación, en los términos que establece la normativa vigente en materia de protección de datos, dirigiendo su petición a la dirección postal Pl. Ausias March 1, 4 planta 08195, Sant Cugat del Vallès (Barcelona) o bien a través de correo electrónico info@pentec-consulting.eu. Si usted lee este mensaje y no es el destinatario señalado, el empleado o el agente responsable

de entregar el mensaje al destinatario, o ha recibido esta comunicación por error, le informamos que está totalmente prohibida, y puede ser ilegal, cualquier divulgación, distribución o reproducción de esta comunicación, y le rogamos que nos lo notifique inmediatamente y nos devuelva el mensaje original a la dirección arriba mencionada. Gracias.

The information contained in this message and/or attached file(s), sent by Pen & Tec Consulting SLU trading as Argenta, is confidential/privileged and is intended to be read solely by the person(s) to whom it is addressed. We hereby inform you that your data will be incorporated into the processing system owned by Pen & Tec Consulting SLU, and that provided it complies with the requirements included in the law, you may exercise the rights of access, rectification, limitation of processing, deletion, portability and opposition by sending your request to the postal address Pl. Ausias March 1, 4 floor 08195, Sant Cugat del Valles (Barcelona) or to the email address info@pentec-consulting.eu. If you read this message and you are neither the intended recipient, employee or agent in charge of delivering the message to the recipient, or if you have received this message as the result of an error, we hereby inform you that distributing, sharing or reproducing any part of this message is totally forbidden and may be illegal. As a result, we request that you immediately inform us of the error and return this message to the address mentioned above. Thank you.

From: Justyna Pałasińska <justyna@pentec-consulting.eu>

Date: Friday, 22 December 2023 at 13:31

To: DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>

Cc: Ioannis Kartanos <ioannis@pentec-consulting.eu>

Subject: Re: [EXTERNAL] GRN 1122 canola concentrate - update contact person

Dear Stephen,

Many thanks for confirming the change of contact person.

I'm following up on my colleague Ioannis e-mail from 12/12/2023. As he mentioned, we have already provided the answers to the questions to USDA-FSIS. Nevertheless, I have included them in a separate document.

Please let us know in case any additional information is required.

In the meantime, we wish you a Happy Holiday Season & all the best in 2024!

Kind regards,

Ing. Justyna Pałasińska

Regulatory Affairs Director – Human Nutrition | Pen & Tec Consulting

T +34 936 758 015 M +34 682 894 653 F +34 936 758 016 www.pentec-consulting.eu

Pl. Ausias March 1 | 4th floor D01 | 08195 Sant Cugat del Vallès | Barcelona | Spain

PEN + TEC
CONSULTING
PART OF THE ARGENTA GROUP

La información contenida en este mensaje y/o archivo(s) adjunto(s), enviada desde Pen & Tec Consulting SLU, es confidencial/privilegiada y está destinada a ser leída sólo por la(s) persona(s) a la(s) que va dirigida. Le recordamos que sus datos han sido incorporados en el sistema de tratamiento de Pen & Tec Consulting SLU y que siempre y cuando se cumplan los requisitos exigidos por la normativa, usted podrá ejercer sus derechos de acceso, rectificación, limitación de tratamiento, supresión, portabilidad y oposición/revocación, en los términos que establece la normativa vigente en materia de protección de datos, dirigiendo su petición a la dirección postal Pl. Ausias March 1, 4 planta 08195, Sant Cugat del Vallès (Barcelona) o bien a través de correo electrónico info@pentec-consulting.eu. Si usted lee este mensaje y no es el destinatario señalado, el empleado o el agente responsable de entregar el mensaje al destinatario, o ha recibido esta comunicación por error, le informamos que está totalmente prohibida, y puede ser ilegal, cualquier divulgación, distribución o reproducción de esta comunicación, y le rogamos que nos lo notifique inmediatamente y nos devuelva el mensaje original a la dirección arriba mencionada. Gracias.

The information contained in this message and/or attached file(s), sent by Pen & Tec Consulting SLU, is confidential/privileged and is intended to be read solely by the person(s) to whom it is addressed. We hereby inform you that your data will be incorporated into the processing system owned by Pen & Tec Consulting SLU, and that provided it complies with the requirements included in the law, you may exercise the rights of access, rectification, limitation of processing, deletion, portability and opposition by sending your request to the

postal address Pl. Ausias March 1, 4 floor 08195, Sant Cugat del Valles (Barcelona) or to the email address info@pentec-consulting.eu. If you read this message and you are neither the intended recipient, employee or agent in charge of delivering the message to the recipient, or if you have received this message as the result of an error, we hereby inform you that distributing, sharing or reproducing any part of this message is totally forbidden and may be illegal. As a result, we request that you immediately inform us of the error and return this message to the address mentioned above. Thank you.

From: DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>

Date: Tuesday, 5 December 2023 at 19:05

To: Nikolaas Tilkin-Franssens <niko@pentec-consulting.eu>

Cc: Justyna Pałasińska <justyna@pentec-consulting.eu>

Subject: RE: [EXTERNAL] GRN 1122 canola concentrate - update contact person

Hello Niko and Justyna,

Just confirming the change of contact person for GRN 1122.

As for timeline, FDA reviews are complete but USDA-FSIS is requesting a few pieces of information regarding the uses of canola concentrate under USDA jurisdiction, namely:

Please provide SDS for the at use concentrations of the substance and include a description of how the use of this technology will not adversely affect the safety of FSIS inspectors. Workplace safety and health hazards include inhalation, direct skin contact (skin, eyes, mouth), and fire/explosion caused by exposure to the product, its working solution or dry mixture and potential by-products formed and/or off-gassed during the application process. The employee safety information should demonstrate how the New Technology will not “jeopardize the safety of Federal inspection personnel” as specified in the [FSIS Compliance Guideline Procedures for New Technology Notifications and Protocols, April 2015](#).

Although I’m not anticipating any issues here, FSIS workplace and employee safety must be specifically addressed. Please refer to Appendix A on page 17, Workplace Safety and Health Criteria, for clarification on what to provide in the response. For additional clarity with respect to employee safety, the following are examples of information that are typically needed by FSIS’ employee safety and health group;

1. Potential workplace exposures that could result from inhalation and direct contact during use of the substance/technology. This information is required in addition to a Safety Data Sheet (SDS) to determine accurate hazard potential and recommended exposure control measures for IPP work areas in accordance with Occupational Safety and Health Administration (OSHA) regulations: 29 CFR 1910.1200, Hazard Communication, 29 CFR 1910.132, Personal Protective Equipment, and 29 CFR 1910.1000, Air Contaminants. The information should be included as a specific section in each of the protocols.
2. If the SDS workplace hazards/precautions do not apply to the type of exposure that would be expected for the FSIS IPP, please have the submitter provide specific information (per the April 2015 FSIS Compliance Guideline Procedures) for the actual type of exposures expected.
3. If no IPP workplace exposures are expected and no control measures are required, please have the submitter state this and provide the reasons why (e.g., such as the substance “as used” [for all concentrations] is not hazardous by inhalation or direct contact and/or IPP would not be exposed to the substance based on the system design, operation and/or control measures that will be in place).
4. Please also indicate how will FSIS IPP be informed of the above information so that it is clear that the information contained in the SDS for the concentrate does not apply to their actual workplace exposure.
5. Are there any potential hazards from chemical mixing or low pH as a result of discharges of the various solutions to floor drains? Are dedicated drain lines or any other enclosures required?

6. With respect to potential airborne exposures to FSIS IPP in the use/application areas, does the submitter have air sampling results taken during the use of the various concentrations of the technology in the listed mixture?

Suitability data;

The intended use of this product in FSIS meat and poultry products is apparently as a binder/extender. The suitability support provided in Appendix 6 does sufficiently support no significant difference in yield and other organoleptic qualities when used as a partial replacement for another binder in a processed meat and poultry product, such as sausage.

However, **additional suitability support is needed:**

- No suitability data was provided for **whole muscle meat and poultry products at the maximum proposed use level**. We would need to see similar data as provided in Appendix 6 for:
 - Whole muscle red meat control containing no other binders, extenders, or moisture retention agents, as compared to a whole muscle red meat product containing 15% isolated canola product.
 - Whole muscle poultry control containing no other binders, extenders, or moisture retention agents as compared to a whole muscle poultry product containing 15% isolated canola product.

You responses can be emailed directly to me and I will distribute to the necessary staff inside FDA and USDA.

Thanks,

Steve

Stephen DiFranco, PhD

Regulatory Review Scientist/Chemist

Center for Food Safety and Applied Nutrition
Office of Food Additive Safety
Division of Food Ingredients
U.S. Food and Drug Administration
Tel: 240-402-2710
stephen.difranco@fda.hhs.gov



From: Nikolaas Tilkin-Franssens <niko@pentec-consulting.eu>

Sent: Monday, December 4, 2023 4:36 AM

To: DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>

Cc: Justyna Pałasińska <justyna@pentec-consulting.eu>

Subject: [EXTERNAL] GRN 1122 canola concentrate - update contact person

CAUTION: This email originated from outside of the organization. Do not click links or open attachments unless you recognize the sender and know the content is safe.

Hi Mr. DiFranco,

Hope this email finds you well.

Due to a change in position, I will no longer be the contact person for the GRAS Notice 1122 (Canola Protein Concentrate). Could you please update your records to ascertain that Justyna Pałasińska, in copy to this email, is informed of any relevant updates?

Could you kindly confirm receipt of this email for our records?

And if possible, let us know if there is any estimate on the timeline re. finalization of the review of this GRAS Notice.

Many thanks for your great and flexible support on this application.

Kind regards,

Niko

Nikolaas Tilkin-Franssens

Regulatory Affairs Manager | Pen & Tec Consulting

T +34 936 758 015 **M** +34 649 840 417 **F** +34 936 758 016 www.pentec-consulting.eu

Pl. Ausias March 1 | 4th floor D01 | 08195 Sant Cugat del Vallès | Barcelona | Spain

PEN + TEC
CONSULTING
PART OF THE ARGENTA GROUP

La información contenida en este mensaje y/o archivo(s) adjunto(s), enviada desde Pen & Tec Consulting SLU, es confidencial/privilegiada y está destinada a ser leída sólo por la(s) persona(s) a la(s) que va dirigida. Le recordamos que sus datos han sido incorporados en el sistema de tratamiento de Pen & Tec Consulting SLU y que siempre y cuando se cumplan los requisitos exigidos por la normativa, usted podrá ejercer sus derechos de acceso, rectificación, limitación de tratamiento, supresión, portabilidad y oposición/revocación, en los términos que establece la normativa vigente en materia de protección de datos, dirigiendo su petición a la dirección postal Pl. Ausias March 1, 4 planta 08195, Sant Cugat del Vallès (Barcelona) o bien a través de correo electrónico info@pentec-consulting.eu. Si usted lee este mensaje y no es el destinatario señalado, el empleado o el agente responsable de entregar el mensaje al destinatario, o ha recibido esta comunicación por error, le informamos que está totalmente prohibida, y puede ser ilegal, cualquier divulgación, distribución o reproducción de esta comunicación, y le rogamos que nos lo notifique inmediatamente y nos devuelva el mensaje original a la dirección arriba mencionada. Gracias.

The information contained in this message and/or attached file(s), sent by Pen & Tec Consulting SLU, is confidential/privileged and is intended to be read solely by the person(s) to whom it is addressed. We hereby inform you that your data will be incorporated into the processing system owned by Pen & Tec Consulting SLU, and that provided it complies with the requirements included in the law, you may exercise the rights of access, rectification, limitation of processing, deletion, portability and opposition by sending your request to the postal address Pl. Ausias March 1, 4 floor 08195, Sant Cugat del Valles (Barcelona) or to the email address info@pentec-consulting.eu. If you read this message and you are neither the intended recipient, employee or agent in charge of delivering the message to the recipient, or if you have received this message as the result of an error, we hereby inform you that distributing, sharing or reproducing any part of this message is totally forbidden and may be illegal. As a result, we request that you immediately inform us of the error and return this message to the address mentioned above. Thank you.

From: DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>

Date: Monday, 17 July 2023 at 17:01

To: Nikolaas Tilkin-Franssens <niko@pentec-consulting.eu>

Subject: RE: [EXTERNAL] Re: GRN 1122 canola concentrate items for clarification - Reply

Hello Niko,

No problem—I'll distribute this to the team for review.

Best,

Steve

Stephen DiFranco, PhD

Regulatory Review Scientist/Chemist

Center for Food Safety and Applied Nutrition

Office of Food Additive Safety

Division of Food Ingredients

U.S. Food and Drug Administration

Tel: 240-402-2710

stephen.difranco@fda.hhs.gov



From: Nikolaas Tilkin-Franssens <niko@pentec-consulting.eu>

Sent: Monday, July 17, 2023 10:35 AM

To: DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>

Subject: [EXTERNAL] Re: GRN 1122 canola concentrate items for clarification - Reply

CAUTION: This email originated from outside of the organization. Do not click links or open attachments unless you recognize the sender and know the content is safe.

Hi Stephen,

Apologies for this inconvenience.

We noticed that the reply to question 9 refers to Canola protein isolate (as per GRN 1103).

I have updated the answer for it to be mentioning Canola protein concentrate (GRN 1122).

We hope this can be taken into consideration.

Kind regards,

Nikolaas Tilkin-Franssens

Regulatory Affairs Manager | Pen & Tec Consulting

T [+34 936 758 015](tel:+34936758015) **M** [+34 649 840 417](tel:+34649840417) **F** [+34 936 758 016](tel:+34936758016) www.pentec-consulting.eu

Pl. Ausias March 1 | 4th floor D01 | 08195 Sant Cugat del Vallès | Barcelona | Spain

La información contenida en este mensaje y/o archivo(s) adjunto(s), enviada desde Pen & Tec Consulting SLU, es confidencial/privilegiada y está destinada a ser leída sólo por la(s) persona(s) a la(s) que va dirigida. Le recordamos que sus datos han sido incorporados en el sistema de tratamiento de Pen & Tec Consulting SLU y que siempre y cuando se cumplan los requisitos exigidos por la normativa, usted podrá ejercer sus derechos de acceso, rectificación, limitación de tratamiento, supresión, portabilidad y oposición/revocación, en los términos que establece la normativa vigente en materia de protección de datos, dirigiendo su petición a la dirección postal Pl. Ausias March 1, 4 planta 08195, Sant Cugat del Vallès (Barcelona) o bien a través de correo electrónico info@pentec-consulting.eu. Si usted lee este mensaje y no es el destinatario señalado, el empleado o el agente responsable de entregar el mensaje al destinatario, o ha recibido esta comunicación por error, le informamos que está totalmente prohibida, y puede ser ilegal, cualquier divulgación, distribución o reproducción de esta comunicación, y le rogamos que nos lo notifique inmediatamente y nos devuelva el mensaje original a la dirección arriba mencionada. Gracias.

The information contained in this message and/or attached file(s), sent by Pen & Tec Consulting SLU, is confidential/privileged and is intended to be read solely by the person(s) to whom it is addressed. We hereby inform you that your data will be incorporated into the processing system owned by Pen & Tec Consulting SLU, and that provided it complies with the requirements included in the law, you may exercise the rights of access, rectification, limitation of processing, deletion, portability and opposition by sending your request to the postal address Pl. Ausias March 1, 4 floor 08195, Sant Cugat del Valles (Barcelona) or to the email address info@pentec-consulting.eu. If you read this message and you are neither the intended recipient, employee or agent in charge of delivering the message to the recipient, or if you have received this message as the result of an error, we hereby inform you that distributing, sharing or reproducing any part of this message is totally forbidden and may be illegal. As a result, we request that you immediately inform us of the error and return this message to the address mentioned above. Thank you.

From: Nikolaas Tilkin-Franssens <niko@pentec-consulting.eu>
Date: Tuesday, 11 July 2023 at 17:03
To: DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>
Cc: Justyna Pałasińska <justyna@pentec-consulting.eu>
Subject: Re: GRN 1122 canola concentrate items for clarification - Reply

Dear Stephen,

Thank you for reaching out with the questions for clarification.
We have worked closely with Napiferyn to close the doubts.

Kindly find attached a Word file including the Questions&Answers, a report on the requested literature review, a SDS sheet as requested by the USDA-FSIS, and a report on the suitability assessment.

We remain available for any further questions or updates.

Thanks for taking the application in further consideration,
best regards,

Nikolaas Tilkin-Franssens

Regulatory Affairs Manager | Pen & Tec Consulting

T +34 936 758 015 M +34 649 840 417 F +34 936 758 016 www.pentec-consulting.eu

Pl. Ausias March 1 | 4th floor D01 | 08195 Sant Cugat del Vallès | Barcelona | Spain

oposición/revocación, en los términos que establece la normativa vigente en materia de protección de datos, dirigiendo su petición a la dirección postal Pl. Ausias March 1, 4 planta 08195, Sant Cugat del Vallès (Barcelona) o bien a través de correo electrónico info@pentec-consulting.eu. Si usted lee este mensaje y no es el destinatario señalado, el empleado o el agente responsable de entregar el mensaje al destinatario, o ha recibido esta comunicación por error, le informamos que está totalmente prohibida, y puede ser ilegal, cualquier divulgación, distribución o reproducción de esta comunicación, y le rogamos que nos lo notifique inmediatamente y nos devuelva el mensaje original a la dirección arriba mencionada. Gracias.

The information contained in this message and/or attached file(s), sent by Pen & Tec Consulting SLU, is confidential/privileged and is intended to be read solely by the person(s) to whom it is addressed. We hereby inform you that your data will be incorporated into the processing system owned by Pen & Tec Consulting SLU, and that provided it complies with the requirements included in the law, you may exercise the rights of access, rectification, limitation of processing, deletion, portability and opposition by sending your request to the postal address Pl. Ausias March 1, 4 floor 08195, Sant Cugat del Valles (Barcelona) or to the email address info@pentec-consulting.eu. If you read this message and you are neither the intended recipient, employee or agent in charge of delivering the message to the recipient, or if you have received this message as the result of an error, we hereby inform you that distributing, sharing or reproducing any part of this message is totally forbidden and may be illegal. As a result, we request that you immediately inform us of the error and return this message to the address mentioned above. Thank you.

From: DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>
Date: Wednesday, 28 June 2023 at 17:41
To: Nicoleta Pasecinic <nicoleta@pentec-consulting.eu>
Cc: Nikolaas Tilkin-Franssens <niko@pentec-consulting.eu>
Subject: [EXTERNAL]: GRN 1122 canola concentrate items for clarification

CAUTION: This email originated from outside of the organization. Do not click links or open attachments unless you recognize the sender and know the content is safe.

Hello Ms. Pasecinic,

After evaluating NapiFeryn's GRAS Notice No. GRN 1122 on canola concentrate we noted a few issues that should be addressed. Please respond to the following points for clarification:

1. On p. 9, NapiFeryn states that the major storage proteins in canola seed are cruciferins and napins, and that canola concentrate consists of 30-45% protein and 40-70% dietary fiber. Please provide the typical cruciferin content and napin content in canola concentrate.
2. Please confirm that all raw materials and processing aids used in the manufacturing process are used in accordance with the U.S. regulations, are GRAS for their respective uses or are the subject of an effective food contact notification. For the record, we note that the food additive regulations cited in Table 4 (p. 15) for ascorbic acid (21 CFR 182.8013), ethanol (21 CFR 184.1293), and ethyl acetate (21 CFR 173.228) do not appear to be applicable to your intended uses of these substances.
3. In Table 6 (p. 18-19), NapiFeryn provides the results from the batch analyses for heavy metals. We would like to bring to your attention a relevant FDA's "[Closer to Zero](#)" initiative that focuses on reducing the levels of heavy metals in foods and recommend that you lower the specification limits for heavy metal to better reflect the batch analyses results and to be as low as possible.
4. In Table 10 (p. 22), NapiFeryn provides batch analyses data for residual solvents and processing aids. In addition, in Table 21 (p. 50), you provided the results from the batch analyses for erucic acid in your canola concentrate ranging from 0.37% to < 0.1%.
Please include limits for residual ethanol, ethyl acetate, and sulphur dioxide as well as a

limit for erucic acid in the specifications for canola concentrate and specify the analytical methods used to test for these parameters.

In addition, please provide an updated Tables 5 and 6 (p. 16-19) to include the additional specification parameters mentioned above, corresponding analytical methods, and batch analyses.

5. Please state that all analytical methods used to test batches were validated and are fit for their respective purpose.
6. Please state that canola concentrate is not intended for use in infant formula or in foods where standards of identity preclude its use.
7. In Table 15 (p.), NapiFeryn provides the results of the batch analyses for total plate count in the raw material (rapeseed press cake). Please address the significant variation in the results (from <10 to 28,000 CFU/g) and discuss whether this will impact safety of the final ingredient.
8. On p. 19, NapiFeryn states that the levels of mycotoxins in canola concentrate are below the limit of quantitation (LOQ) and provide the results from the analyses of five batches to support your statement. Please clarify whether you expect mycotoxins to be present in canola concentrate manufactured in accordance with good manufacturing practices.
9. In Part 1.4 (p. 6) and Part 3.1 (p. 33), NapiFeryn states that the intended use of canola concentrate is as a source of protein and/or fiber, thickener, or texturizer. However, we note that on p. 33 you also state the intended use of canola concentrate is as a flavoring agent or binder in various comminuted or whole muscle meat and poultry products. In addition, in Appendix 3 (p. 5) you state that canola concentrate may also be used “to create a flavored salt” or as “a flavor enhancer like monosodium glutamate”. Please confirm these additional uses of canola concentrate are within the scope of GRN 001122.
10. On p. 10, the notifier describes the protein composition of canola concentrate, being primarily cruciferins, napin, oleosin, and squalene monooxygenase. However, the pivotal safety data provided appear to only be relevant to the cruciferin and napin fractions of the canola concentrate. Please provide a brief narrative to confirm the safety of oleosin and squalene monooxygenase exposure from the intended uses.
11. On p. 31-32 of the notice, the notifier clearly establishes that canola concentrate is intended to be substitutive to protein and fiber consumption and will not contribute to additional exposure to protein or fiber in general. Please elaborate on this conclusion, and clarify if the intended uses of canola concentrate are additive or substitutive to other canola protein products currently on the market (i.e., GRNs 327, 386, and 683)?
12. On p. 37, the notifier concludes exposure to canola concentrate from the intended uses is safe since the EDI reported is “still much lower (approximately 7- to 22-fold lower) than the no-observed-adverse-effect level (NOAEL) values established” for cruciferin- and napin-rich

protein isolates in male rats following a 13-week oral exposure regimen (Mejia *et al.*, 2009a & 2009b). We note that an uncertainty factor, or margin of safety (MOS), of 100 (10 for interindividual variability × 10 for interspecies variability) is normally used when assessing safety of a food ingredient by comparing estimated human exposure levels to the NOAEL from animal toxicology data. Therefore, it is not clear why MOS that is ~5-10-fold lower can be concluded as safe without proper justification. Additionally, we note that potential thyrotoxic effects were observed at the highest doses in these two rat studies, as well as for rapeseed products in general tested in other species, as cited in Table 20 of the GRAS notice. This effect was mostly attributed to the presence of glucosinolate; however, we note that since the level of glucosinolate was low or absent in both the test articles from Mejia *et al.* and the article of commerce, the rationale used by the study authors to conclude that the observed NOAEL was not in fact the LOAEL may be questionable. Regardless, it appears that the provided safety narrative lacks sufficient basis to conclude MOS of 7-22 is adequate to reach the conclusion of “reasonable certainty of no harm.” Based on generally available data and information, please provide additional narrative to explain your rationale for your GRAS conclusion.

13. We note that when discussing the absorption, distribution, metabolism, and excretion of canola concentrate (p. 49), the notifier reports unpublished data from an EU Novel Foods application for “defatted rapeseed powder” to support their conclusion. Similarly, genotoxicity conclusions are made using unpublished data from an EFSA Panel conclusion on defatted rapeseed powder. Given other data and information have been used in prior GRAS notices for canola ingredients (e.g., GRN 327), please confirm that the EFSA Panel and EU Novel Foods conclusions are only considered as corroborative, not pivotal, to the safety determination of canola concentrate at its intended use level?
14. On p. 40, the notifier discusses the allergenicity potential of canola concentrate being determined via a “bioinformatics approach” and concludes that canola concentrate “may elicit possible allergenic effects.” Additionally, on p. 59 the notifier reiterates that the bioinformatics analysis indicated “possible allergenic effects” of canola concentrate, but no further discussion is provided. While data from an allergen online database search is provided as part of Appendix 4, no discussion of these data are included in the current GRAS notice. Please briefly detail the “possible allergenic effects” of canola concentrate similar to previous notices (e.g., GRN 683), and discuss why they would not be expected to pose a safety concern from the intended use.
15. We note that a recent study on rapeseed protein isolate was published (Xiong *et al.*, 2022).
 - a. Please discuss if this study presents additional safety concerns for the article of commerce or contradicts the current GRAS conclusion.
 - b. Please also perform an updated literature review from 2021 to present and discuss if any additional studies relevant to the safety of canola concentrate were identified that would contradict the current GRAS conclusion.

References cited:

Xiong Z, Fu Y, Yao J, Zhang N, He R, Ju X, Wang Z. Removal of anti-nutritional factors of rapeseed protein isolate (RPI) and toxicity assessment of RPI. *Food Funct.* 2022 Jan 24;13(2):664-674.

doi: 10.1039/d1fo03217h. PMID: 34933325.

Additionally, we received the following questions from USDA FSIS regarding their review of the uses of GRN 1122 concerning products within their purview. Please respond to the following and we will pass your responses along to them.

Please provide Safety Data Sheet (SDS) for the at use concentrations of the substance and include a description of how the use of this technology will not adversely affect the safety of FSIS inspectors. Workplace safety and health hazards include inhalation, direct skin contact (skin, eyes, mouth), and fire/explosion caused by exposure to the product, its working solution or dry mixture and potential by-products formed and/or off-gassed during the application process. The employee safety information should demonstrate how the New Technology will not “jeopardize the safety of Federal inspection personnel” as specified in the [FSIS Compliance Guideline Procedures for New Technology Notifications and Protocols, April 2015](#). FSIS workplace and employee safety must be specifically addressed. Please refer to Appendix A on p. 17, Workplace Safety and Health Criteria, for clarification on what to provide in the response. For additional clarity with respect to employee safety, the following are examples of information that are typically needed by FSIS’ employee safety and health group;

1. Potential workplace exposures that could result from inhalation and direct contact during use of the substance/technology. This information is required in addition to a SDS to determine accurate hazard potential and recommended exposure control measures for IPP work areas in accordance with Occupational Safety and Health Administration (OSHA) regulations: 29 CFR 1910.1200, Hazard Communication, 29 CFR 1910.132, Personal Protective Equipment, and 29 CFR 1910.1000, Air Contaminants. The information should be included as a specific section in each of the protocols.
2. If the SDS workplace hazards/precautions do not apply to the type of exposure that would be expected for the FSIS IPP, please have the submitter provide specific information (per the April 2015 FSIS Compliance Guideline Procedures) for the actual type of exposures expected.
3. If no IPP workplace exposures are expected and no control measures are required, please have the submitter state this and provide the reasons why (e.g., such as the substance “as used” [for all concentrations] is not hazardous by inhalation or direct contact and/or IPP would not be exposed to the substance based on the system design, operation and/or control measures that will be in place).
4. Please also indicate how will FSIS IPP be informed of the above information so that it is clear that the information contained in the SDS for the concentrate does not apply to their actual workplace exposure.
5. Are there any potential hazards from chemical mixing or low pH as a result of discharges of the various solutions to floor drains? Are dedicated drain lines or any other enclosures required?
6. With respect to potential airborne exposures to FSIS IPP in the use/application areas, does the submitter have air sampling results taken during the use of the various concentrations of the technology in the listed mixture?
7. The intended use of this product in FSIS meat and poultry products is apparently as a binder/extender. The suitability support provided in Appendix 6 does sufficiently support no

significant difference in yield and other organoleptic qualities when used as a partial replacement for another binder in a processed meat and poultry product, such as sausage. However, **additional suitability support is needed:**

- a. No suitability data was provided for **whole muscle meat and poultry products at the maximum proposed use level**. We would need to see similar data as provided in Appendix 6 for:

Whole muscle red meat control containing no other binders, extenders, or moisture retention agents, as compared to a whole muscle red meat product containing 15% isolated canola product.

Whole muscle poultry control containing no other binders, extenders, or moisture retention agents as compared to a whole muscle poultry product containing 15% isolated canola product.

Responses may be sent in an email or in a separate document. We respectfully request a response within 10 business days. If you are unable to complete the response within that time frame, please contact me to discuss further options.

If you have any additional questions or concerns, please don't hesitate to contact me at stephen.difranco@fda.hhs.gov or by phone at 240.402.2710.

Best,

Steve

Stephen DiFranco, PhD

Regulatory Review Scientist/Chemist

Center for Food Safety and Applied Nutrition

Office of Food Additive Safety

Division of Food Ingredients

U.S. Food and Drug Administration

Tel: 240-402-2710

stephen.difranco@fda.hhs.gov



CAUTION: This email, including any attachments, is confidential. If you are not the intended recipient, please notify the sender and delete the email and any attachments from your system. In addition, you must not use, distribute or reproduce this email or any attachments. Opinions and other information in this email and any attachments which do not relate to the official business of Argenta are neither given by nor endorsed by Argenta. While Argenta uses anti-virus software, Argenta accepts no liability for any viruses in this email or any attachment, or for any effects this email or any attachment may have on your network or computer system.

CAUTION: This email, including any attachments, is confidential. If you are not the intended recipient, please notify the sender and delete the email and any attachments from your system. In addition, you must not use, distribute or reproduce this email or any attachments. Opinions and other information in this email and any attachments which do not relate to the official business of Argenta are neither given by nor endorsed by Argenta. While Argenta uses anti-virus software, Argenta accepts no liability for any viruses in this email or any attachment, or for any effects this email or any attachment may have on your network or computer system.

Este correo electrónico y los archivos adjuntos, enviados por Pen & Tec Consulting SLU, que opera bajo el nombre comercial de Argenta® (Argenta), son confidenciales y pueden estar protegidos por ley. Si usted no es el destinatario, cualquier divulgación, reproducción, copia, distribución u otro tipo de difusión o uso de esta comunicación está estrictamente prohibido. Si ha recibido esta transmisión por error, notifíquelo al remitente y elimine inmediatamente el correo electrónico y cualquier archivo adjunto de su sistema. Argenta no emite ni respalda las opiniones y demás información contenida en este correo electrónico y en sus anexos que no estén relacionadas con las actividades oficiales de Argenta. Aunque Argenta utiliza software antivirus, Argenta no acepta ninguna responsabilidad por cualquier virus en este correo electrónico o cualquier archivo adjunto, o por cualquier efecto que este correo electrónico o cualquier archivo adjunto pueda tener en su red o sistema informático. Argenta registra y almacena los correos electrónicos enviados a nosotros o a nuestros afiliados de acuerdo con nuestras políticas y procedimientos internos. Consulte www.pentec-consulting.eu para obtener información sobre Argenta y/o nuestra política de privacidad.

This email and any attached file(s), sent by Pen & Tec Consulting SLU trading as Argenta® (Argenta), are confidential and may be legally privileged. If you are not the intended recipient, any disclosure, reproduction, copying, distribution, or other dissemination or use of this communication is strictly prohibited. If you have received this transmission in error, please notify the sender and delete the email and any attachments from your system immediately. Opinions and other information in this email and any attachments which do not relate to the official business of Argenta are neither given by nor endorsed by Argenta. While Argenta uses anti-virus software, Argenta accepts no liability for any viruses in this email or any attachment, or for any effects this email or any attachment may have on your network or computer system. Argenta records and stores emails sent to us or our affiliates in keeping with our internal policies and procedures. Please see www.pentec-consulting.eu for information regarding Argenta and/or our privacy policy.

Este correo electrónico y los archivos adjuntos, enviados por Pen & Tec Consulting SLU, que opera bajo el nombre comercial de Argenta® (Argenta), son confidenciales y pueden estar protegidos por ley. Si usted no es el destinatario, cualquier divulgación, reproducción, copia, distribución u otro tipo de difusión o uso de esta comunicación está estrictamente prohibido. Si ha recibido esta transmisión por error, notifíquelo al remitente y elimine inmediatamente el correo electrónico y cualquier archivo adjunto de su sistema. Argenta no emite ni respalda las opiniones y demás información contenida en este correo electrónico y en sus anexos que no estén relacionadas con las actividades oficiales de Argenta. Aunque Argenta utiliza software antivirus, Argenta no acepta ninguna responsabilidad por cualquier virus en este correo electrónico o cualquier archivo adjunto, o por cualquier efecto que este correo electrónico o cualquier archivo adjunto pueda tener en su red o sistema informático. Argenta registra y almacena los correos electrónicos enviados a nosotros o a nuestros afiliados de acuerdo con nuestras políticas y procedimientos internos. Consulte www.pentec-consulting.eu para obtener información sobre Argenta y/o nuestra política de privacidad.

This email and any attached file(s), sent by Pen & Tec Consulting SLU trading as Argenta® (Argenta), are confidential and may be legally privileged. If you are not the intended recipient, any disclosure, reproduction, copying, distribution, or other dissemination or use of this communication is strictly prohibited. If you have received this transmission in error, please notify the sender and delete the email and any attachments from your system immediately. Opinions and other information in this email and any attachments which do not relate to the official business of Argenta are neither given by nor endorsed by Argenta. While Argenta uses anti-virus software, Argenta accepts no liability for any viruses in this email or any attachment, or for any effects this email or any attachment may have on your network or computer system. Argenta records and stores emails sent to us or our affiliates in keeping with our internal policies and procedures. Please see www.pentec-consulting.eu for information regarding Argenta and/or our privacy policy.

Este correo electrónico y los archivos adjuntos, enviados por Pen & Tec Consulting SLU, que opera bajo el nombre comercial de Argenta® (Argenta), son confidenciales y pueden estar protegidos por ley. Si usted no es el destinatario, cualquier divulgación, reproducción, copia, distribución u otro tipo de difusión o uso de esta comunicación está estrictamente prohibido. Si ha recibido esta

transmisión por error, notifíquelo al remitente y elimine inmediatamente el correo electrónico y cualquier archivo adjunto de su sistema. Argenta no emite ni respalda las opiniones y demás información contenida en este correo electrónico y en sus anexos que no estén relacionadas con las actividades oficiales de Argenta. Aunque Argenta utiliza software antivirus, Argenta no acepta ninguna responsabilidad por cualquier virus en este correo electrónico o cualquier archivo adjunto, o por cualquier efecto que este correo electrónico o cualquier archivo adjunto pueda tener en su red o sistema informático. Argenta registra y almacena los correos electrónicos enviados a nosotros o a nuestros afiliados de acuerdo con nuestras políticas y procedimientos internos. Consulte www.pentec-consulting.eu para obtener información sobre Argenta y/o nuestra política de privacidad.

This email and any attached file(s), sent by Pen & Tec Consulting SLU trading as Argenta® (Argenta), are confidential and may be legally privileged. If you are not the intended recipient, any disclosure, reproduction, copying, distribution, or other dissemination or use of this communication is strictly prohibited. If you have received this transmission in error, please notify the sender and delete the email and any attachments from your system immediately. Opinions and other information in this email and any attachments which do not relate to the official business of Argenta are neither given by nor endorsed by Argenta. While Argenta uses anti-virus software, Argenta accepts no liability for any viruses in this email or any attachment, or for any effects this email or any attachment may have on your network or computer system. Argenta records and stores emails sent to us or our affiliates in keeping with our internal policies and procedures. Please see www.pentec-consulting.eu for information regarding Argenta and/or our privacy policy.

From: [Justyna Pałasińska](#)
To: [DiFranco, Stephen](#)
Subject: Re: [EXTERNAL] GRN 1122 canola concentrate status
Date: Tuesday, July 2, 2024 10:59:39 AM
Attachments: [image001.png](#)
[image007.png](#)
[image008.png](#)
[image009.png](#)
[image010.png](#)
[image011.png](#)
[image012.png](#)
[Outlook-Image.png](#)
[Outlook-Image.png](#)

CAUTION: This email originated from outside of the organization. Do not click links or open attachments unless you recognize the sender and know the content is safe.

Many thanks for your swift reply, Steve.

We will update the GRAS & get the updated version to you shortly. I wanted to check a couple questions with you:

- understand the issue is with 'source of fiber' & not with other claims, e.g. 'source of protein'. Could you confirm?
- one of the intended uses is 'protein-fiber and nutritional powders'. I understand that we can keep this category, as the product is a source of protein & therefore can be used as an ingredient for this category of foods. Could you confirm?
- Is it OK for us to send the updated GRAS document by e-mail or do you require a CD-submission?

I look forward to your reply.

Kind regards,

Justyna Pałasińska

Regulatory Affairs Director – Human Nutrition, Argenta Barcelona



M +34 682 894 653 T +34 936 758 015



La información contenida en este mensaje y/o archivo(s) adjunto(s), enviada desde Pen & Tec Consulting SLU cotiza como Argenta, es confidencial/privilegiada y está destinada a ser leída sólo por la(s) persona(s) a la(s) que va dirigida. Le recordamos que sus datos han sido incorporados en el sistema de tratamiento de Pen & Tec Consulting SLU cotiza como Argenta, y que siempre y cuando se cumplan los requisitos exigidos por la normativa, usted podrá ejercer sus derechos de acceso, rectificación, limitación de tratamiento, supresión, portabilidad y oposición/revocación, en los términos que establece la normativa vigente en materia de protección de datos, dirigiendo su petición a la dirección postal OneCoWork, Portal de l'Àngel 40, 08002, Barcelona o bien a través de correo electrónico info@pentec-consulting.eu. Si usted lee este mensaje y no es el destinatario señalado, el empleado o el agente responsable de entregar el mensaje al destinatario, o ha recibido esta comunicación por error, le informamos que está totalmente prohibida, y puede ser ilegal, cualquier divulgación, distribución o reproducción de esta comunicación, y le rogamos que nos lo notifique inmediatamente y nos devuelva el mensaje original a la dirección arriba mencionada. Gracias.

The information contained in this message and/or attached file(s), sent by Pen & Tec Consulting SLU trading as Argenta, is confidential/privileged and is intended to be read solely by the person(s) to whom it is addressed. We hereby inform you that your data will be incorporated into the processing system owned by Pen & Tec Consulting SLU, and that provided it complies with the requirements included in the law, you may exercise the rights of access, rectification, limitation of processing, deletion, portability and opposition by sending your request to the postal address OneCoWork, Portal de l'Àngel 40, 08002, Barcelona or to the email address info@pentec-consulting.eu. If you read this message and you are neither the intended recipient, employee or agent in charge of delivering the message to the recipient, or if you have received this message as the result of an error, we hereby inform you that distributing, sharing or reproducing any part of this message is totally forbidden and may be illegal. As a result, we request that you immediately inform us of the error and return this message to the address mentioned above. Thank you.

From: DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>
Sent: 01 July 2024 21:32
To: Justyna Pałasińska <justyna.palasinaska@argentaglobal.com>
Subject: RE: [EXTERNAL] GRN 1122 canola concentrate status

Hello Justyna,

In finalizing our response letter we ran into a bit of an issue regarding the notice's claim that the ingredient is a source of dietary fiber, as this is a legally defined area in US regulations. I got the following from our review team for your consideration:

NapiFeryn states that canola concentrate is intended to be used as a source of dietary fiber amongst other intended uses (i.e., source of protein, formulation aid, stabilizer, thickener, or texturizer). We note that FDA defines dietary fiber as "non-digestible soluble and insoluble carbohydrates (with 3 or more monomeric units), and lignin that are intrinsic and intact in plants; isolated or synthetic non-digestible carbohydrates (with 3 or more monomeric units) determined by FDA to have physiological effects that are beneficial to human health" (21 CFR 101.9(c)(6)(i)). Additional information related to dietary fiber can be found at <https://www.fda.gov/food/food-labeling-nutrition/questions-and-answers-dietary-fiber>.

During our evaluation of GRN 001122 we were not able to determine whether canola concentrate meets the definition of dietary fiber. To proceed with our evaluation of GRN 001122, we recommend that NapiFeryn reconsider the description of the intended uses of canola concentrate by replacing the intended use as "a source of dietary fiber" with the use as "an ingredient".

If NapiFeryn wishes to use canola concentrate as a source of dietary fiber, we recommend that you consult with FDA's Office of Nutrition and Food Labeling (ONFL) on whether the ingredient meets the definition of dietary fiber. After ONFL provides a favorable determination, NapiFeryn may choose to inform FDA about their GRAS conclusion for the use of canola concentrate as a source of dietary fiber by submitting a supplement to GRN 001122.

Again, amending the notice to state the use is simply as "an ingredient" will allow us to close out this GRAS notice while still allowing the

ingredient to be used in foods. If you then wish to have the use as a source of dietary fiber included in the notice and/or displayed on the [GRAS Notice inventory](#), we can go back and amend as appropriate pending the outcome with ONFL.

Happy to discuss if this is unclear.

Thanks,

Steve

Stephen DiFranco, PhD

Regulatory Review Scientist/Chemist

Center for Food Safety and Applied Nutrition
Office of Food Additive Safety
Division of Food Ingredients
U.S. Food and Drug Administration
Tel: 240-402-2710
stephen.difranco@fda.hhs.gov



From: Justyna Pałasińska <justyna.palasinaska@argentaglobal.com>
Sent: Monday, July 1, 2024 8:16 AM
To: DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>
Subject: Re: [EXTERNAL] GRN 1122 canola concentrate status

CAUTION: This email originated from outside of the organization. Do not click links or open attachments unless you recognize the sender and know the content is safe.

Hi Steve,

I hope you are doing well.

Could you let me know when the letter is expected to receive clearance & be shared with the applicant?

Kind regards,

Justyna Pałasińska

Regulatory Affairs Director – Human Nutrition, Argenta Barcelona



M +34 682 894 653 T +34 936 758 015

www.argentaglobal.com

La información contenida en este mensaje y/o archivo(s) adjunto(s), enviada desde Pen & Tec Consulting SLU cotiza como Argenta, es confidencial/privilegiada y está destinada a ser leída sólo por la(s) persona(s) a la(s) que va dirigida. Le recordamos que sus datos han sido incorporados en el sistema de tratamiento de Pen & Tec Consulting SLU cotiza como Argenta, y que siempre y cuando se cumplan los requisitos exigidos por la normativa, usted podrá ejercer sus derechos de acceso, rectificación, limitación de tratamiento, supresión, portabilidad y oposición/revocación, en los términos que establece la normativa vigente en materia de protección de datos, dirigiendo su petición a la dirección postal OneCoWork, Portal de l'Àngel 40, 08002, Barcelona o bien a través de correo electrónico info@pentec-consulting.eu. Si usted lee este mensaje y no es el destinatario señalado, el empleado o el agente responsable de entregar el mensaje al destinatario, o ha recibido esta comunicación por error, le informamos que está totalmente prohibida, y puede ser ilegal, cualquier divulgación, distribución o reproducción de esta comunicación, y le rogamos que nos lo notifique inmediatamente y nos devuelva el mensaje original a la dirección arriba mencionada. Gracias.
The information contained in this message and/or attached file(s), sent by Pen & Tec Consulting SLU trading as Argenta, is confidential/privileged and is intended to be read solely by the person(s) to whom it is addressed. We hereby inform you that your data will be incorporated into the processing system owned by Pen & Tec Consulting SLU, and that provided it complies with the requirements included in the law, you may exercise the rights of access, rectification, limitation of processing, deletion, portability and opposition by sending your request to the postal address OneCoWork, Portal de l'Àngel 40, 08002, Barcelona or to the email address info@pentec-consulting.eu. If you read this message and you are neither the intended recipient, employee or agent in charge of delivering the message to the recipient, or if you have received this message as the result of an error, we hereby inform you that distributing, sharing or reproducing any part of this message is totally forbidden and may be illegal. As a result, we request that you immediately inform us of the error and return this message to the address mentioned above. Thank you.

From: Justyna Pałasińska <justyna.palasinaska@argentaglobal.com>
Sent: 30 May 2024 16:09
To: DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>
Subject: Re: [EXTERNAL] GRN 1122 canola concentrate status

Indeed, great news, thank you Steve!

Kind regards,

Justyna Pałasińska

Regulatory Affairs Director – Human Nutrition, Argenta Barcelona



M +34 682 894 653 T +34 936 758 015

www.argentaglobal.com

La información contenida en este mensaje y/o archivo(s) adjunto(s), enviada desde Pen & Tec Consulting SLU cotiza como Argenta, es confidencial/privilegiada y está destinada a ser leída sólo por la(s) persona(s) a la(s) que va dirigida. Le recordamos que sus datos han sido incorporados en el sistema de tratamiento de Pen & Tec Consulting SLU cotiza como Argenta, y que siempre y cuando se cumplan los requisitos exigidos por la normativa, usted podrá ejercer sus derechos de acceso, rectificación, limitación de tratamiento, supresión, portabilidad y oposición/revocación, en los términos que establece la normativa vigente en materia de protección de datos, dirigiendo su petición a la dirección postal OneCoWork, Portal de l'Àngel 40, 08002, Barcelona o bien a través de correo electrónico info@pentec-consulting.eu. Si usted lee este mensaje y no es el destinatario señalado, el empleado o el agente responsable de entregar el mensaje al destinatario, o ha recibido esta comunicación por error, le informamos que está totalmente prohibida, y puede ser ilegal, cualquier divulgación, distribución o reproducción de esta comunicación, y le rogamos que nos lo notifique inmediatamente y nos devuelva el mensaje original a la dirección arriba mencionada. Gracias.
The information contained in this message and/or attached file(s), sent by Pen & Tec Consulting SLU trading as Argenta, is confidential/privileged and is intended to be read solely by the person(s) to whom it is addressed. We hereby inform you that your data will be incorporated into the processing system owned by Pen & Tec Consulting SLU, and that provided it complies with the requirements included in the law, you may exercise the rights of access, rectification, limitation of processing, deletion, portability and opposition by sending your request to the postal address OneCoWork, Portal de l'Àngel 40, 08002, Barcelona or to the email address info@pentec-consulting.eu. If you read this message and you are neither the intended recipient, employee or agent in charge of delivering the message to the recipient, or if you have received this message as the result of an error, we hereby inform you that distributing, sharing or reproducing any part of this message is totally forbidden and may be illegal. As a result, we request that you immediately inform us of the error and return this message to the address mentioned above. Thank you.

From: DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>
Sent: 30 May 2024 16:06
To: Justyna Pałasińska <justyna.palasinaska@argentaglobal.com>
Subject: RE: [EXTERNAL] GRN 1122 canola concentrate status

Hi Justyna,

I finally have some good news for you—FSIS has just finished their review. I have drafted a response letter and it is currently making its way through clearance, so you should hear back soon.

Best,

Steve

Stephen DiFranco, PhD

Regulatory Review Scientist/Chemist

Center for Food Safety and Applied Nutrition
Office of Food Additive Safety
Division of Food Ingredients
U.S. Food and Drug Administration
Tel: 240-402-2710
stephen.difranco@fda.hhs.gov



From: Justyna Pałasińska <justyna.palasinaska@argentaglobal.com>
Sent: Thursday, May 30, 2024 9:48 AM
To: DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>
Subject: Re: [EXTERNAL] GRN 1122 canola concentrate status

CAUTION: This email originated from outside of the organization. Do not click links or open attachments unless you recognize the sender and know the content is safe.

Dear Stephen,

I hope this e-mail finds you well. I was wondering if there is any update from FSIS on this GRN?

Kind regards,

Justyna Pałasińska

Regulatory Affairs Director – Human Nutrition, Argenta Barcelona



M +34 682 894 653 T +34 936 758 015

www.argentaglobal.com

La información contenida en este mensaje y/o archivo(s) adjunto(s), enviada desde Pen & Tec Consulting SLU cotiza como Argenta, es confidencial/privilegiada y está destinada a ser leída sólo por la(s) persona(s) a la(s) que va dirigida. Le recordamos que sus datos han sido incorporados en el sistema de tratamiento de Pen & Tec Consulting SLU cotiza como Argenta, y que siempre y cuando se cumplan los requisitos exigidos por la normativa, usted podrá ejercer sus derechos de acceso, rectificación, limitación de tratamiento, supresión, portabilidad y oposición/revocación, en

los términos que establece la normativa vigente en materia de protección de datos, dirigiendo su petición a la dirección postal OneCoWork, Portal de l'Àngel 40, 08002. Barcelona o bien a través de correo electrónico info@pentec-consulting.eu. Si usted lee este mensaje y no es el destinatario señalado, el empleado o el agente responsable de entregar el mensaje al destinatario, o ha recibido esta comunicación por error, le informamos que está totalmente prohibida, y puede ser ilegal, cualquier divulgación, distribución o reproducción de esta comunicación, y le rogamos que nos lo notifique inmediatamente y nos devuelva el mensaje original a la dirección arriba mencionada. Gracias.

The information contained in this message and/or attached file(s), sent by Pen & Tec Consulting SLU trading as Argenta, is confidential/privileged and is intended to be read solely by the person(s) to whom it is addressed. We hereby inform you that your data will be incorporated into the processing system owned by Pen & Tec Consulting SLU, and that provided it complies with the requirements included in the law, you may exercise the rights of access, rectification, limitation of processing, deletion, portability and opposition by sending your request to the postal address OneCoWork, Portal de l'Àngel 40, 08002. Barcelona or to the email address info@pentec-consulting.eu. If you read this message and you are neither the intended recipient, employee or agent in charge of delivering the message to the recipient, or if you have received this message as the result of an error, we hereby inform you that distributing, sharing or reproducing any part of this message is totally forbidden and may be illegal. As a result, we request that you immediately inform us of the error and return this message to the address mentioned above. Thank you.

From: DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>
Sent: 04 April 2024 17:26
To: Justyna Pałasińska <justyna.palasinaska@argentaglobal.com>
Subject: RE: [EXTERNAL] GRN 1122 canola concentrate status

Thanks Justyna,

I've passed the information to FSIS for review. Hopefully we will hear back shortly.

Best,

Steve

Stephen DiFranco, PhD
Regulatory Review Scientist/Chemist

Center for Food Safety and Applied Nutrition
Office of Food Additive Safety
Division of Food Ingredients
U.S. Food and Drug Administration
Tel: 240-402-2710
stephen.difranco@fda.hhs.gov



From: Justyna Pałasińska <justyna.palasinaska@argentaglobal.com>
Sent: Thursday, April 4, 2024 7:38 AM
To: DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>
Subject: Re: [EXTERNAL] GRN 1122 canola concentrate status

CAUTION: This email originated from outside of the organization. Do not click links or open attachments unless you recognize the sender and know the content is safe.

Dear Stephen,

Please find our reply below:

It is the applicant's understanding that OSHA OELs for heavy metals indicated by FSIS relate to the risk of exposure to heavy metals in the material under assessment via inhalation route only. The material indeed may create dust hazard if handled improperly. We note that the safety data sheet provided for the material (attached for reference) not only informs about the potential to form dust if handled improperly but also includes information on precautionary measures and personal protection and engineering controls aimed at eliminating or greatly reducing the risk of exposure to airborne particles. Proper handling of the material / adherence to these measures and controls by extension would eliminate or greatly reduce the risk of exposure to heavy metals that may be present in the material.

In case the above does not sufficiently address the potential risk of exposure to heavy metals present in the material via inhalation route, the applicant would like to inform that the bulk density of the material ranges between 0.1 and 0.3 g/cm³. A confirmation whether this information is sufficient to proceed with the calculations would be much appreciated. It would also be helpful to understand the assumptions being made by FSIS (e.g. concentration of airborne particles) when assessing whether the levels of heavy metals in the product may exceed OSHA OELs.

Kind regards,
Justyna Pałasińska
Regulatory Affairs Director – Human Nutrition, Argenta Barcelona

M +34 682 894 653 T +34 936 758 015


www.argentaglobal.com

La información contenida en este mensaje y/o archivo(s) adjunto(s), enviada desde Pen & Tec Consulting SLU cotiza como Argenta, es confidencial/privilegiada y está destinada a ser leída sólo por la(s) persona(s) a la(s) que va dirigida. Le recordamos que sus datos han sido incorporados en el sistema de tratamiento de Pen & Tec Consulting SLU cotiza como Argenta, y que siempre y cuando se cumplan los requisitos exigidos

por la normativa, usted podrá ejercer sus derechos de acceso, rectificación, limitación de tratamiento, supresión, portabilidad y oposición/revocación, en los términos que establece la normativa vigente en materia de protección de datos, dirigiendo su petición a la dirección postal OneCoWork, Portal de l'Àngel 40, 08002, Barcelona o bien a través de correo electrónico info@pentec-consulting.eu. Si usted lee este mensaje y no es el destinatario señalado, el empleado o el agente responsable de entregar el mensaje al destinatario, o ha recibido esta comunicación por error, le informamos que está totalmente prohibida, y puede ser ilegal, cualquier divulgación, distribución o reproducción de esta comunicación, y le rogamos que nos lo notifique inmediatamente y nos devuelva el mensaje original a la dirección arriba mencionada. Gracias.

The information contained in this message and/or attached file(s), sent by Pen & Tec Consulting SLU trading as Argenta, is confidential/privileged and is intended to be read solely by the person(s) to whom it is addressed. We hereby inform you that your data will be incorporated into the processing system owned by Pen & Tec Consulting SLU, and that provided it complies with the requirements included in the law, you may exercise the rights of access, rectification, limitation of processing, deletion, portability and opposition by sending your request to the postal address OneCoWork, Portal de l'Àngel 40, 08002, Barcelona or to the email address info@pentec-consulting.eu. If you read this message and you are neither the intended recipient, employee or agent in charge of delivering the message to the recipient, or if you have received this message as the result of an error, we hereby inform you that distributing, sharing or reproducing any part of this message is totally forbidden and may be illegal. As a result, we request that you immediately inform us of the error and return this message to the address mentioned above. Thank you.

From: DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>
Date: Thursday, 28 March 2024 at 20:47
To: Justyna Pałasińska <justyna.palasinaska@argentaglobal.com>
Subject: RE: [EXTERNAL] GRN 1122 canola concentrate status

Hello Justyna,

I got feedback from FSIS about their review of GRN 1122. They send the following:

I have now completed the review of the documentation submitted for the approval of the above-referenced compound. I noted that it contains Lead (≤ 0.5 mg/kg), Arsenic (≤ 0.2 mg/kg), Cadmium (≤ 0.2 mg/kg), and Mercury (≤ 0.1 mg/kg). OSHA has established OEL for these substances at 0.05 mg/m³, 0.01 mg/m³, 0.01 mg/m³, 0.025 mg/m³ (depending on presentation) respectively.

To finalize my analysis, I require the composition in mg/m³ of each of these elements or the density so I may calculate their composition accurately and evaluate them against their OSHA standards.

Are you able to provide the density of the canola concentrate? I believe this is the easiest way to answer their questions. From the density and the specified ppm levels, the reviewer should be able to calculate the maximum amount by weight of each heavy metal contaminate for a given volume of canola concentrate.

Best,

Steve

Stephen DiFranco, PhD
Regulatory Review Scientist/Chemist

Center for Food Safety and Applied Nutrition
Office of Food Additive Safety
Division of Food Ingredients
U.S. Food and Drug Administration
Tel: 240-402-2710
stephen.difranco@fda.hhs.gov



From: Justyna Pałasińska <justyna.palasinaska@argentaglobal.com>
Sent: Monday, March 4, 2024 5:04 AM
To: DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>
Subject: Re: [EXTERNAL] GRN 1122 canola concentrate status

CAUTION: This email originated from outside of the organization. Do not click links or open attachments unless you recognize the sender and know the content is safe.

Many thanks for the update, Stephen. We look forward to hearing an update, hopefully soon!

Kind regards,
Justyna Pałasińska
Regulatory Affairs Director – Human Nutrition, Argenta Barcelona

M +34 682 894 653 T +34 936 758 015


www.argentaglobal.com



La información contenida en este mensaje y/o archivo(s) adjunto(s), enviada desde Pen & Tec Consulting SLU cotiza como Argenta, es confidencial/privilegiada y está destinada a ser leída sólo por la(s) persona(s) a la(s) que va dirigida. Le recordamos que sus datos han sido incorporados en el sistema de tratamiento de Pen & Tec Consulting SLU cotiza como Argenta, y que siempre y cuando se cumplan los requisitos exigidos por la normativa, usted podrá ejercer sus derechos de acceso, rectificación, limitación de tratamiento, supresión, portabilidad y oposición/revocación, en los términos que establece la normativa vigente en materia de protección de datos, dirigiendo su petición a la dirección postal Pl. Ausias March 1, 4 planta 08195, Sant Cugat del Vallès (Barcelona) o bien a través de correo electrónico info@pentec-consulting.eu. Si usted lee este mensaje y no es el destinatario señalado, el empleado o el agente responsable de entregar el mensaje al destinatario, o ha recibido esta comunicación por error, le informamos que está totalmente prohibida, y puede ser ilegal, cualquier divulgación, distribución o reproducción de esta comunicación, y le rogamos que nos lo notifique inmediatamente y nos devuelva el mensaje original a la dirección arriba mencionada. Gracias.

The information contained in this message and/or attached file(s), sent by Pen & Tec Consulting SLU trading as Argenta, is confidential/privileged and is intended to be read solely by the person(s) to whom it is addressed. We hereby inform you that your data will be incorporated into the processing system owned by Pen & Tec Consulting SLU, and that provided it complies with the requirements included in the law, you may exercise the rights of access, rectification, limitation of processing, deletion, portability and opposition by sending your request to the postal address Pl. Ausias March 1, 4 floor 08195, Sant Cugat del Valles (Barcelona) or to the email address info@pentec-consulting.eu. If you read this message and you are neither the intended recipient, employee or agent in charge of delivering the message to the recipient, or if you have received this message as the result of an error, we hereby inform you that distributing, sharing or reproducing any part of this message is totally forbidden and may be illegal. As a result, we request that you immediately inform us of the error and return this message to the address mentioned above. Thank you.

From: DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>
Date: Monday, 26 February 2024 at 17:20
To: Justyna Pałasińska <justyna.palasinaska@argentaglobal.com>
Subject: RE: [EXTERNAL] GRN 1122 canola concentrate status

Hello Justyna,

Regarding GRN 1122; FDA has completed its review and has drafted a response letter. Unfortunately, we cannot move forward before USDA-FSIS completes their review of the uses under their jurisdiction. I have been periodically inquiring with FSIS as to the status and will get this to you as soon as possible.

We appreciate your continued patience.

Best,

Steve

Stephen DiFranco, PhD
Regulatory Review Scientist/Chemist

Center for Food Safety and Applied Nutrition
Office of Food Additive Safety
Division of Food Ingredients
U.S. Food and Drug Administration
Tel: 240-402-2710
stephen.difranco@fda.hhs.gov



From: Justyna Pałasińska <justyna.palasinaska@argentaglobal.com>
Sent: Wednesday, February 14, 2024 12:07 PM
To: Premarkt <Premarkt@fda.hhs.gov>
Cc: DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>; Ioannis Kartanos <ioannis.kartanos@argentaglobal.com>
Subject: [EXTERNAL] GRN 1122 canola concentrate status

CAUTION: This email originated from outside of the organization. Do not click links or open attachments unless you recognize the sender and know the content is safe.

Dear HHS team,

I am writing to enquire about a GRAS notice that was submitted to the FDA & filed April 19, 2023 (GRN 1122). We have been in touch with Mr Stephen DiFranco & at the beginning of December he has informed us that the FDA reviews are complete & the notice is now with USDA-FSIS.

Mr DiFranco has been very helpful through the whole process. However, we have tried to contact him several times since December without success. We were wondering if there is someone else we can get in touch with for an update on this application. We would be happy to provide any information that would help finalize the process.

I look forward to hearing from you.

Kind regards,
Justyna Pałasińska
Regulatory Affairs Director – Human Nutrition, Argenta Barcelona



M +34 682 894 653 T +34 936 758 015

www.argentaglobal.com

La información contenida en este mensaje y/o archivo(s) adjunto(s), enviada desde Pen & Tec Consulting SLU cotiza como Argenta, es confidencial/privilegiada y está destinada a ser leída sólo por la(s) persona(s) a la(s) que va dirigida. Le recordamos que sus datos han sido incorporados en el sistema de tratamiento de Pen & Tec Consulting SLU cotiza como Argenta, y que siempre y cuando se cumplan los requisitos exigidos por la normativa, usted podrá ejercer sus derechos de acceso, rectificación, limitación de tratamiento, supresión, portabilidad y oposición/revocación, en los términos que establece la normativa vigente en materia de protección de datos, dirigiendo su petición a la dirección postal Pl. Ausias March 1, 4 planta 08195, Sant Cugat del Vallès (Barcelona) o bien a través de correo electrónico info@pentec-consulting.eu. Si usted lee este mensaje y no es el destinatario señalado, el empleado o el agente responsable de entregar el mensaje al destinatario, o ha recibido esta comunicación por error, le informamos que está totalmente prohibida, y puede ser ilegal, cualquier divulgación, distribución o reproducción de esta comunicación, y le rogamos que nos lo notifique inmediatamente y nos devuelva el mensaje original a la dirección arriba mencionada. Gracias.

The information contained in this message and/or attached file(s), sent by Pen & Tec Consulting SLU trading as Argenta, is confidential/privileged and is intended to be read solely by the person(s) to whom it is addressed. We hereby inform you that your data will be incorporated into the processing system owned by Pen & Tec Consulting SLU, and that provided it complies with the requirements included in the law, you may exercise the rights of access, rectification, limitation of processing, deletion, portability and opposition by sending your request to the postal address Pl. Ausias March 1, 4 floor 08195, Sant Cugat del Valles (Barcelona) or to the email address info@pentec-consulting.eu. If you read this message and you are neither the intended recipient, employee or agent in charge of delivering the message to the recipient, or if you have received this message as the result of an error, we hereby inform you that distributing, sharing or reproducing any part of this message is totally forbidden and may be illegal. As a result, we request that you immediately inform us of the error and return this message to the address mentioned above. Thank you.

From: Justyna Pałasińska <justyna.palasinaska@argentaglobal.com>

Date: Wednesday, 31 January 2024 at 17:53

To: Justyna Pałasińska <justyna.palasinaska@argentaglobal.com>, DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>

Cc: Ioannis Kartanos <ioannis.kartanos@argentaglobal.com>

Subject: Re: [EXTERNAL] GRN 1122 canola concentrate - update contact person

Dear Steve,

I hope this e-mail finds you well. I was wondering if there are any updates on the finalization of this notification?

Is there any additional information that needs to be provided?

Kind regards,

Justyna Pałasińska

Regulatory Affairs Director – Human Nutrition, Argenta Barcelona



M +34 682 894 653 T +34 936 758 015

www.argentaglobal.com

La información contenida en este mensaje y/o archivo(s) adjunto(s), enviada desde Pen & Tec Consulting SLU cotiza como Argenta, es confidencial/privilegiada y está destinada a ser leída sólo por la(s) persona(s) a la(s) que va dirigida. Le recordamos que sus datos han sido incorporados en el sistema de tratamiento de Pen & Tec Consulting SLU cotiza como Argenta, y que siempre y cuando se cumplan los requisitos exigidos por la normativa, usted podrá ejercer sus derechos de acceso, rectificación, limitación de tratamiento, supresión, portabilidad y oposición/revocación, en los términos que establece la normativa vigente en materia de protección de datos, dirigiendo su petición a la dirección postal Pl. Ausias March 1, 4 planta 08195, Sant Cugat del Vallès (Barcelona) o bien a través de correo electrónico info@pentec-consulting.eu. Si usted lee este mensaje y no es el destinatario señalado, el empleado o el agente responsable de entregar el mensaje al destinatario, o ha recibido esta comunicación por error, le informamos que está totalmente prohibida, y puede ser ilegal, cualquier divulgación, distribución o reproducción de esta comunicación, y le rogamos que nos lo notifique inmediatamente y nos devuelva el mensaje original a la dirección arriba mencionada. Gracias.

The information contained in this message and/or attached file(s), sent by Pen & Tec Consulting SLU trading as Argenta, is confidential/privileged and is intended to be read solely by the person(s) to whom it is addressed. We hereby inform you that your data will be incorporated into the processing system owned by Pen & Tec Consulting SLU, and that provided it complies with the requirements included in the law, you may exercise the rights of access, rectification, limitation of processing, deletion, portability and opposition by sending your request to the postal address Pl. Ausias March 1, 4 floor 08195, Sant Cugat del Valles (Barcelona) or to the email address info@pentec-consulting.eu. If you read this message and you are neither the intended recipient, employee or agent in charge of delivering the message to the recipient, or if you have received this message as the result of an error, we hereby inform you that distributing, sharing or reproducing any part of this message is totally forbidden and may be illegal. As a result, we request that you immediately inform us of the error and return this message to the address mentioned above. Thank you.

From: Justyna Pałasińska <justyna@pentec-consulting.eu>

Date: Friday, 22 December 2023 at 13:31

To: DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>

Cc: Ioannis Kartanos <ioannis@pentec-consulting.eu>

Subject: Re: [EXTERNAL] GRN 1122 canola concentrate - update contact person

Dear Stephen,

Many thanks for confirming the change of contact person.

I'm following up on my colleague Ioannis e-mail from 12/12/2023. As he mentioned, we have already provided the answers to the questions to USDA-FSIS. Nevertheless, I have included them in a separate document.

Please let us know in case any additional information is required.

In the meantime, we wish you a Happy Holiday Season & all the best in 2024!

Kind regards,

Ing. Justyna Pałasińska

Regulatory Affairs Director – Human Nutrition | Pen & Tec Consulting
T +34 936 758 015 M +34 682 894 653 F +34 936 758 016 www.pentec-consulting.eu
Pl. Ausias March 1 | 4th floor D01 | 08195 Sant Cugat del Vallès | Barcelona | Spain

PEN + TEC
CONSULTING
PART OF THE ARGENTA GROUP

La información contenida en este mensaje y/o archivo(s) adjunto(s), enviada desde Pen & Tec Consulting SLU, es confidencial/privilegiada y está destinada a ser leída sólo por la(s) persona(s) a la(s) que va dirigida. Le recordamos que sus datos han sido incorporados en el sistema de tratamiento de Pen & Tec Consulting SLU y que siempre y cuando se cumplan los requisitos exigidos por la normativa, usted podrá ejercer sus derechos de acceso, rectificación, limitación de tratamiento, supresión, portabilidad y oposición/revocación, en los términos que establece la normativa vigente en materia de protección de datos, dirigiendo su petición a la dirección postal Pl. Ausias March 1, 4 planta 08195, Sant Cugat del Vallès (Barcelona) o bien a través de correo electrónico info@pentec-consulting.eu. Si usted lee este mensaje y no es el destinatario señalado, el empleado o el agente responsable de entregar el mensaje al destinatario, o ha recibido esta comunicación por error, le informamos que está totalmente prohibida, y puede ser ilegal, cualquier divulgación, distribución o reproducción de esta comunicación, y le rogamos que nos lo notifique inmediatamente y nos devuelva el mensaje original a la dirección arriba mencionada. Gracias.

The information contained in this message and/or attached file(s), sent by Pen & Tec Consulting SLU, is confidential/privileged and is intended to be read solely by the person(s) to whom it is addressed. We hereby inform you that your data will be incorporated into the processing system owned by Pen & Tec Consulting SLU, and that provided it complies with the requirements included in the law, you may exercise the rights of access, rectification, limitation of processing, deletion, portability and opposition by sending your request to the postal address Pl. Ausias March 1, 4 floor 08195, Sant Cugat del Vallès (Barcelona) or to the email address info@pentec-consulting.eu. If you read this message and you are neither the intended recipient, employee or agent in charge of delivering the message to the recipient, or if you have received this message as the result of an error, we hereby inform you that distributing, sharing or reproducing any part of this message is totally forbidden and may be illegal. As a result, we request that you immediately inform us of the error and return this message to the address mentioned above. Thank you.

From: DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>
Date: Tuesday, 5 December 2023 at 19:05
To: Nikolaas Tilkin-Franssens <niko@pentec-consulting.eu>
Cc: Justyna Pałasińska <justyna@pentec-consulting.eu>
Subject: RE: [EXTERNAL] GRN 1122 canola concentrate - update contact person

Hello Niko and Justyna,

Just confirming the change of contact person for GRN 1122.

As for timeline, FDA reviews are complete but USDA-FSIS is requesting a few pieces of information regarding the uses of canola concentrate under USDA jurisdiction, namely:

Please provide SDS for the at use concentrations of the substance and include a description of how the use of this technology will not adversely affect the safety of FSIS inspectors. Workplace safety and health hazards include inhalation, direct skin contact (skin, eyes, mouth), and fire/explosion caused by exposure to the product, its working solution or dry mixture and potential by-products formed and/or off-gassed during the application process. The employee safety information should demonstrate how the New Technology will not “jeopardize the safety of Federal inspection personnel” as specified in the [FSIS Compliance Guideline Procedures for New Technology Notifications and Protocols, April 2015](#).

Although I’m not anticipating any issues here, FSIS workplace and employee safety must be specifically addressed. Please refer to Appendix A on page 17, Workplace Safety and Health Criteria, for clarification on what to provide in the response. For additional clarity with respect to employee safety, the following are examples of information that are typically needed by FSIS’ employee safety and health group;

1. Potential workplace exposures that could result from inhalation and direct contact during use of the substance/technology. This information is required in addition to a Safety Data Sheet (SDS) to determine accurate hazard potential and recommended exposure control measures for IPP work areas in accordance with Occupational Safety and Health Administration (OSHA) regulations: 29 CFR 1910.1200, Hazard Communication, 29 CFR 1910.132, Personal Protective Equipment, and 29 CFR 1910.1000, Air Contaminants. The information should be included as a specific section in each of the protocols.
2. If the SDS workplace hazards/precautions do not apply to the type of exposure that would be expected for the FSIS IPP, please have the submitter provide specific information (per the April 2015 FSIS Compliance Guideline Procedures) for the actual type of exposures expected.
3. If no IPP workplace exposures are expected and no control measures are required, please have the submitter state this and provide the reasons why (e.g., such as the substance “as used” [for all concentrations] is not hazardous by inhalation or direct contact and/or IPP would not be exposed to the substance based on the system design, operation and/or control measures that will be in place).
4. Please also indicate how will FSIS IPP be informed of the above information so that it is clear that the information contained in the SDS for the concentrate does not apply to their actual workplace exposure.
5. Are there any potential hazards from chemical mixing or low pH as a result of discharges of the various solutions to floor drains? Are dedicated drain lines or any other enclosures required?
6. With respect to potential airborne exposures to FSIS IPP in the use/application areas, does the submitter have air sampling results taken during the use of the various concentrations of the technology in the listed mixture?

Suitability data;

The intended use of this product in FSIS meat and poultry products is apparently as a binder/extender. The suitability support provided in Appendix 6 does sufficiently support no significant difference in yield and other organoleptic qualities when used as a partial replacement for another binder in a processed meat and poultry product, such as sausage.

However, **additional suitability support is needed:**

- No suitability data was provided for **whole muscle meat and poultry products at the maximum proposed use level**. We would need to see similar data as provided in Appendix 6 for:
 - Whole muscle red meat control containing no other binders, extenders, or moisture retention agents, as compared to a whole

- muscle red meat product containing 15% isolated canola product.
- Whole muscle poultry control containing no other binders, extenders, or moisture retention agents as compared to a whole muscle poultry product containing 15% isolated canola product.

You responses can be emailed directly to me and I will distribute to the necessary staff inside FDA and USDA.

Thanks,

Steve

Stephen DiFranco, PhD

Regulatory Review Scientist/Chemist

Center for Food Safety and Applied Nutrition

Office of Food Additive Safety

Division of Food Ingredients

U.S. Food and Drug Administration

Tel: 240-402-2710

stephen.difranco@fda.hhs.gov



From: Nikolaas Tilkin-Franssens <niko@pentec-consulting.eu>
Sent: Monday, December 4, 2023 4:36 AM
To: DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>
Cc: Justyna Pałasińska <justyna@pentec-consulting.eu>
Subject: [EXTERNAL] GRN 1122 canola concentrate - update contact person

CAUTION: This email originated from outside of the organization. Do not click links or open attachments unless you recognize the sender and know the content is safe.

Hi Mr. DiFranco,

Hope this email finds you well.

Due to a change in position, I will no longer be the contact person for the GRAS Notice 1122 (Canola Protein Concentrate). Could you please update your records to ascertain that Justyna Pałasińska, in copy to this email, is informed of any relevant updates?

Could you kindly confirm receipt of this email for our records?
And if possible, let us know if there is any estimate on the timeline re. finalization of the review of this GRAS Notice.

Many thanks for your great and flexible support on this application.

Kind regards,

Niko

Nikolaas Tilkin-Franssens

Regulatory Affairs Manager | Pen & Tec Consulting

T +34 936 758 015 M +34 649 840 417 F +34 936 758 016 www.pentec-consulting.eu

Pl. Ausias March 1 | 4th floor D01 | 08195 Sant Cugat del Vallès | Barcelona | Spain



La información contenida en este mensaje y/o archivo(s) adjunto(s), enviada desde Pen & Tec Consulting SLU, es confidencial/privilegiada y está destinada a ser leída sólo por la(s) persona(s) a la(s) que va dirigida. Le recordamos que sus datos han sido incorporados en el sistema de tratamiento de Pen & Tec Consulting SLU y que siempre y cuando se cumplan los requisitos exigidos por la normativa, usted podrá ejercer sus derechos de acceso, rectificación, limitación de tratamiento, supresión, portabilidad y oposición/revocación, en los términos que establece la normativa vigente en materia de protección de datos, dirigiendo su petición a la dirección postal Pl. Ausias March 1, 4 planta 08195, Sant Cugat del Vallès (Barcelona) o bien a través de correo electrónico info@pentec-consulting.eu. Si usted lee este mensaje y no es el destinatario señalado, el empleado o el agente responsable de entregar el mensaje al destinatario, o ha recibido esta comunicación por error, le informamos que está totalmente prohibida, y puede ser ilegal, cualquier divulgación, distribución o reproducción de esta comunicación, y le rogamos que nos lo notifique inmediatamente y nos devuelva el mensaje original a la dirección arriba mencionada. Gracias.

The information contained in this message and/or attached file(s), sent by Pen & Tec Consulting SLU, is confidential/privileged and is intended to be read solely by the person(s) to whom it is addressed. We hereby inform you that your data will be incorporated into the processing system owned by Pen & Tec Consulting SLU, and that provided it complies with the requirements included in the law, you may exercise the rights of access, rectification, limitation of processing, deletion, portability and opposition by sending your request to the postal address Pl. Ausias March 1, 4 floor 08195, Sant Cugat del Valles (Barcelona) or to the email address info@pentec-consulting.eu. If you read this message and you are neither the intended recipient, employee or agent in charge of delivering the message to the recipient, or if you have received this message as the result of an error, we hereby inform you that distributing, sharing or reproducing any part of this message is totally forbidden and may be illegal. As a result, we request that you immediately inform us of the error and return this message to the address mentioned above. Thank you.

From: DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>
Date: Monday, 17 July 2023 at 17:01
To: Nikolaas Tilkin-Franssens <niko@pentec-consulting.eu>
Subject: RE: [EXTERNAL] Re: GRN 1122 canola concentrate items for clarification - Reply

Hello Niko,

No problem—I'll distribute this to the team for review.

Best,

Steve

Stephen DiFranco, PhD

Regulatory Review Scientist/Chemist

Center for Food Safety and Applied Nutrition
Office of Food Additive Safety
Division of Food Ingredients
U.S. Food and Drug Administration
Tel: 240-402-2710
stephen.difranco@fda.hhs.gov



From: Nikolaas Tilkin-Franssens <niko@pentec-consulting.eu>
Sent: Monday, July 17, 2023 10:35 AM
To: DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>
Subject: [EXTERNAL] Re: GRN 1122 canola concentrate items for clarification - Reply

CAUTION: This email originated from outside of the organization. Do not click links or open attachments unless you recognize the sender and know the content is safe.

Hi Stephen,

Apologies for this inconvenience.

We noticed that the reply to question 9 refers to Canola protein isolate (as per GRN 1103). I have updated the answer for it to be mentioning Canola protein concentrate (GRN 1122).

We hope this can be taken into consideration.

Kind regards,

Nikolaas Tilkin-Franssens

Regulatory Affairs Manager | Pen & Tec Consulting

T +34 936 758 015 M +34 649 840 417 F +34 936 758 016 www.pentec-consulting.eu

Pl. Ausias March 1 | 4th floor D01 | 08195 Sant Cugat del Vallès | Barcelona | Spain



La información contenida en este mensaje y/o archivo(s) adjunto(s), enviada desde Pen & Tec Consulting SLU, es confidencial/privilegiada y está destinada a ser leída sólo por la(s) persona(s) a la(s) que va dirigida. Le recordamos que sus datos han sido incorporados en el sistema de tratamiento de Pen & Tec Consulting SLU y que siempre y cuando se cumplan los requisitos exigidos por la normativa, usted podrá ejercer sus derechos de acceso, rectificación, limitación de tratamiento, supresión, portabilidad y oposición/revocación, en los términos que establece la normativa vigente en materia de protección de datos, dirigiendo su petición a la dirección postal Pl. Ausias March 1, 4 planta 08195, Sant Cugat del Vallès (Barcelona) o bien a través de correo electrónico info@pentec-consulting.eu. Si usted lee este mensaje y no es el destinatario señalado, el empleado o el agente responsable de entregar el mensaje al destinatario, o ha recibido esta comunicación por error, le informamos que está totalmente prohibida, y puede ser ilegal, cualquier divulgación, distribución o reproducción de esta comunicación, y le rogamos que nos lo notifique inmediatamente y nos devuelva el mensaje original a la dirección arriba mencionada. Gracias.

The information contained in this message and/or attached file(s), sent by Pen & Tec Consulting SLU, is confidential/privileged and is intended to be read solely by the person(s) to whom it is addressed. We hereby inform you that your data will be incorporated into the processing system owned by Pen & Tec Consulting SLU, and that provided it complies with the requirements included in the law, you may exercise the rights of access, rectification, limitation of processing, deletion, portability and opposition by sending your request to the postal address Pl. Ausias March 1, 4 floor 08195, Sant Cugat del Vallès (Barcelona) or to the email address info@pentec-consulting.eu. If you read this message and you are neither the intended recipient, employee or agent in charge of delivering the message to the recipient, or if you have received this message as the result of an error, we hereby inform you that distributing, sharing or reproducing any part of this message is totally forbidden and may be illegal. As a result, we request that you immediately inform us of the error and return this message to the address mentioned above. Thank you.

From: Nikolaas Tilkin-Franssens <niko@pentec-consulting.eu>

Date: Tuesday, 11 July 2023 at 17:03
To: DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>
Cc: Justyna Pałasińska <justyna@pentec-consulting.eu>
Subject: Re: GRN 1122 canola concentrate items for clarification - Reply

Dear Stephen,

Thank you for reaching out with the questions for clarification.
We have worked closely with Napiferyn to close the doubts.

Kindly find attached a Word file including the Questions&Answers, a report on the requested literature review, a SDS sheet as requested by the USDA-FSIS, and a report on the suitability assessment.

We remain available for any further questions or updates.

Thanks for taking the application in further consideration,
best regards,

Nikolaas Tilkin-Franssens

Regulatory Affairs Manager | Pen & Tec Consulting

T +34 936 758 015 M +34 649 840 417 F +34 936 758 016 www.pentec-consulting.eu

Pl. Ausias March 1 | 4th floor D01 | 08195 Sant Cugat del Vallès | Barcelona | Spain

PEN + TEC
CONSULTING

PART OF THE ARGENTA GROUP

La información contenida en este mensaje y/o archivo(s) adjunto(s), enviada desde Pen & Tec Consulting SLU, es confidencial/privilegiada y está destinada a ser leída sólo por la(s) persona(s) a la(s) que va dirigida. Le recordamos que sus datos han sido incorporados en el sistema de tratamiento de Pen & Tec Consulting SLU y que siempre y cuando se cumplan los requisitos exigidos por la normativa, usted podrá ejercer sus derechos de acceso, rectificación, limitación de tratamiento, supresión, portabilidad y oposición/revocación, en los términos que establece la normativa vigente en materia de protección de datos, dirigiendo su petición a la dirección postal Pl. Ausias March 1, 4 planta 08195, Sant Cugat del Vallès (Barcelona) o bien a través de correo electrónico info@pentec-consulting.eu. Si usted lee este mensaje y no es el destinatario señalado, el empleado o el agente responsable de entregar el mensaje al destinatario, o ha recibido esta comunicación por error, le informamos que está totalmente prohibida, y puede ser ilegal, cualquier divulgación, distribución o reproducción de esta comunicación, y le rogamos que nos lo notifique inmediatamente y nos devuelva el mensaje original a la dirección arriba mencionada. Gracias.

The information contained in this message and/or attached file(s), sent by Pen & Tec Consulting SLU, is confidential/privileged and is intended to be read solely by the person(s) to whom it is addressed. We hereby inform you that your data will be incorporated into the processing system owned by Pen & Tec Consulting SLU, and that provided it complies with the requirements included in the law, you may exercise the rights of access, rectification, limitation of processing, deletion, portability and opposition by sending your request to the postal address Pl. Ausias March 1, 4 floor 08195, Sant Cugat del Vallès (Barcelona) or to the email address info@pentec-consulting.eu. If you read this message and you are neither the intended recipient, employee or agent in charge of delivering the message to the recipient, or if you have received this message as the result of an error, we hereby inform you that distributing, sharing or reproducing any part of this message is totally forbidden and may be illegal. As a result, we request that you immediately inform us of the error and return this message to the address mentioned above. Thank you.

From: DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>
Date: Wednesday, 28 June 2023 at 17:41
To: Nicoleta Pasecinic <nicoleta@pentec-consulting.eu>
Cc: Nikolaas Tilkin-Franssens <niko@pentec-consulting.eu>
Subject: [EXTERNAL]: GRN 1122 canola concentrate items for clarification

CAUTION: This email originated from outside of the organization. Do not click links or open attachments unless you recognize the sender and know the content is safe.

Hello Ms. Pasecinic,

After evaluating NapiFeryn's GRAS Notice No. GRN 1122 on canola concentrate we noted a few issues that should be addressed. Please respond to the following points for clarification:

1. On p. 9, NapiFeryn states that the major storage proteins in canola seed are cruciferins and napins, and that canola concentrate consists of 30-45% protein and 40-70% dietary fiber. Please provide the typical cruciferin content and napin content in canola concentrate.
2. Please confirm that all raw materials and processing aids used in the manufacturing process are used in accordance with the U.S. regulations, are GRAS for their respective uses or are the subject of an effective food contact notification. For the record, we note that the food additive regulations cited in Table 4 (p. 15) for ascorbic acid (21 CFR 182.8013), ethanol (21 CFR 184.1293), and ethyl acetate (21 CFR 173.228) do not appear to be applicable to your intended uses of these substances.
3. In Table 6 (p. 18-19), NapiFeryn provides the results from the batch analyses for heavy metals. We would like to bring to your attention a relevant FDA's "[Closer to Zero](#)" initiative that focuses on reducing the levels of heavy metals in foods and recommend that you lower the specification limits for heavy metal to better reflect the batch analyses results and to be as low as possible.
4. In Table 10 (p. 22), NapiFeryn provides batch analyses data for residual solvents and processing aids. In addition, in Table 21 (p. 50), you provided the results from the batch analyses for erucic acid in your canola concentrate ranging from 0.37% to < 0.1%.
Please include limits for residual ethanol, ethyl acetate, and sulphur dioxide as well as a limit for erucic acid in the specifications for canola concentrate and specify the analytical methods used to test for these parameters.
In addition, please provide an updated Tables 5 and 6 (p. 16-19) to include the additional specification parameters mentioned

above, corresponding analytical methods, and batch analyses.

5. Please state that all analytical methods used to test batches were validated and are fit for their respective purpose.
6. Please state that canola concentrate is not intended for use in infant formula or in foods where standards of identity preclude its use.
7. In Table 15 (p.), NapiFeryn provides the results of the batch analyses for total plate count in the raw material (rapeseed press cake). Please address the significant variation in the results (from <10 to 28,000 CFU/g) and discuss whether this will impact safety of the final ingredient.
8. On p. 19, NapiFeryn states that the levels of mycotoxins in canola concentrate are below the limit of quantitation (LOQ) and provide the results from the analyses of five batches to support your statement. Please clarify whether you expect mycotoxins to be present in canola concentrate manufactured in accordance with good manufacturing practices.
9. In Part 1.4 (p. 6) and Part 3.1 (p. 33), NapiFeryn states that the intended use of canola concentrate is as a source of protein and/or fiber, thickener, or texturizer. However, we note that on p. 33 you also state the intended use of canola concentrate is as a flavoring agent or binder in various comminuted or whole muscle meat and poultry products. In addition, in Appendix 3 (p. 5) you state that canola concentrate may also be used “to create a flavored salt” or as “a flavor enhancer like monosodium glutamate”. Please confirm these additional uses of canola concentrate are within the scope of GRN 001122.
10. On p. 10, the notifier describes the protein composition of canola concentrate, being primarily cruciferins, napin, oleosin, and squalene monooxygenase. However, the pivotal safety data provided appear to only be relevant to the cruciferin and napin fractions of the canola concentrate. Please provide a brief narrative to confirm the safety of oleosin and squalene monooxygenase exposure from the intended uses.
11. On p. 31-32 of the notice, the notifier clearly establishes that canola concentrate is intended to be substitutive to protein and fiber consumption and will not contribute to additional exposure to protein or fiber in general. Please elaborate on this conclusion, and clarify if the intended uses of canola concentrate are additive or substitutive to other canola protein products currently on the market (i.e., GRNs 327, 386, and 683)?
12. On p. 37, the notifier concludes exposure to canola concentrate from the intended uses is safe since the EDI reported is “still much lower (approximately 7- to 22-fold lower) than the no-observed-adverse-effect level (NOAEL) values established” for cruciferin- and napin-rich protein isolates in male rats following a 13-week oral exposure regimen (Mejia *et al.*, 2009a & 2009b). We note that an uncertainty factor, or margin of safety (MOS), of 100 (10 for interindividual variability × 10 for interspecies variability) is normally used when assessing safety of a food ingredient by comparing estimated human exposure levels to the NOAEL from animal toxicology data. Therefore, it is not clear why MOS that is ~5-10-fold lower can be concluded as safe without proper justification. Additionally, we note that potential thyrotoxic effects were observed at the highest doses in these two rat studies, as well as for rapeseed products in general tested in other species, as cited in Table 20 of the GRAS notice. This effect was mostly attributed to the presence of glucosinolate; however, we note that since the level of glucosinolate was low or absent in both the test articles from Mejia *et al.* and the article of commerce, the rationale used by the study authors to conclude that the observed NOAEL was not in fact the LOAEL may be questionable. Regardless, it appears that the provided safety narrative lacks sufficient basis to conclude MOS of 7-22 is adequate to reach the conclusion of “reasonable certainty of no harm.” Based on generally available data and information, please provide additional narrative to explain your rationale for your GRAS conclusion.
13. We note that when discussing the absorption, distribution, metabolism, and excretion of canola concentrate (p. 49), the notifier reports unpublished data from an EU Novel Foods application for “defatted rapeseed powder” to support their conclusion. Similarly, genotoxicity conclusions are made using unpublished data from an EFSA Panel conclusion on defatted rapeseed powder. Given other data and information have been used in prior GRAS notices for canola ingredients (e.g., GRN 327), please confirm that the EFSA Panel and EU Novel Foods conclusions are only considered as corroborative, not pivotal, to the safety determination of canola concentrate at its intended use level?
14. On p. 40, the notifier discusses the allergenicity potential of canola concentrate being determined via a “bioinformatics approach” and concludes that canola concentrate “may elicit possible allergenic effects.” Additionally, on p. 59 the notifier reiterates that the bioinformatics analysis indicated “possible allergenic effects” of canola concentrate, but no further discussion is provided. While data from an allergen online database search is provided as part of Appendix 4, no discussion of these data are included in the current GRAS notice. Please briefly detail the “possible allergenic effects” of canola concentrate similar to previous notices (e.g., GRN 683), and discuss why they would not be expected to pose a safety concern from the intended use.
15. We note that a recent study on rapeseed protein isolate was published (Xiong *et al.*, 2022).
 - a. Please discuss if this study presents additional safety concerns for the article of commerce or contradicts the current GRAS conclusion.
 - b. Please also perform an updated literature review from 2021 to present and discuss if any additional studies relevant to the safety of canola concentrate were identified that would contradict the current GRAS conclusion.

References cited:

Xiong Z, Fu Y, Yao J, Zhang N, He R, Ju X, Wang Z. Removal of anti-nutritional factors of rapeseed protein isolate (RPI) and toxicity assessment of RPI. *Food Funct.* 2022 Jan 24;13(2):664-674. doi: 10.1039/d1fo03217h. PMID: 34933325.

Additionally, we received the following questions from USDA FSIS regarding their review of the uses of GRN 1122 concerning products within their purview. Please respond to the following and we will pass your responses along to them.

Please provide Safety Data Sheet (SDS) for the at use concentrations of the substance and include a description of how the use of this technology will not adversely affect the safety of FSIS inspectors. Workplace safety and health hazards include inhalation, direct skin contact (skin, eyes, mouth), and fire/explosion caused by exposure to the product, its working solution or dry mixture and potential by-products formed and/or off-gassed during the application process. The employee safety information should demonstrate how the New Technology will not “jeopardize the safety of Federal inspection personnel” as specified in the [FSIS Compliance Guideline Procedures for New Technology Notifications and Protocols, April 2015](#). FSIS workplace and employee safety must be specifically addressed. Please refer to Appendix A on p. 17, Workplace Safety and Health Criteria, for clarification on what to provide in the response. For additional clarity with respect to employee safety, the following are examples of information that are typically needed by FSIS’ employee safety and health group;

1. Potential workplace exposures that could result from inhalation and direct contact during use of the substance/technology. This information is required in addition to a SDS to determine accurate hazard potential and recommended exposure control measures for IPP work areas in accordance with Occupational Safety and Health Administration (OSHA) regulations: 29 CFR 1910.1200, Hazard Communication, 29 CFR 1910.132, Personal Protective Equipment, and 29 CFR 1910.1000, Air Contaminants. The information should be included as a specific section in each of the protocols.
2. If the SDS workplace hazards/precautions do not apply to the type of exposure that would be expected for the FSIS IPP, please have the submitter provide specific information (per the April 2015 FSIS Compliance Guideline Procedures) for the actual type of exposures expected.
3. If no IPP workplace exposures are expected and no control measures are required, please have the submitter state this and provide the reasons why (e.g., such as the substance “as used” [for all concentrations] is not hazardous by inhalation or direct contact and/or IPP would not be exposed to the substance based on the system design, operation and/or control measures that will be in place).
4. Please also indicate how will FSIS IPP be informed of the above information so that it is clear that the information contained in the SDS for the concentrate does not apply to their actual workplace exposure.
5. Are there any potential hazards from chemical mixing or low pH as a result of discharges of the various solutions to floor drains? Are dedicated drain lines or any other enclosures required?
6. With respect to potential airborne exposures to FSIS IPP in the use/application areas, does the submitter have air sampling results taken during the use of the various concentrations of the technology in the listed mixture?
7. The intended use of this product in FSIS meat and poultry products is apparently as a binder/extender. The suitability support provided in Appendix 6 does sufficiently support no significant difference in yield and other organoleptic qualities when used as a partial replacement for another binder in a processed meat and poultry product, such as sausage.
However, **additional suitability support is needed:**
 - a. No suitability data was provided for **whole muscle meat and poultry products at the maximum proposed use level**. We would need to see similar data as provided in Appendix 6 for:
 - Whole muscle red meat control containing no other binders, extenders, or moisture retention agents, as compared to a whole muscle red meat product containing 15% isolated canola product.
 - Whole muscle poultry control containing no other binders, extenders, or moisture retention agents as compared to a whole muscle poultry product containing 15% isolated canola product.

Responses may be sent in an email or in a separate document. We respectfully request a response within 10 business days. If you are unable to complete the response within that time frame, please contact me to discuss further options.

If you have any further additional questions or concerns, please don't hesitate to contact me at stephen.difranco@fda.hhs.gov or by phone at 240.402.2710.

Best,
Steve

Stephen DiFranco, PhD
Regulatory Review Scientist/Chemist

Center for Food Safety and Applied Nutrition
Office of Food Additive Safety
Division of Food Ingredients
U.S. Food and Drug Administration
Tel: 240-402-2710
stephen.difranco@fda.hhs.gov



CAUTION: This email, including any attachments, is confidential. If you are not the intended recipient, please notify the sender and delete the email and any attachments from your system. In addition, you must not use, distribute or reproduce this email or any attachments. Opinions and other information in this email and any attachments which do not relate to the official business of Argenta are neither given by nor endorsed by Argenta. While Argenta uses anti-virus software, Argenta accepts no liability for any viruses in this email or any attachment, or for any effects this email or any attachment may have on your network or computer system.

CAUTION: This email, including any attachments, is confidential. If you are not the intended recipient, please notify the sender and delete the email and any attachments from your system. In addition, you must not use, distribute or reproduce this email or any attachments. Opinions and other information in this email and any attachments which do not relate to the official business of Argenta are neither given by nor endorsed by Argenta. While Argenta uses anti-virus software, Argenta accepts no liability for any viruses in this email or any attachment, or for any effects this email or any attachment may have on your network or computer system.

Este correo electrónico y los archivos adjuntos, enviados por Pen & Tec Consulting SLU, que opera bajo el nombre comercial de Argenta® (Argenta), son confidenciales y pueden estar protegidos por ley. Si usted no es el destinatario, cualquier divulgación, reproducción, copia, distribución u otro tipo de difusión o uso de esta comunicación está estrictamente prohibido. Si ha recibido esta transmisión por error, notifíquelo al remitente y elimine inmediatamente el correo electrónico y cualquier archivo adjunto de su sistema. Argenta no emite ni respalda las opiniones y demás información contenida en este correo electrónico y en sus anexos que no estén relacionadas con las actividades oficiales de Argenta. Aunque Argenta utiliza software antivirus, Argenta no acepta ninguna responsabilidad por cualquier virus en este correo electrónico o cualquier archivo adjunto, o por cualquier efecto que este correo electrónico o cualquier archivo adjunto pueda tener en su red o sistema informático. Argenta registra y almacena los correos electrónicos enviados a nosotros o a nuestros afiliados de acuerdo con nuestras políticas y procedimientos internos. Consulte www.pentec-consulting.eu para obtener información sobre Argenta y/o nuestra política de privacidad.

This email and any attached file(s), sent by Pen & Tec Consulting SLU trading as Argenta® (Argenta), are confidential and may be legally privileged. If you are not the intended recipient, any disclosure, reproduction, copying, distribution, or other dissemination or use of this communication is strictly prohibited. If you have received this transmission in error, please notify the sender and delete the email and any attachments from your system immediately. Opinions and other information in this email and any attachments which do not relate to the official business of Argenta are neither given by nor endorsed by Argenta. While Argenta uses anti-virus software, Argenta accepts no liability for any viruses in this email or any attachment, or for any effects this email or any attachment may have on your network or computer system. Argenta records and stores emails sent to us or our affiliates in keeping with our internal policies and procedures. Please see www.pentec-consulting.eu for information regarding Argenta and/or our privacy policy.

Este correo electrónico y los archivos adjuntos, enviados por Pen & Tec Consulting SLU, que opera bajo el nombre comercial de Argenta® (Argenta), son confidenciales y pueden estar protegidos por ley. Si usted no es el destinatario, cualquier divulgación, reproducción, copia, distribución u otro tipo de difusión o uso de esta comunicación está estrictamente prohibido. Si ha recibido esta transmisión por error, notifíquelo al remitente y elimine inmediatamente el correo electrónico y cualquier archivo adjunto de su sistema. Argenta no emite ni respalda las opiniones y demás información contenida en este correo electrónico y en sus anexos que no estén relacionadas con las actividades oficiales de Argenta. Aunque Argenta utiliza software antivirus, Argenta no acepta ninguna responsabilidad por cualquier virus en este correo electrónico o cualquier archivo adjunto, o por cualquier efecto que este correo electrónico o cualquier archivo adjunto pueda tener en su red o sistema informático. Argenta registra y almacena los correos electrónicos enviados a nosotros o a nuestros afiliados de acuerdo con nuestras políticas y procedimientos internos. Consulte www.pentec-consulting.eu para obtener información sobre Argenta y/o nuestra política de privacidad.

This email and any attached file(s), sent by Pen & Tec Consulting SLU trading as Argenta® (Argenta), are confidential and may be legally privileged. If you are not the intended recipient, any disclosure, reproduction, copying, distribution, or other dissemination or use of this communication is strictly prohibited. If you have received this transmission in error, please notify the sender and delete the email and any attachments from your system immediately. Opinions and other information in this email and any attachments which do not relate to the official business of Argenta are neither given by nor endorsed by Argenta. While Argenta uses anti-virus software, Argenta accepts no liability for any viruses in this email or any attachment, or for any effects this email or any attachment may have on your network or computer system. Argenta records and stores emails sent to us or our affiliates in keeping with our internal policies and procedures. Please see www.pentec-consulting.eu for information regarding Argenta and/or our privacy policy.

Este correo electrónico y los archivos adjuntos, enviados por Pen & Tec Consulting SLU, que opera bajo el nombre comercial de Argenta® (Argenta), son confidenciales y pueden estar protegidos por ley. Si usted no es el destinatario, cualquier divulgación, reproducción, copia, distribución u otro tipo de difusión o uso de esta comunicación está estrictamente prohibido. Si ha recibido esta transmisión por error, notifíquelo al remitente y elimine inmediatamente el correo electrónico y cualquier archivo adjunto de su sistema. Argenta no emite ni respalda las opiniones y demás información contenida en este correo electrónico y en sus anexos que no estén relacionadas con las actividades oficiales de Argenta. Aunque Argenta utiliza software antivirus, Argenta no acepta ninguna responsabilidad por cualquier virus en este correo electrónico o cualquier archivo adjunto, o por cualquier efecto que este correo electrónico o cualquier archivo adjunto pueda tener en su red o sistema informático. Argenta registra y almacena los correos electrónicos enviados a nosotros o a nuestros afiliados de acuerdo con nuestras políticas y procedimientos internos. Consulte www.pentec-consulting.eu para obtener información sobre Argenta y/o nuestra política de privacidad.

This email and any attached file(s), sent by Pen & Tec Consulting SLU trading as Argenta® (Argenta), are confidential and may be legally privileged. If you are not the intended recipient, any disclosure, reproduction, copying, distribution, or other dissemination or use of this communication is strictly prohibited. If you have received this transmission in error, please notify the sender and delete the email and any attachments from your system immediately. Opinions and other information in this email and any attachments which do not relate to the official business of Argenta are neither given by nor endorsed by Argenta. While Argenta uses anti-virus software, Argenta accepts no liability for any viruses in this email or any attachment, or for any effects this email or any attachment may have on your network or computer system. Argenta records and stores emails sent to us or our affiliates in keeping with our internal policies and procedures. Please see www.pentec-consulting.eu for information regarding Argenta and/or our privacy policy.

Este correo electrónico y los archivos adjuntos, enviados por Pen & Tec Consulting SLU, que opera bajo el nombre comercial de Argenta® (Argenta), son confidenciales y pueden estar protegidos por ley. Si usted no es el destinatario, cualquier divulgación, reproducción, copia, distribución u otro tipo de difusión o uso de esta comunicación está estrictamente prohibido. Si ha recibido esta transmisión por error, notifíquelo al remitente y elimine inmediatamente el correo electrónico y cualquier archivo adjunto de su sistema. Argenta no emite ni respalda las opiniones y demás información contenida en este correo electrónico y en sus anexos que no estén relacionadas con las actividades oficiales de Argenta. Aunque Argenta utiliza software antivirus, Argenta no acepta ninguna responsabilidad por cualquier virus en este correo electrónico o cualquier archivo adjunto, o por cualquier efecto que este correo electrónico o cualquier archivo adjunto pueda tener en su red o sistema informático. Argenta registra y almacena los correos electrónicos enviados a nosotros o a nuestros afiliados de acuerdo con nuestras políticas y procedimientos internos. Consulte www.pentec-consulting.eu para obtener información sobre Argenta y/o nuestra política de privacidad.

This email and any attached file(s), sent by Pen & Tec Consulting SLU trading as Argenta® (Argenta), are confidential and may be legally privileged. If you are not the intended recipient, any disclosure, reproduction, copying, distribution, or other dissemination or use of this communication is strictly prohibited. If you have received this transmission in error, please notify the sender and delete the email and any attachments from your system immediately. Opinions and other information in this email and any attachments which do not relate to the official business of Argenta are neither given by nor endorsed by Argenta. While Argenta uses anti-virus software, Argenta accepts no liability for any viruses in this email or any attachment, or for any effects this email or any attachment may have on your network or computer system. Argenta records and stores emails sent to us or our affiliates in keeping with our internal policies and procedures. Please see www.pentec-consulting.eu for information regarding Argenta and/or our privacy policy.

Este correo electrónico y los archivos adjuntos, enviados por Pen & Tec Consulting SLU, que opera bajo el nombre comercial de Argenta® (Argenta), son confidenciales y pueden estar protegidos por ley. Si usted no es el destinatario, cualquier divulgación, reproducción, copia, distribución u otro tipo de difusión o uso de esta comunicación está estrictamente prohibido. Si ha recibido esta transmisión por error, notifíquelo al remitente y elimine inmediatamente el correo electrónico y cualquier archivo adjunto de su sistema. Argenta no emite ni respalda las opiniones y demás información contenida en este correo electrónico y en sus anexos que no estén relacionadas con las actividades oficiales de Argenta. Aunque Argenta utiliza software antivirus, Argenta no acepta ninguna responsabilidad por cualquier virus en este correo electrónico o cualquier archivo adjunto, o por cualquier efecto que este correo electrónico o cualquier archivo adjunto pueda tener en su red o sistema informático. Argenta registra y almacena los correos electrónicos enviados a nosotros o a nuestros afiliados de acuerdo con nuestras políticas y procedimientos internos. Consulte www.pentec-consulting.eu para obtener información sobre Argenta y/o nuestra política de privacidad.

This email and any attached file(s), sent by Pen & Tec Consulting SLU trading as Argenta® (Argenta), are confidential and may be legally privileged. If you are not the intended recipient, any disclosure, reproduction, copying, distribution, or other dissemination or use of this communication is strictly prohibited. If you have received this transmission in error, please notify the sender and delete the email and any attachments from your system immediately. Opinions and other information in this email and any attachments which do not relate to the official business of Argenta

are neither given by nor endorsed by Argenta. While Argenta uses anti-virus software, Argenta accepts no liability for any viruses in this email or any attachment, or for any effects this email or any attachment may have on your network or computer system. Argenta records and stores emails sent to us or our affiliates in keeping with our internal policies and procedures. Please see www.pentec-consulting.eu for information regarding Argenta and/or our privacy policy.

Este correo electrónico y los archivos adjuntos, enviados por Pen & Tec Consulting SLU, que opera bajo el nombre comercial de Argenta® (Argenta), son confidenciales y pueden estar protegidos por ley. Si usted no es el destinatario, cualquier divulgación, reproducción, copia, distribución u otro tipo de difusión o uso de esta comunicación está estrictamente prohibido. Si ha recibido esta transmisión por error, notifíquelo al remitente y elimine inmediatamente el correo electrónico y cualquier archivo adjunto de su sistema. Argenta no emite ni respalda las opiniones y demás información contenida en este correo electrónico y en sus anexos que no estén relacionadas con las actividades oficiales de Argenta. Aunque Argenta utiliza software antivirus, Argenta no acepta ninguna responsabilidad por cualquier virus en este correo electrónico o cualquier archivo adjunto, o por cualquier efecto que este correo electrónico o cualquier archivo adjunto pueda tener en su red o sistema informático. Argenta registra y almacena los correos electrónicos enviados a nosotros o a nuestros afiliados de acuerdo con nuestras políticas y procedimientos internos. Consulte www.pentec-consulting.eu para obtener información sobre Argenta y/o nuestra política de privacidad.

This email and any attached file(s), sent by Pen & Tec Consulting SLU trading as Argenta® (Argenta), are confidential and may be legally privileged. If you are not the intended recipient, any disclosure, reproduction, copying, distribution, or other dissemination or use of this communication is strictly prohibited. If you have received this transmission in error, please notify the sender and delete the email and any attachments from your system immediately. Opinions and other information in this email and any attachments which do not relate to the official business of Argenta are neither given by nor endorsed by Argenta. While Argenta uses anti-virus software, Argenta accepts no liability for any viruses in this email or any attachment, or for any effects this email or any attachment may have on your network or computer system. Argenta records and stores emails sent to us or our affiliates in keeping with our internal policies and procedures. Please see www.pentec-consulting.eu for information regarding Argenta and/or our privacy policy.

From: [Justyna Pałasińska](#)
To: [DiFranco, Stephen](#)
Subject: Re: [EXTERNAL] GRN 1122 canola concentrate status
Date: Wednesday, July 3, 2024 11:45:16 AM
Attachments: [image001.png](#)
[image007.png](#)
[image008.png](#)
[image009.png](#)
[image010.png](#)
[image011.png](#)
[image012.png](#)
[Outlook-Image.png](#)
[Outlook-Image.png](#)

CAUTION: This email originated from outside of the organization. Do not click links or open attachments unless you recognize the sender and know the content is safe.

Thank you very much for your clarification, Steve.

Following your advice: we wish to amend the notice by removing the claim that this ingredient is used as a source of dietary fiber and that we wish to add that it may be used "as an ingredient" in the food categories listed within the notice.

Please let me know if anything else is needed from our side.

Kind regards,

Justyna Pałasińska

Regulatory Affairs Director – Human Nutrition, Argenta Barcelona



M +34 682 894 653 T +34 936 758 015

La información contenida en este mensaje y/o archivo(s) adjunto(s), enviada desde Pen & Tec Consulting SLU cotiza como Argenta, es confidencial/privilegiada y está destinada a ser leída sólo por la(s) persona(s) a la(s) que va dirigida. Le recordamos que sus datos han sido incorporados en el sistema de tratamiento de Pen & Tec Consulting SLU cotiza como Argenta, y que siempre y cuando se cumplan los requisitos exigidos por la normativa, usted podrá ejercer sus derechos de acceso, rectificación, limitación de tratamiento, supresión, portabilidad y oposición/revocación, en los términos que establece la normativa vigente en materia de protección de datos, dirigiendo su petición a la dirección postal OneCoWork, Portal de l'Àngel 40, 08002, Barcelona o bien a través de correo electrónico info@pentec-consulting.eu. Si usted lee este mensaje y no es el destinatario señalado, el empleado o el agente responsable de entregar el mensaje al destinatario, o ha recibido esta comunicación por error, le informamos que está totalmente prohibida, y puede ser ilegal, cualquier divulgación, distribución o reproducción de esta comunicación, y le rogamos que nos lo notifique inmediatamente y nos devuelva el mensaje original a la dirección arriba mencionada. Gracias.

The information contained in this message and/or attached file(s), sent by Pen & Tec Consulting SLU trading as Argenta, is confidential/privileged and is intended to be read solely by the person(s) to whom it is addressed. We hereby inform you that your data will be incorporated into the processing system owned by Pen & Tec Consulting SLU, and that provided it complies with the requirements included in the law, you may exercise the rights of access, rectification, limitation of processing, deletion, portability and opposition by sending your request to the postal address OneCoWork, Portal de l'Àngel 40, 08002, Barcelona or to the email address info@pentec-consulting.eu. If you read this message and you are neither the intended recipient, employee or agent in charge of delivering the message to the recipient, or if you have received this message as the result of an error, we hereby inform you that distributing, sharing or reproducing any part of this message is totally forbidden and may be illegal. As a result, we request that you immediately inform us of the error and return this message to the address mentioned above. Thank you.

From: DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>
Sent: 02 July 2024 20:49
To: Justyna Pałasińska <justyna.palasinaska@argentaglobal.com>
Subject: RE: [EXTERNAL] GRN 1122 canola concentrate status

Hello Justyna,

I appreciate the quick response. Per your questions:

- The issue is only with the claim that the ingredient is a source of fiber. You may still make the other claims and claim it is a source of protein—and just add the technical effect "as an ingredient". This is kind of a general, catch all term. There are different regulations addressing claims of source of protein, and this fits.
- You may keep use in all categories that are currently in the notice. This change does not require a different exposure estimate or any other change such as in use. The issue is really about what nutritional claims you can make about the ingredient, not its safety in these uses.
- You do not have to do any sort of rewrite or resubmit the notice. You can simply email me stating you wish to amend the notice by removing the claim that this ingredient is used as a source of dietary fiber and that you wish to add that it may be used "as an ingredient" in the food categories listed. In other words you are adding "as an ingredient" to the notified technical effects of the substance in food. That will be sufficient and we should be able to get this closed out shortly thereafter.

Happy to discuss if you have any other questions.

Best,

Steve

Stephen DiFranco, PhD
Regulatory Review Scientist/Chemist

Center for Food Safety and Applied Nutrition
Office of Food Additive Safety
Division of Food Ingredients
U.S. Food and Drug Administration
Tel: 240-402-2710
stephen.difranco@fda.hhs.gov



From: Justyna Pałasińska <justyna.palasincka@argentaglobal.com>
Sent: Tuesday, July 2, 2024 10:59 AM
To: DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>
Subject: Re: [EXTERNAL] GRN 1122 canola concentrate status

CAUTION: This email originated from outside of the organization. Do not click links or open attachments unless you recognize the sender and know the content is safe.

Many thanks for your swift reply, Steve.

We will update the GRAS & get the updated version to you shortly. I wanted to check a couple questions with you:

- understand the issue is with 'source of fiber' & not with other claims, e.g. 'source of protein'. Could you confirm?
- one of the intended uses is 'protein-fiber and nutritional powders'. I understand that we can keep this category, as the product is a source of protein & therefore can be used as an ingredient for this category of foods. Could you confirm?
- Is it OK for us to send the updated GRAS document by e-mail or do you require a CD-submission?

I look forward to your reply.

Kind regards,
Justyna Pałasińska
Regulatory Affairs Director – Human Nutrition, Argenta Barcelona



M +34 682 894 653 T +34 936 758 015

www.argentaglobal.com

La información contenida en este mensaje y/o archivo(s) adjunto(s), enviada desde Pen & Tec Consulting SLU cotiza como Argenta, es confidencial/privilegiada y está destinada a ser leída sólo por la(s) persona(s) a la(s) que va dirigida. Le recordamos que sus datos han sido incorporados en el sistema de tratamiento de Pen & Tec Consulting SLU cotiza como Argenta, y que siempre y cuando se cumplan los requisitos exigidos por la normativa, usted podrá ejercer sus derechos de acceso, rectificación, limitación de tratamiento, supresión, portabilidad y oposición/revocación, en los términos que establece la normativa vigente en materia de protección de datos, dirigiendo su petición a la dirección postal OneCoWork, Portal de l'Àngel 40, 08002, Barcelona o bien a través de correo electrónico info@pentec-consulting.eu. Si usted lee este mensaje y no es el destinatario señalado, el empleado o el agente responsable de entregar el mensaje al destinatario, o ha recibido esta comunicación por error, le informamos que está totalmente prohibida, y puede ser ilegal, cualquier divulgación, distribución o reproducción de esta comunicación, y le rogamos que nos lo notifique inmediatamente y nos devuelva el mensaje original a la dirección arriba mencionada. Gracias.

The information contained in this message and/or attached file(s), sent by Pen & Tec Consulting SLU trading as Argenta, is confidential/privileged and is intended to be read solely by the person(s) to whom it is addressed. We hereby inform you that your data will be incorporated into the processing system owned by Pen & Tec Consulting SLU, and that provided it complies with the requirements included in the law, you may exercise the rights of access, rectification, limitation of processing, deletion, portability and opposition by sending your request to the postal address OneCoWork, Portal de l'Àngel 40, 08002, Barcelona or to the email address info@pentec-consulting.eu. If you read this message and you are neither the intended recipient, employee or agent in charge of delivering the message to the recipient, or if you have received this message as the result of an error, we hereby inform you that distributing, sharing or reproducing any part of this message is totally forbidden and may be illegal. As a result, we request that you immediately inform us of the error and return this message to the address mentioned above. Thank you.

From: DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>
Sent: 01 July 2024 21:32
To: Justyna Pałasińska <justyna.palasincka@argentaglobal.com>
Subject: RE: [EXTERNAL] GRN 1122 canola concentrate status

Hello Justyna,

In finalizing our response letter we ran into a bit of an issue regarding the notice's claim that the ingredient is a source of dietary fiber, as this is a legally defined area in US regulations. I got the following from our review team for your consideration:

NapiFeryn states that canola concentrate is intended to be used as a source of dietary fiber amongst other intended uses (i.e., source of protein, formulation aid, stabilizer, thickener, or texturizer). We note that FDA defines dietary fiber as "non-digestible soluble and insoluble carbohydrates (with 3 or more monomeric units), and lignin that are intrinsic and intact in plants; isolated or synthetic non-digestible carbohydrates (with 3 or more monomeric units) determined by FDA to have physiological effects that are beneficial to human health" (21 CFR 101.9(c)(6)(i)). Additional information related to dietary fiber can be found at <https://www.fda.gov/food/food-labeling-nutrition/questions-and-answers-dietary-fiber>.

During our evaluation of GRN 001122 we were not able to determine whether canola concentrate meets the definition of dietary fiber. To proceed with our evaluation of GRN 001122, we recommend that Napiferyn reconsider the description of the intended uses of canola concentrate by replacing the intended use as “a source of dietary fiber” with the use as “an ingredient”.

If NapiFeryn wishes to use canola concentrate as a source of dietary fiber, we recommend that you consult with FDA’s Office of Nutrition and Food Labeling (ONFL) on whether the ingredient meets the definition of dietary fiber. After ONFL provides a favorable determination, Napiferyn may choose to inform FDA about their GRAS conclusion for the use of canola concentrate as a source of dietary fiber by submitting a supplement to GRN 001122.

Again, amending the notice to state the use is simply as “an ingredient” will allow us to close out this GRAS notice while still allowing the ingredient to be used in foods. If you then wish to have the use as a source of dietary fiber included in the notice and/or displayed on the [GRAS Notice inventory](#), we can go back and amend as appropriate pending the outcome with ONFL.

Happy to discuss if this is unclear.

Thanks,

Steve

Stephen DiFranco, PhD

Regulatory Review Scientist/Chemist

Center for Food Safety and Applied Nutrition
Office of Food Additive Safety
Division of Food Ingredients
U.S. Food and Drug Administration
Tel: 240-402-2710
stephen.difranco@fda.hhs.gov



From: Justyna Pałasińska <justyna.palasincka@argentaglobal.com>
Sent: Monday, July 1, 2024 8:16 AM
To: DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>
Subject: Re: [EXTERNAL] GRN 1122 canola concentrate status

CAUTION: This email originated from outside of the organization. Do not click links or open attachments unless you recognize the sender and know the content is safe.

Hi Steve,

I hope you are doing well.

Could you let me know when the letter is expected to receive clearance & be shared with the applicant?

Kind regards,

Justyna Pałasińska

Regulatory Affairs Director – Human Nutrition, Argenta Barcelona

M +34 682 894 653 T +34 936 758 015

www.argentaglobal.com



La información contenida en este mensaje y/o archivo(s) adjunto(s), enviada desde Pen & Tec Consulting SLU cotiza como Argenta, es confidencial/privilegiada y está destinada a ser leída sólo por la(s) persona(s) a la(s) que va dirigida. Le recordamos que sus datos han sido incorporados en el sistema de tratamiento de Pen & Tec Consulting SLU cotiza como Argenta, y que siempre y cuando se cumplan los requisitos exigidos por la normativa, usted podrá ejercer sus derechos de acceso, rectificación, limitación de tratamiento, supresión, portabilidad y oposición/revocación, en los términos que establece la normativa vigente en materia de protección de datos, dirigiendo su petición a la dirección postal OneCoWork, Portal de l'Àngel 40, 08002, Barcelona o bien a través de correo electrónico info@pentec-consulting.eu. Si usted lee este mensaje y no es el destinatario señalado, el empleado o el agente responsable de entregar el mensaje al destinatario, o ha recibido esta comunicación por error, le informamos que está totalmente prohibida, y puede ser ilegal, cualquier divulgación, distribución o reproducción de esta comunicación, y le rogamos que nos lo notifique inmediatamente y nos devuelva el mensaje original a la dirección arriba mencionada. Gracias.

The information contained in this message and/or attached file(s), sent by Pen & Tec Consulting SLU trading as Argenta, is confidential/privileged and is intended to be read solely by the person(s) to whom it is addressed. We hereby inform you that your data will be incorporated into the processing system owned by Pen & Tec Consulting SLU, and that provided it complies with the requirements included in the law, you may exercise the rights of access, rectification, limitation of processing, deletion, portability and opposition by sending your request to the postal address OneCoWork, Portal de l'Àngel 40, 08002, Barcelona or to the email address info@pentec-consulting.eu. If you read this message and you are neither the intended recipient, employee or agent in charge of delivering the message to the recipient, or if you have received this message as the result of an error, we hereby inform you that distributing, sharing or reproducing any part of this message is totally forbidden and may be illegal. As a result, we request that you immediately inform us of the error and return this message to the address mentioned above. Thank you.

From: Justyna Pałasińska <justyna.palasincka@argentaglobal.com>

Sent: 30 May 2024 16:09
To: DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>
Subject: Re: [EXTERNAL] GRN 1122 canola concentrate status

Indeed, great news, thank you Steve!

Kind regards,
Justyna Pałasińska
Regulatory Affairs Director – Human Nutrition, Argenta Barcelona



M +34 682 894 653 T +34 936 758 015

www.argentaglobal.com

La información contenida en este mensaje y/o archivo(s) adjunto(s), enviada desde Pen & Tec Consulting SLU cotiza como Argenta, es confidencial/privilegiada y está destinada a ser leída sólo por la(s) persona(s) a la(s) que va dirigida. Le recordamos que sus datos han sido incorporados en el sistema de tratamiento de Pen & Tec Consulting SLU cotiza como Argenta, y que siempre y cuando se cumplan los requisitos exigidos por la normativa, usted podrá ejercer sus derechos de acceso, rectificación, limitación de tratamiento, supresión, portabilidad y oposición/revocación, en los términos que establece la normativa vigente en materia de protección de datos, dirigiendo su petición a la dirección postal OneCoWork, Portal de l'Àngel 40, 08002, Barcelona o bien a través de correo electrónico info@pentec-consulting.eu. Si usted lee este mensaje y no es el destinatario señalado, el empleado o el agente responsable de entregar el mensaje al destinatario, o ha recibido esta comunicación por error, le informamos que está totalmente prohibida, y puede ser ilegal, cualquier divulgación, distribución o reproducción de esta comunicación, y le rogamos que nos lo notifique inmediatamente y nos devuelva el mensaje original a la dirección arriba mencionada. Gracias.
The information contained in this message and/or attached file(s), sent by Pen & Tec Consulting SLU trading as Argenta, is confidential/privileged and is intended to be read solely by the person(s) to whom it is addressed. We hereby inform you that your data will be incorporated into the processing system owned by Pen & Tec Consulting SLU, and that provided it complies with the requirements included in the law, you may exercise the rights of access, rectification, limitation of processing, deletion, portability and opposition by sending your request to the postal address OneCoWork, Portal de l'Àngel 40, 08002, Barcelona or to the email address info@pentec-consulting.eu. If you read this message and you are neither the intended recipient, employee or agent in charge of delivering the message to the recipient, or if you have received this message as the result of an error, we hereby inform you that distributing, sharing or reproducing any part of this message is totally forbidden and may be illegal. As a result, we request that you immediately inform us of the error and return this message to the address mentioned above. Thank you.

From: DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>
Sent: 30 May 2024 16:06
To: Justyna Pałasińska <justyna.palasinaska@argentaglobal.com>
Subject: RE: [EXTERNAL] GRN 1122 canola concentrate status

Hi Justyna,

I finally have some good news for you—FSIS has just finished their review. I have drafted a response letter and it is currently making its way through clearance, so you should hear back soon.

Best,

Steve

Stephen DiFranco, PhD
Regulatory Review Scientist/Chemist

Center for Food Safety and Applied Nutrition
Office of Food Additive Safety
Division of Food Ingredients
U.S. Food and Drug Administration
Tel: 240-402-2710
stephen.difranco@fda.hhs.gov



From: Justyna Pałasińska <justyna.palasinaska@argentaglobal.com>
Sent: Thursday, May 30, 2024 9:48 AM
To: DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>
Subject: Re: [EXTERNAL] GRN 1122 canola concentrate status

CAUTION: This email originated from outside of the organization. Do not click links or open attachments unless you recognize the sender and know the content is safe.

Dear Stephen,

I hope this e-mail finds you well. I was wondering if there is any update from FSIS on this GRN?

Kind regards,
Justyna Pałasińska
Regulatory Affairs Director – Human Nutrition, Argenta Barcelona



M +34 682 894 653 T +34 936 758 015

www.argentaglobal.com

La información contenida en este mensaje y/o archivo(s) adjunto(s), enviada desde Pen & Tec Consulting SLU cotiza como Argenta, es confidencial/privilegiada y está destinada a ser leída sólo por la(s) persona(s) a la(s) que va dirigida. Le recordamos que sus datos han sido incorporados en el sistema de tratamiento de Pen & Tec Consulting SLU cotiza como Argenta, y que siempre y cuando se cumplan los requisitos exigidos por la normativa, usted podrá ejercer sus derechos de acceso, rectificación, limitación de tratamiento, supresión, portabilidad y oposición/revocación, en los términos que establece la normativa vigente en materia de protección de datos, dirigiendo su petición a la dirección postal OneCoWork, Portal de l'Àngel 40, 08002, Barcelona o bien a través de correo electrónico info@pentec-consulting.eu. Si usted lee este mensaje y no es el destinatario señalado, el empleado o el agente responsable de entregar el mensaje al destinatario, o ha recibido esta comunicación por error, le informamos que está totalmente prohibida, y puede ser ilegal, cualquier divulgación, distribución o reproducción de esta comunicación, y le rogamos que nos lo notifique inmediatamente y nos devuelva el mensaje original a la dirección arriba mencionada. Gracias.

The information contained in this message and/or attached file(s), sent by Pen & Tec Consulting SLU trading as Argenta, is confidential/privileged and is intended to be read solely by the person(s) to whom it is addressed. We hereby inform you that your data will be incorporated into the processing system owned by Pen & Tec Consulting SLU, and that provided it complies with the requirements included in the law, you may exercise the rights of access, rectification, limitation of processing, deletion, portability and opposition by sending your request to the postal address OneCoWork, Portal de l'Àngel 40, 08002, Barcelona or to the email address info@pentec-consulting.eu. If you read this message and you are neither the intended recipient, employee or agent in charge of delivering the message to the recipient, or if you have received this message as the result of an error, we hereby inform you that distributing, sharing or reproducing any part of this message is totally forbidden and may be illegal. As a result, we request that you immediately inform us of the error and return this message to the address mentioned above. Thank you.

From: DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>
Sent: 04 April 2024 17:26
To: Justyna Pałasińska <justyna.palasinaska@argentaglobal.com>
Subject: RE: [EXTERNAL] GRN 1122 canola concentrate status

Thanks Justyna,

I've passed the information to FSIS for review. Hopefully we will hear back shortly.

Best,

Steve

Stephen DiFranco, PhD
Regulatory Review Scientist/Chemist

Center for Food Safety and Applied Nutrition
Office of Food Additive Safety
Division of Food Ingredients
U.S. Food and Drug Administration
Tel: 240-402-2710
stephen.difranco@fda.hhs.gov



From: Justyna Pałasińska <justyna.palasinaska@argentaglobal.com>
Sent: Thursday, April 4, 2024 7:38 AM
To: DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>
Subject: Re: [EXTERNAL] GRN 1122 canola concentrate status

CAUTION: This email originated from outside of the organization. Do not click links or open attachments unless you recognize the sender and know the content is safe.

Dear Stephen,

Please find our reply below:

It is the applicant's understanding that OSHA OELs for heavy metals indicated by FSIS relate to the risk of exposure to heavy metals in the material under assessment via inhalation route only. The material indeed may create dust hazard if handled improperly. We note that the safety data sheet provided for the material (attached for reference) not only informs about the potential to form dust if handled improperly but also includes information on precautionary measures and personal protection and engineering controls aimed at eliminating or greatly reducing the risk of exposure to airborne particles. Proper handling of the material / adherence to these measures and controls by extension would eliminate or greatly reduce the risk of exposure to heavy metals that may be present in the material.

In case the above does not sufficiently address the potential risk of exposure to heavy metals present in the material via inhalation route, the applicant would like to inform that the bulk density of the material ranges between 0.1 and 0.3 g/cm³. A confirmation whether this information is sufficient to proceed with the calculations would be much appreciated. It would also be helpful to understand the assumptions being made by FSIS (e.g. concentration of airborne particles) when assessing whether the levels of heavy metals in the product may exceed OSHA OELs.

Kind regards,
Justyna Pałasińska



M +34 682 894 653 T +34 936 758 015

www.argentaglobal.com

La informació contenida en este missatge y/o arxivo(s) adjunt(s), enviada desde Pen & Tec Consulting SLU cotiza como Argenta, es confidencial/privilegiada y está destinada a ser leída sólo por la(s) persona(s) a la(s) que va dirigida. Le recordamos que sus datos han sido incorporados en el sistema de tratamiento de Pen & Tec Consulting SLU cotiza como Argenta, y que siempre y cuando se cumplan los requisitos exigidos por la normativa, usted podrá ejercer sus derechos de acceso, rectificación, limitación de tratamiento, supresión, portabilidad y oposición/revocación, en los términos que establece la normativa vigente en materia de protección de datos, dirigiendo su petición a la dirección postal OneCoWork, Portal de l'Àngel 40, 08002, Barcelona o bien a través de correo electrónico info@pentec-consulting.eu. Si usted lee este mensaje y no es el destinatario señalado, el empleado o el agente responsable de entregar el mensaje al destinatario, o ha recibido esta comunicación por error, le informamos que está totalmente prohibida, y puede ser ilegal, cualquier divulgación, distribución o reproducción de esta comunicación, y le rogamos que nos lo notifique inmediatamente y nos devuelva el mensaje original a la dirección arriba mencionada. Gracias.

The information contained in this message and/or attached file(s), sent by Pen & Tec Consulting SLU trading as Argenta, is confidential/privileged and is intended to be read solely by the person(s) to whom it is addressed. We hereby inform you that your data will be incorporated into the processing system owned by Pen & Tec Consulting SLU, and that provided it complies with the requirements included in the law, you may exercise the rights of access, rectification, limitation of processing, deletion, portability and opposition by sending your request to the postal address OneCoWork, Portal de l'Àngel 40, 08002, Barcelona or to the email address info@pentec-consulting.eu. If you read this message and you are neither the intended recipient, employee or agent in charge of delivering the message to the recipient, or if you have received this message as the result of an error, we hereby inform you that distributing, sharing or reproducing any part of this message is totally forbidden and may be illegal. As a result, we request that you immediately inform us of the error and return this message to the address mentioned above. Thank you.

From: DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>
Date: Thursday, 28 March 2024 at 20:47
To: Justyna Pałasińska <justyna.palasinaska@argentaglobal.com>
Subject: RE: [EXTERNAL] GRN 1122 canola concentrate status

Hello Justyna,

I got feedback from FSIS about their review of GRN 1122. They send the following:

I have now completed the review of the documentation submitted for the approval of the above-referenced compound. I noted that it contains Lead (≤ 0.5 mg/kg), Arsenic (≤ 0.2 mg/kg), Cadmium (≤ 0.2 mg/kg), and Mercury (≤ 0.1 mg/kg). OSHA has established OEL for these substances at 0.05 mg/m³, 0.01 mg/m³, 0.01 mg/m³, 0.025 mg/m³ (depending on presentation) respectively.

To finalize my analysis, I require the composition in mg/m³ of each of these elements or the density so I may calculate their composition accurately and evaluate them against their OSHA standards.

Are you able to provide the density of the canola concentrate? I believe this is the easiest way to answer their questions. From the density and the specified ppm levels, the reviewer should be able to calculate the maximum amount by weight of each heavy metal contaminate for a given volume of canola concentrate.

Best,

Steve

Stephen DiFranco, PhD

Regulatory Review Scientist/Chemist

Center for Food Safety and Applied Nutrition
Office of Food Additive Safety
Division of Food Ingredients
U.S. Food and Drug Administration
Tel: 240-402-2710
stephen.difranco@fda.hhs.gov



From: Justyna Pałasińska <justyna.palasinaska@argentaglobal.com>
Sent: Monday, March 4, 2024 5:04 AM
To: DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>
Subject: Re: [EXTERNAL] GRN 1122 canola concentrate status

CAUTION: This email originated from outside of the organization. Do not click links or open attachments unless you recognize the sender and know the content is safe.

Many thanks for the update, Stephen. We look forward to hearing an update, hopefully soon!

Kind regards,

Justyna Pałasińska
Regulatory Affairs Director – Human Nutrition, Argenta Barcelona



M +34 682 894 653 T +34 936 758 015

www.argentaglobal.com

La información contenida en este mensaje y/o archivo(s) adjunto(s), enviada desde Pen & Tec Consulting SLU cotiza como Argenta, es confidencial/privilegiada y está destinada a ser leída sólo por la(s) persona(s) a la(s) que va dirigida. Le recordamos que sus datos han sido incorporados en el sistema de tratamiento de Pen & Tec Consulting SLU cotiza como Argenta, y que siempre y cuando se cumplan los requisitos exigidos por la normativa, usted podrá ejercer sus derechos de acceso, rectificación, limitación de tratamiento, supresión, portabilidad y oposición/revocación, en los términos que establece la normativa vigente en materia de protección de datos, dirigiendo su petición a la dirección postal Pl. Ausias March 1, 4 planta 08195, Sant Cugat del Vallès (Barcelona) o bien a través de correo electrónico info@pentec-consulting.eu. Si usted lee este mensaje y no es el destinatario señalado, el empleado o el agente responsable de entregar el mensaje al destinatario, o ha recibido esta comunicación por error, le informamos que está totalmente prohibida, y puede ser ilegal, cualquier divulgación, distribución o reproducción de esta comunicación, y le rogamos que nos lo notifique inmediatamente y nos devuelva el mensaje original a la dirección arriba mencionada. Gracias.

The information contained in this message and/or attached file(s), sent by Pen & Tec Consulting SLU trading as Argenta, is confidential/privileged and is intended to be read solely by the person(s) to whom it is addressed. We hereby inform you that your data will be incorporated into the processing system owned by Pen & Tec Consulting SLU, and that provided it complies with the requirements included in the law, you may exercise the rights of access, rectification, limitation of processing, deletion, portability and opposition by sending your request to the postal address Pl. Ausias March 1, 4 floor 08195, Sant Cugat del Valles (Barcelona) or to the email address info@pentec-consulting.eu. If you read this message and you are neither the intended recipient, employee or agent in charge of delivering the message to the recipient, or if you have received this message as the result of an error, we hereby inform you that distributing, sharing or reproducing any part of this message is totally forbidden and may be illegal. As a result, we request that you immediately inform us of the error and return this message to the address mentioned above. Thank you.

From: DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>
Date: Monday, 26 February 2024 at 17:20
To: Justyna Pałasińska <justyna.palasinaska@argentaglobal.com>
Subject: RE: [EXTERNAL] GRN 1122 canola concentrate status

Hello Justyna,

Regarding GRN 1122; FDA has completed its review and has drafted a response letter. Unfortunately, we cannot move forward before USDA-FSIS completes their review of the uses under their jurisdiction. I have been periodically inquiring with FSIS as to the status and will get this to you as soon as possible.

We appreciate your continued patience.

Best,

Steve

Stephen DiFranco, PhD
Regulatory Review Scientist/Chemist

Center for Food Safety and Applied Nutrition
Office of Food Additive Safety
Division of Food Ingredients
U.S. Food and Drug Administration
Tel: 240-402-2710
stephen.difranco@fda.hhs.gov



From: Justyna Pałasińska <justyna.palasinaska@argentaglobal.com>
Sent: Wednesday, February 14, 2024 12:07 PM
To: Premarkt <Premarkt@fda.hhs.gov>
Cc: DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>; Ioannis Kartanos <ioannis.kartanos@argentaglobal.com>
Subject: [EXTERNAL] GRN 1122 canola concentrate status

CAUTION: This email originated from outside of the organization. Do not click links or open attachments unless you recognize the sender and know the content is safe.

Dear HHS team,

I am writing to enquire about a GRAS notice that was submitted to the FDA & filed April 19, 2023 (GRN 1122). We have been in touch with Mr Stephen DiFranco & at the beginning of December he has informed us that the FDA reviews are complete & the notice is now with USDA-FSIS.

Mr DiFranco has been very helpful through the whole process. However, we have tried to contact him several times since December without success.

We were wondering if there is someone else we can get in touch with for an update on this application. We would be happy to provide any information that would help finalize the process.

I look forward to hearing from you.

Kind regards,

Justyna Pałasińska

Regulatory Affairs Director – Human Nutrition, Argenta Barcelona

The logo for Argenta, featuring the word "argenta" in a lowercase, sans-serif font with a blue and white graphic element above the letter 'a'.

M +34 682 894 653 T +34 936 758 015

www.argentaglobal.com

La información contenida en este mensaje y/o archivo(s) adjunto(s), enviada desde Pen & Tec Consulting SLU cotiza como Argenta, es confidencial/privilegiada y está destinada a ser leída sólo por la(s) persona(s) a la(s) que va dirigida. Le recordamos que sus datos han sido incorporados en el sistema de tratamiento de Pen & Tec Consulting SLU cotiza como Argenta, y que siempre y cuando se cumplan los requisitos exigidos por la normativa, usted podrá ejercer sus derechos de acceso, rectificación, limitación de tratamiento, supresión, portabilidad y oposición/revocación, en los términos que establece la normativa vigente en materia de protección de datos, dirigiendo su petición a la dirección postal Pl. Ausias March 1, 4 planta 08195, Sant Cugat del Vallès (Barcelona) o bien a través de correo electrónico info@pentec-consulting.eu. Si usted lee este mensaje y no es el destinatario señalado, el empleado o el agente responsable de entregar el mensaje al destinatario, o ha recibido esta comunicación por error, le informamos que está totalmente prohibida, y puede ser ilegal, cualquier divulgación, distribución o reproducción de esta comunicación, y le rogamos que nos lo notifique inmediatamente y nos devuelva el mensaje original a la dirección arriba mencionada. Gracias.

The information contained in this message and/or attached file(s), sent by Pen & Tec Consulting SLU trading as Argenta, is confidential/privileged and is intended to be read solely by the person(s) to whom it is addressed. We hereby inform you that your data will be incorporated into the processing system owned by Pen & Tec Consulting SLU, and that provided it complies with the requirements included in the law, you may exercise the rights of access, rectification, limitation of processing, deletion, portability and opposition by sending your request to the postal address Pl. Ausias March 1, 4 floor 08195, Sant Cugat del Valles (Barcelona) or to the email address info@pentec-consulting.eu. If you read this message and you are neither the intended recipient, employee or agent in charge of delivering the message to the recipient, or if you have received this message as the result of an error, we hereby inform you that distributing, sharing or reproducing any part of this message is totally forbidden and may be illegal. As a result, we request that you immediately inform us of the error and return this message to the address mentioned above. Thank you.

From: Justyna Pałasińska <justyna.palasinaska@argentaglobal.com>

Date: Wednesday, 31 January 2024 at 17:53

To: Justyna Pałasińska <justyna.palasinaska@argentaglobal.com>, DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>

Cc: Ioannis Kartanos <ioannis.kartanos@argentaglobal.com>

Subject: Re: [EXTERNAL] GRN 1122 canola concentrate - update contact person

Dear Steve,

I hope this e-mail finds you well. I was wondering if there are any updates on the finalization of this notification?

Is there any additional information that needs to be provided?

Kind regards,

Justyna Pałasińska

Regulatory Affairs Director – Human Nutrition, Argenta Barcelona

The logo for Argenta, featuring the word "argenta" in a lowercase, sans-serif font with a blue and white graphic element above the letter 'a'.

M +34 682 894 653 T +34 936 758 015

www.argentaglobal.com

La información contenida en este mensaje y/o archivo(s) adjunto(s), enviada desde Pen & Tec Consulting SLU cotiza como Argenta, es confidencial/privilegiada y está destinada a ser leída sólo por la(s) persona(s) a la(s) que va dirigida. Le recordamos que sus datos han sido incorporados en el sistema de tratamiento de Pen & Tec Consulting SLU cotiza como Argenta, y que siempre y cuando se cumplan los requisitos exigidos por la normativa, usted podrá ejercer sus derechos de acceso, rectificación, limitación de tratamiento, supresión, portabilidad y oposición/revocación, en los términos que establece la normativa vigente en materia de protección de datos, dirigiendo su petición a la dirección postal Pl. Ausias March 1, 4 planta 08195, Sant Cugat del Vallès (Barcelona) o bien a través de correo electrónico info@pentec-consulting.eu. Si usted lee este mensaje y no es el destinatario señalado, el empleado o el agente responsable de entregar el mensaje al destinatario, o ha recibido esta comunicación por error, le informamos que está totalmente prohibida, y puede ser ilegal, cualquier divulgación, distribución o reproducción de esta comunicación, y le rogamos que nos lo notifique inmediatamente y nos devuelva el mensaje original a la dirección arriba mencionada. Gracias.

The information contained in this message and/or attached file(s), sent by Pen & Tec Consulting SLU trading as Argenta, is confidential/privileged and is intended to be read solely by the person(s) to whom it is addressed. We hereby inform you that your data will be incorporated into the processing system owned by Pen & Tec Consulting SLU, and that provided it complies with the requirements included in the law, you may exercise the rights of access, rectification, limitation of processing, deletion, portability and opposition by sending your request to the postal address Pl. Ausias March 1, 4 floor 08195, Sant Cugat del Valles (Barcelona) or to the email address info@pentec-consulting.eu. If you read this message and you are neither the intended recipient, employee or agent in charge of delivering the message to the recipient, or if you have received this message as the result of an error, we hereby inform you that distributing, sharing or reproducing any part of this message is totally forbidden and may be illegal. As a result, we request that you immediately inform us of the error and return this message to the address mentioned above. Thank you.

From: Justyna Pałasińska <justyna@pentec-consulting.eu>

Date: Friday, 22 December 2023 at 13:31

To: DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>

Cc: Ioannis Kartanos <ioannis@pentec-consulting.eu>

Subject: Re: [EXTERNAL] GRN 1122 canola concentrate - update contact person

Dear Stephen,

Many thanks for confirming the change of contact person.

I'm following up on my colleague Ioannis e-mail from 12/12/2023. As he mentioned, we have already provided the answers to the questions to USDA-FSIS. Nevertheless, I have included them in a separate document.

Please let us know in case any additional information is required.

In the meantime, we wish you a Happy Holiday Season & all the best in 2024!

Kind regards,

Ing. Justyna Pałasińska

Regulatory Affairs Director – Human Nutrition | Pen & Tec Consulting
T +34 936 758 015 M +34 682 894 653 F +34 936 758 016 www.pentec-consulting.eu
Pl. Ausias March 1 | 4th floor D01 | 08195 Sant Cugat del Vallès | Barcelona | Spain



La información contenida en este mensaje y/o archivo(s) adjunto(s), enviada desde Pen & Tec Consulting SLU, es confidencial/privilegiada y está destinada a ser leída sólo por la(s) persona(s) a la(s) que va dirigida. Le recordamos que sus datos han sido incorporados en el sistema de tratamiento de Pen & Tec Consulting SLU y que siempre y cuando se cumplan los requisitos exigidos por la normativa, usted podrá ejercer sus derechos de acceso, rectificación, limitación de tratamiento, supresión, portabilidad y oposición/revocación, en los términos que establece la normativa vigente en materia de protección de datos, dirigiendo su petición a la dirección postal Pl. Ausias March 1, 4 planta 08195, Sant Cugat del Vallès (Barcelona) o bien a través de correo electrónico info@pentec-consulting.eu. Si usted lee este mensaje y no es el destinatario señalado, el empleado o el agente responsable de entregar el mensaje al destinatario, o ha recibido esta comunicación por error, le informamos que está totalmente prohibida, y puede ser ilegal, cualquier divulgación, distribución o reproducción de esta comunicación, y le rogamos que nos lo notifique inmediatamente y nos devuelva el mensaje original a la dirección arriba mencionada. Gracias.

The information contained in this message and/or attached file(s), sent by Pen & Tec Consulting SLU, is confidential/privileged and is intended to be read solely by the person(s) to whom it is addressed. We hereby inform you that your data will be incorporated into the processing system owned by Pen & Tec Consulting SLU, and that provided it complies with the requirements included in the law, you may exercise the rights of access, rectification, limitation of processing, deletion, portability and opposition by sending your request to the postal address Pl. Ausias March 1, 4 floor 08195, Sant Cugat del Vallès (Barcelona) or to the email address info@pentec-consulting.eu. If you read this message and you are neither the intended recipient, employee or agent in charge of delivering the message to the recipient, or if you have received this message as the result of an error, we hereby inform you that distributing, sharing or reproducing any part of this message is totally forbidden and may be illegal. As a result, we request that you immediately inform us of the error and return this message to the address mentioned above. Thank you.

From: DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>
Date: Tuesday, 5 December 2023 at 19:05
To: Nikolaas Tilkin-Franssens <niko@pentec-consulting.eu>
Cc: Justyna Pałasińska <justyna@pentec-consulting.eu>
Subject: RE: [EXTERNAL] GRN 1122 canola concentrate - update contact person

Hello Niko and Justyna,

Just confirming the change of contact person for GRN 1122.

As for timeline, FDA reviews are complete but USDA-FSIS is requesting a few pieces of information regarding the uses of canola concentrate under USDA jurisdiction, namely:

Please provide SDS for the at use concentrations of the substance and include a description of how the use of this technology will not adversely affect the safety of FSIS inspectors. Workplace safety and health hazards include inhalation, direct skin contact (skin, eyes, mouth), and fire/explosion caused by exposure to the product, its working solution or dry mixture and potential by-products formed and/or off-gassed during the application process. The employee safety information should demonstrate how the New Technology will not “jeopardize the safety of Federal inspection personnel” as specified in the [FSIS Compliance Guideline Procedures for New Technology Notifications and Protocols, April 2015](#).

Although I'm not anticipating any issues here, FSIS workplace and employee safety must be specifically addressed. Please refer to Appendix A on page 17, Workplace Safety and Health Criteria, for clarification on what to provide in the response. For additional clarity with respect to employee safety, the following are examples of information that are typically needed by FSIS' employee safety and health group;

1. Potential workplace exposures that could result from inhalation and direct contact during use of the substance/technology. This information is required in addition to a Safety Data Sheet (SDS) to determine accurate hazard potential and recommended exposure control measures for IPP work areas in accordance with Occupational Safety and Health Administration (OSHA) regulations: 29 CFR 1910.1200, Hazard Communication, 29 CFR 1910.132, Personal Protective Equipment, and 29 CFR 1910.1000, Air Contaminants. The information should be included as a specific section in each of the protocols.
2. If the SDS workplace hazards/precautions do not apply to the type of exposure that would be expected for the FSIS IPP, please have the submitter provide specific information (per the April 2015 FSIS Compliance Guideline Procedures) for the actual type of exposures expected.
3. If no IPP workplace exposures are expected and no control measures are required, please have the submitter state this and provide the reasons why (e.g., such as the substance “as used” [for all concentrations] is not hazardous by inhalation or direct contact and/or IPP would not be exposed to the substance based on the system design, operation and/or control measures that will be in place).
4. Please also indicate how will FSIS IPP be informed of the above information so that it is clear that the information contained in the SDS for the concentrate does not apply to their actual workplace exposure.
5. Are there any potential hazards from chemical mixing or low pH as a result of discharges of the various solutions to floor drains? Are dedicated drain lines or any other enclosures required?
6. With respect to potential airborne exposures to FSIS IPP in the use/application areas, does the submitter have air sampling results taken during the use of the various concentrations of the technology in the listed mixture?

Suitability data;

The intended use of this product in FSIS meat and poultry products is apparently as a binder/extender. The suitability support provided in Appendix 6 does sufficiently support no significant difference in yield and other organoleptic qualities when used as a partial replacement for another binder in a processed meat and poultry product, such as sausage.

However, **additional suitability support is needed:**

- No suitability data was provided for **whole muscle meat and poultry products at the maximum proposed use level**. We would need to see similar data as provided in Appendix 6 for:
 - Whole muscle red meat control containing no other binders, extenders, or moisture retention agents, as compared to a whole muscle red meat product containing 15% isolated canola product.
 - Whole muscle poultry control containing no other binders, extenders, or moisture retention agents as compared to a whole muscle poultry product containing 15% isolated canola product.

You responses can be emailed directly to me and I will distribute to the necessary staff inside FDA and USDA.

Thanks,

Steve

Stephen DiFranco, PhD

Regulatory Review Scientist/Chemist

Center for Food Safety and Applied Nutrition
Office of Food Additive Safety
Division of Food Ingredients
U.S. Food and Drug Administration
Tel: 240-402-2710
stephen.difranco@fda.hhs.gov



From: Nikolaas Tilkin-Franssens <niko@pentec-consulting.eu>
Sent: Monday, December 4, 2023 4:36 AM
To: DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>
Cc: Justyna Pałasińska <justyna@pentec-consulting.eu>
Subject: [EXTERNAL] GRN 1122 canola concentrate - update contact person

CAUTION: This email originated from outside of the organization. Do not click links or open attachments unless you recognize the sender and know the content is safe.

Hi Mr. DiFranco,

Hope this email finds you well.

Due to a change in position, I will no longer be the contact person for the GRAS Notice 1122 (Canola Protein Concentrate). Could you please update your records to ascertain that Justyna Pałasińska, in copy to this email, is informed of any relevant updates?

Could you kindly confirm receipt of this email for our records?

And if possible, let us know if there is any estimate on the timeline re. finalization of the review of this GRAS Notice.

Many thanks for your great and flexible support on this application.

Kind regards,

Niko

Nikolaas Tilkin-Franssens

Regulatory Affairs Manager | Pen & Tec Consulting

T +34 936 758 015 M +34 649 840 417 F +34 936 758 016 www.pentec-consulting.eu

Pl. Ausias March 1 | 4th floor D01 | 08195 Sant Cugat del Vallès | Barcelona | Spain



La información contenida en este mensaje y/o archivo(s) adjunto(s), enviada desde Pen & Tec Consulting SLU, es confidencial/privilegiada y está destinada a ser leída sólo por la(s) persona(s) a la(s) que va dirigida. Le recordamos que sus datos han sido incorporados en el sistema de tratamiento de Pen & Tec Consulting SLU y que siempre y cuando se cumplan los requisitos exigidos por la normativa, usted podrá ejercer sus derechos de acceso, rectificación, limitación de tratamiento, supresión, portabilidad y oposición/revocación, en los términos que establece la normativa

vigente en materia de protección de datos, dirigiendo su petición a la dirección postal Pl. Ausias March 1, 4 planta 08195, Sant Cugat del Vallès (Barcelona) o bien a través de correo electrónico info@pentec-consulting.eu. Si usted lee este mensaje y no es el destinatario señalado, el empleado o el agente responsable de entregar el mensaje al destinatario, o ha recibido esta comunicación por error, le informamos que está totalmente prohibida, y puede ser ilegal, cualquier divulgación, distribución o reproducción de esta comunicación, y le rogamos que nos lo notifique inmediatamente y nos devuelva el mensaje original a la dirección arriba mencionada. Gracias.

The information contained in this message and/or attached file(s), sent by Pen & Tec Consulting SLU, is confidential/privileged and is intended to be read solely by the person(s) to whom it is addressed. We hereby inform you that your data will be incorporated into the processing system owned by Pen & Tec Consulting SLU, and that provided it complies with the requirements included in the law, you may exercise the rights of access, rectification, limitation of processing, deletion, portability and opposition by sending your request to the postal address Pl. Ausias March 1, 4 floor 08195, Sant Cugat del Vallès (Barcelona) or to the email address info@pentec-consulting.eu. If you read this message and you are neither the intended recipient, employee or agent in charge of delivering the message to the recipient, or if you have received this message as the result of an error, we hereby inform you that distributing, sharing or reproducing any part of this message is totally forbidden and may be illegal. As a result, we request that you immediately inform us of the error and return this message to the address mentioned above. Thank you.

From: DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>
Date: Monday, 17 July 2023 at 17:01
To: Nikolaas Tilkin-Franssens <niko@pentec-consulting.eu>
Subject: RE: [EXTERNAL] Re: GRN 1122 canola concentrate items for clarification - Reply

Hello Niko,

No problem—I'll distribute this to the team for review.

Best,

Steve

Stephen DiFranco, PhD
Regulatory Review Scientist/Chemist

Center for Food Safety and Applied Nutrition
Office of Food Additive Safety
Division of Food Ingredients
U.S. Food and Drug Administration
Tel: 240-402-2710
stephen.difranco@fda.hhs.gov



From: Nikolaas Tilkin-Franssens <niko@pentec-consulting.eu>
Sent: Monday, July 17, 2023 10:35 AM
To: DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>
Subject: [EXTERNAL] Re: GRN 1122 canola concentrate items for clarification - Reply

CAUTION: This email originated from outside of the organization. Do not click links or open attachments unless you recognize the sender and know the content is safe.

Hi Stephen,

Apologies for this inconvenience.

We noticed that the reply to question 9 refers to Canola protein isolate (as per GRN 1103). I have updated the answer for it to be mentioning Canola protein concentrate (GRN 1122).

We hope this can be taken into consideration.

Kind regards,

Nikolaas Tilkin-Franssens
Regulatory Affairs Manager | Pen & Tec Consulting

T +34 936 758 015 M +34 649 840 417 F +34 936 758 016 www.pentec-consulting.eu
Pl. Ausias March 1 | 4th floor D01 | 08195 Sant Cugat del Vallès | Barcelona | Spain

PEN + TEC
CONSULTING
PART OF THE ARGENTA GROUP

La información contenida en este mensaje y/o archivo(s) adjunto(s), enviada desde Pen & Tec Consulting SLU, es confidencial/privilegiada y está destinada a ser leída sólo por la(s) persona(s) a la(s) que va dirigida. Le recordamos que sus datos han sido incorporados en el sistema de tratamiento de Pen & Tec Consulting SLU y que siempre y cuando se cumplan los requisitos exigidos por la normativa, usted podrá ejercer sus derechos de acceso, rectificación, limitación de tratamiento, supresión, portabilidad y oposición/revocación, en los términos que establezca la normativa vigente en materia de protección de datos, dirigiendo su petición a la dirección postal Pl. Ausias March 1, 4 planta 08195, Sant Cugat del Vallès (Barcelona) o bien a través de correo electrónico info@pentec-consulting.eu. Si usted lee este mensaje y no es el destinatario señalado, el empleado o el agente responsable de entregar el mensaje al destinatario, o ha recibido esta comunicación por error, le informamos que está totalmente prohibida, y puede ser ilegal, cualquier divulgación, distribución o reproducción de esta comunicación, y le rogamos que nos lo notifique

inmediatamente y nos devuelve el mensaje original a la dirección arriba mencionada. Gracias.

The information contained in this message and/or attached file(s), sent by Pen & Tec Consulting SLU, is confidential/privileged and is intended to be read solely by the person(s) to whom it is addressed. We hereby inform you that your data will be incorporated into the processing system owned by Pen & Tec Consulting SLU, and that provided it complies with the requirements included in the law, you may exercise the rights of access, rectification, limitation of processing, deletion, portability and opposition by sending your request to the postal address Pl. Ausias March 1, 4 floor 08195, Sant Cugat del Valles (Barcelona) or to the email address info@pentec-consulting.eu. If you read this message and you are neither the intended recipient, employee or agent in charge of delivering the message to the recipient, or if you have received this message as the result of an error, we hereby inform you that distributing, sharing or reproducing any part of this message is totally forbidden and may be illegal. As a result, we request that you immediately inform us of the error and return this message to the address mentioned above. Thank you.

From: Nikolaas Tilkin-Franssens <niko@pentec-consulting.eu>
Date: Tuesday, 11 July 2023 at 17:03
To: DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>
Cc: Justyna Pałasińska <justyna@pentec-consulting.eu>
Subject: Re: GRN 1122 canola concentrate items for clarification - Reply

Dear Stephen,

Thank you for reaching out with the questions for clarification.
We have worked closely with Napiferyn to close the doubts.

Kindly find attached a Word file including the Questions&Answers, a report on the requested literature review, a SDS sheet as requested by the USDA-FSIS, and a report on the suitability assessment.

We remain available for any further questions or updates.

Thanks for taking the application in further consideration,
best regards,

Nikolaas Tilkin-Franssens

Regulatory Affairs Manager | Pen & Tec Consulting

T +34 936 758 015 M +34 649 840 417 F +34 936 758 016 www.pentec-consulting.eu

Pl. Ausias March 1 | 4th floor D01 | 08195 Sant Cugat del Vallès | Barcelona | Spain

PEN + TEC
CONSULTING
PART OF THE ARGENTA GROUP

La información contenida en este mensaje y/o archivo(s) adjunto(s), enviada desde Pen & Tec Consulting SLU, es confidencial/privilegiada y está destinada a ser leída sólo por la(s) persona(s) a la(s) que va dirigida. Le recordamos que sus datos han sido incorporados en el sistema de tratamiento de Pen & Tec Consulting SLU y que siempre y cuando se cumplan los requisitos exigidos por la normativa, usted podrá ejercer sus derechos de acceso, rectificación, limitación de tratamiento, supresión, portabilidad y oposición/revocación, en los términos que establece la normativa vigente en materia de protección de datos, dirigiendo su petición a la dirección postal Pl. Ausias March 1, 4 planta 08195, Sant Cugat del Vallès (Barcelona) o bien a través de correo electrónico info@pentec-consulting.eu. Si usted lee este mensaje y no es el destinatario señalado, el empleado o el agente responsable de entregar el mensaje al destinatario, o ha recibido esta comunicación por error, le informamos que está totalmente prohibida, y puede ser ilegal, cualquier divulgación, distribución o reproducción de esta comunicación, y le rogamos que nos lo notifique inmediatamente y nos devuelva el mensaje original a la dirección arriba mencionada. Gracias.

The information contained in this message and/or attached file(s), sent by Pen & Tec Consulting SLU, is confidential/privileged and is intended to be read solely by the person(s) to whom it is addressed. We hereby inform you that your data will be incorporated into the processing system owned by Pen & Tec Consulting SLU, and that provided it complies with the requirements included in the law, you may exercise the rights of access, rectification, limitation of processing, deletion, portability and opposition by sending your request to the postal address Pl. Ausias March 1, 4 floor 08195, Sant Cugat del Valles (Barcelona) or to the email address info@pentec-consulting.eu. If you read this message and you are neither the intended recipient, employee or agent in charge of delivering the message to the recipient, or if you have received this message as the result of an error, we hereby inform you that distributing, sharing or reproducing any part of this message is totally forbidden and may be illegal. As a result, we request that you immediately inform us of the error and return this message to the address mentioned above. Thank you.

From: DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>
Date: Wednesday, 28 June 2023 at 17:41
To: Nicoleta Pasecinic <nicoleta@pentec-consulting.eu>
Cc: Nikolaas Tilkin-Franssens <niko@pentec-consulting.eu>
Subject: [EXTERNAL]: GRN 1122 canola concentrate items for clarification

CAUTION: This email originated from outside of the organization. Do not click links or open attachments unless you recognize the sender and know the content is safe.

Hello Ms. Pasecinic,

After evaluating Napiferyn's GRAS Notice No. GRN 1122 on canola concentrate we noted a few issues that should be addressed. Please respond to the following points for clarification:

1. On p. 9, Napiferyn states that the major storage proteins in canola seed are cruciferins and napins, and that canola concentrate consists of 30-45% protein and 40-70% dietary fiber. Please provide the typical cruciferin content and napin content in canola concentrate.
2. Please confirm that all raw materials and processing aids used in the manufacturing process are used in accordance with the U.S. regulations, are GRAS for their respective uses or are the subject of an effective food contact notification. For the record, we note that the food additive regulations cited in Table 4 (p. 15) for ascorbic acid (21 CFR 182.8013), ethanol (21 CFR 184.1293), and ethyl acetate (21 CFR 173.228) do not appear to be applicable to your intended uses of these substances.
3. In Table 6 (p. 18-19), Napiferyn provides the results from the batch analyses for heavy metals. We would like to bring to your attention a relevant FDA's "[Closer to Zero](#)" initiative that focuses on reducing the levels of heavy metals in foods and recommend that you lower the

specification limits for heavy metal to better reflect the batch analyses results and to be as low as possible.

4. In Table 10 (p. 22), NapiFeryn provides batch analyses data for residual solvents and processing aids. In addition, in Table 21 (p. 50), you provided the results from the batch analyses for erucic acid in your canola concentrate ranging from 0.37% to < 0.1%.
Please include limits for residual ethanol, ethyl acetate, and sulphur dioxide as well as a limit for erucic acid in the specifications for canola concentrate and specify the analytical methods used to test for these parameters.
In addition, please provide an updated Tables 5 and 6 (p. 16-19) to include the additional specification parameters mentioned above, corresponding analytical methods, and batch analyses.
5. Please state that all analytical methods used to test batches were validated and are fit for their respective purpose.
6. Please state that canola concentrate is not intended for use in infant formula or in foods where standards of identity preclude its use.
7. In Table 15 (p.), NapiFeryn provides the results of the batch analyses for total plate count in the raw material (rapeseed press cake). Please address the significant variation in the results (from <10 to 28,000 CFU/g) and discuss whether this will impact safety of the final ingredient.
8. On p. 19, NapiFeryn states that the levels of mycotoxins in canola concentrate are below the limit of quantitation (LOQ) and provide the results from the analyses of five batches to support your statement. Please clarify whether you expect mycotoxins to be present in canola concentrate manufactured in accordance with good manufacturing practices.
9. In Part 1.4 (p. 6) and Part 3.1 (p. 33), NapiFeryn states that the intended use of canola concentrate is as a source of protein and/or fiber, thickener, or texturizer. However, we note that on p. 33 you also state the intended use of canola concentrate is as a flavoring agent or binder in various comminuted or whole muscle meat and poultry products. In addition, in Appendix 3 (p. 5) you state that canola concentrate may also be used “to create a flavored salt” or as “a flavor enhancer like monosodium glutamate”. Please confirm these additional uses of canola concentrate are within the scope of GRN 001122.
10. On p. 10, the notifier describes the protein composition of canola concentrate, being primarily cruciferins, napin, oleosin, and squalene monooxygenase. However, the pivotal safety data provided appear to only be relevant to the cruciferin and napin fractions of the canola concentrate. Please provide a brief narrative to confirm the safety of oleosin and squalene monooxygenase exposure from the intended uses.
11. On p. 31-32 of the notice, the notifier clearly establishes that canola concentrate is intended to be substitutive to protein and fiber consumption and will not contribute to additional exposure to protein or fiber in general. Please elaborate on this conclusion, and clarify if the intended uses of canola concentrate are additive or substitutive to other canola protein products currently on the market (i.e., GRNs 327, 386, and 683)?
12. On p. 37, the notifier concludes exposure to canola concentrate from the intended uses is safe since the EDI reported is “still much lower (approximately 7- to 22-fold lower) than the no-observed-adverse-effect level (NOAEL) values established” for cruciferin- and napin-rich protein isolates in male rats following a 13-week oral exposure regimen (Mejia *et al.*, 2009a & 2009b). We note that an uncertainty factor, or margin of safety (MOS), of 100 (10 for interindividual variability × 10 for interspecies variability) is normally used when assessing safety of a food ingredient by comparing estimated human exposure levels to the NOAEL from animal toxicology data. Therefore, it is not clear why MOS that is ~5-10-fold lower can be concluded as safe without proper justification. Additionally, we note that potential thyrotoxic effects were observed at the highest doses in these two rat studies, as well as for rapeseed products in general tested in other species, as cited in Table 20 of the GRAS notice. This effect was mostly attributed to the presence of glucosinolate; however, we note that since the level of glucosinolate was low or absent in both the test articles from Mejia *et al.* and the article of commerce, the rationale used by the study authors to conclude that the observed NOAEL was not in fact the LOAEL may be questionable. Regardless, it appears that the provided safety narrative lacks sufficient basis to conclude MOS of 7-22 is adequate to reach the conclusion of “reasonable certainty of no harm.” Based on generally available data and information, please provide additional narrative to explain your rationale for your GRAS conclusion.
13. We note that when discussing the absorption, distribution, metabolism, and excretion of canola concentrate (p. 49), the notifier reports unpublished data from an EU Novel Foods application for “defatted rapeseed powder” to support their conclusion. Similarly, genotoxicity conclusions are made using unpublished data from an EFSA Panel conclusion on defatted rapeseed powder. Given other data and information have been used in prior GRAS notices for canola ingredients (e.g., GRN 327), please confirm that the EFSA Panel and EU Novel Foods conclusions are only considered as corroborative, not pivotal, to the safety determination of canola concentrate at its intended use level?
14. On p. 40, the notifier discusses the allergenicity potential of canola concentrate being determined via a “bioinformatics approach” and concludes that canola concentrate “may elicit possible allergenic effects.” Additionally, on p. 59 the notifier reiterates that the bioinformatics analysis indicated “possible allergenic effects” of canola concentrate, but no further discussion is provided. While data from an allergen online database search is provided as part of Appendix 4, no discussion of these data are included in the current GRAS notice. Please briefly detail the “possible allergenic effects” of canola concentrate similar to previous notices (e.g., GRN 683), and discuss why they would not be expected to pose a safety concern from the intended use.

15. We note that a recent study on rapeseed protein isolate was published (Xiong et al., 2022).
 - a. Please discuss if this study presents additional safety concerns for the article of commerce or contradicts the current GRAS conclusion.
 - b. Please also perform an updated literature review from 2021 to present and discuss if any additional studies relevant to the safety of canola concentrate were identified that would contradict the current GRAS conclusion.

References cited:

Xiong Z, Fu Y, Yao J, Zhang N, He R, Ju X, Wang Z. Removal of anti-nutritional factors of rapeseed protein isolate (RPI) and toxicity assessment of RPI. *Food Funct.* 2022 Jan 24;13(2):664-674. doi: 10.1039/d1fo03217h. PMID: 34933325.

Additionally, we received the following questions from USDA FSIS regarding their review of the uses of GRN 1122 concerning products within their purview. Please respond to the following and we will pass your responses along to them.

Please provide Safety Data Sheet (SDS) for the at use concentrations of the substance and include a description of how the use of this technology will not adversely affect the safety of FSIS inspectors. Workplace safety and health hazards include inhalation, direct skin contact (skin, eyes, mouth), and fire/explosion caused by exposure to the product, its working solution or dry mixture and potential by-products formed and/or off-gassed during the application process. The employee safety information should demonstrate how the New Technology will not “jeopardize the safety of Federal inspection personnel” as specified in the [FSIS Compliance Guideline Procedures for New Technology Notifications and Protocols, April 2015](#). FSIS workplace and employee safety must be specifically addressed. Please refer to Appendix A on p. 17, Workplace Safety and Health Criteria, for clarification on what to provide in the response. For additional clarity with respect to employee safety, the following are examples of information that are typically needed by FSIS’ employee safety and health group;

1. Potential workplace exposures that could result from inhalation and direct contact during use of the substance/technology. This information is required in addition to a SDS to determine accurate hazard potential and recommended exposure control measures for IPP work areas in accordance with Occupational Safety and Health Administration (OSHA) regulations: 29 CFR 1910.1200, Hazard Communication, 29 CFR 1910.132, Personal Protective Equipment, and 29 CFR 1910.1000, Air Contaminants. The information should be included as a specific section in each of the protocols.
2. If the SDS workplace hazards/precautions do not apply to the type of exposure that would be expected for the FSIS IPP, please have the submitter provide specific information (per the April 2015 FSIS Compliance Guideline Procedures) for the actual type of exposures expected.
3. If no IPP workplace exposures are expected and no control measures are required, please have the submitter state this and provide the reasons why (e.g., such as the substance “as used” [for all concentrations] is not hazardous by inhalation or direct contact and/or IPP would not be exposed to the substance based on the system design, operation and/or control measures that will be in place).
4. Please also indicate how will FSIS IPP be informed of the above information so that it is clear that the information contained in the SDS for the concentrate does not apply to their actual workplace exposure.
5. Are there any potential hazards from chemical mixing or low pH as a result of discharges of the various solutions to floor drains? Are dedicated drain lines or any other enclosures required?
6. With respect to potential airborne exposures to FSIS IPP in the use/application areas, does the submitter have air sampling results taken during the use of the various concentrations of the technology in the listed mixture?
7. The intended use of this product in FSIS meat and poultry products is apparently as a binder/extender. The suitability support provided in Appendix 6 does sufficiently support no significant difference in yield and other organoleptic qualities when used as a partial replacement for another binder in a processed meat and poultry product, such as sausage.

However, **additional suitability support is needed:**

- a. No suitability data was provided for **whole muscle meat and poultry products at the maximum proposed use level**. We would need to see similar data as provided in Appendix 6 for:
 - Whole muscle red meat control containing no other binders, extenders, or moisture retention agents, as compared to a whole muscle red meat product containing 15% isolated canola product.
 - Whole muscle poultry control containing no other binders, extenders, or moisture retention agents as compared to a whole muscle poultry product containing 15% isolated canola product.

Responses may be sent in an email or in a separate document. We respectfully request a response within 10 business days. If you are unable to complete the response within that time frame, please contact me to discuss further options.

If you have any additional questions or concerns, please don't hesitate to contact me at stephen.difranco@fda.hhs.gov or by phone at 240.402.2710.

Best,
Steve

Stephen DiFranco, PhD

Regulatory Review Scientist/Chemist

Center for Food Safety and Applied Nutrition
Office of Food Additive Safety
Division of Food Ingredients



CAUTION: This email, including any attachments, is confidential. If you are not the intended recipient, please notify the sender and delete the email and any attachments from your system. In addition, you must not use, distribute or reproduce this email or any attachments. Opinions and other information in this email and any attachments which do not relate to the official business of Argenta are neither given by nor endorsed by Argenta. While Argenta uses anti-virus software, Argenta accepts no liability for any viruses in this email or any attachment, or for any effects this email or any attachment may have on your network or computer system.

CAUTION: This email, including any attachments, is confidential. If you are not the intended recipient, please notify the sender and delete the email and any attachments from your system. In addition, you must not use, distribute or reproduce this email or any attachments. Opinions and other information in this email and any attachments which do not relate to the official business of Argenta are neither given by nor endorsed by Argenta. While Argenta uses anti-virus software, Argenta accepts no liability for any viruses in this email or any attachment, or for any effects this email or any attachment may have on your network or computer system.

Este correo electrónico y los archivos adjuntos, enviados por Pen & Tec Consulting SLU, que opera bajo el nombre comercial de Argenta® (Argenta), son confidenciales y pueden estar protegidos por ley. Si usted no es el destinatario, cualquier divulgación, reproducción, copia, distribución u otro tipo de difusión o uso de esta comunicación está estrictamente prohibido. Si ha recibido esta transmisión por error, notifíquelo al remitente y elimine inmediatamente el correo electrónico y cualquier archivo adjunto de su sistema. Argenta no emite ni respalda las opiniones y demás información contenida en este correo electrónico y en sus anexos que no estén relacionadas con las actividades oficiales de Argenta. Aunque Argenta utiliza software antivirus, Argenta no acepta ninguna responsabilidad por cualquier virus en este correo electrónico o cualquier archivo adjunto, o por cualquier efecto que este correo electrónico o cualquier archivo adjunto pueda tener en su red o sistema informático. Argenta registra y almacena los correos electrónicos enviados a nosotros o a nuestros afiliados de acuerdo con nuestras políticas y procedimientos internos. Consulte www.pentec-consulting.eu para obtener información sobre Argenta y/o nuestra política de privacidad.

This email and any attached file(s), sent by Pen & Tec Consulting SLU trading as Argenta® (Argenta), are confidential and may be legally privileged. If you are not the intended recipient, any disclosure, reproduction, copying, distribution, or other dissemination or use of this communication is strictly prohibited. If you have received this transmission in error, please notify the sender and delete the email and any attachments from your system immediately. Opinions and other information in this email and any attachments which do not relate to the official business of Argenta are neither given by nor endorsed by Argenta. While Argenta uses anti-virus software, Argenta accepts no liability for any viruses in this email or any attachment, or for any effects this email or any attachment may have on your network or computer system. Argenta records and stores emails sent to us or our affiliates in keeping with our internal policies and procedures. Please see www.pentec-consulting.eu for information regarding Argenta and/or our privacy policy.

Este correo electrónico y los archivos adjuntos, enviados por Pen & Tec Consulting SLU, que opera bajo el nombre comercial de Argenta® (Argenta), son confidenciales y pueden estar protegidos por ley. Si usted no es el destinatario, cualquier divulgación, reproducción, copia, distribución u otro tipo de difusión o uso de esta comunicación está estrictamente prohibido. Si ha recibido esta transmisión por error, notifíquelo al remitente y elimine inmediatamente el correo electrónico y cualquier archivo adjunto de su sistema. Argenta no emite ni respalda las opiniones y demás información contenida en este correo electrónico y en sus anexos que no estén relacionadas con las actividades oficiales de Argenta. Aunque Argenta utiliza software antivirus, Argenta no acepta ninguna responsabilidad por cualquier virus en este correo electrónico o cualquier archivo adjunto, o por cualquier efecto que este correo electrónico o cualquier archivo adjunto pueda tener en su red o sistema informático. Argenta registra y almacena los correos electrónicos enviados a nosotros o a nuestros afiliados de acuerdo con nuestras políticas y procedimientos internos. Consulte www.pentec-consulting.eu para obtener información sobre Argenta y/o nuestra política de privacidad.

This email and any attached file(s), sent by Pen & Tec Consulting SLU trading as Argenta® (Argenta), are confidential and may be legally privileged. If you are not the intended recipient, any disclosure, reproduction, copying, distribution, or other dissemination or use of this communication is strictly prohibited. If you have received this transmission in error, please notify the sender and delete the email and any attachments from your system immediately. Opinions and other information in this email and any attachments which do not relate to the official business of Argenta are neither given by nor endorsed by Argenta. While Argenta uses anti-virus software, Argenta accepts no liability for any viruses in this email or any attachment, or for any effects this email or any attachment may have on your network or computer system. Argenta records and stores emails sent to us or our affiliates in keeping with our internal policies and procedures. Please see www.pentec-consulting.eu for information regarding Argenta and/or our privacy policy.

Este correo electrónico y los archivos adjuntos, enviados por Pen & Tec Consulting SLU, que opera bajo el nombre comercial de Argenta® (Argenta), son confidenciales y pueden estar protegidos por ley. Si usted no es el destinatario, cualquier divulgación, reproducción, copia, distribución u otro tipo de difusión o uso de esta comunicación está estrictamente prohibido. Si ha recibido esta transmisión por error, notifíquelo al remitente y elimine inmediatamente el correo electrónico y cualquier archivo adjunto de su sistema. Argenta no emite ni respalda las opiniones y demás información contenida en este correo electrónico y en sus anexos que no estén relacionadas con las actividades oficiales de Argenta. Aunque Argenta utiliza software antivirus, Argenta no acepta ninguna responsabilidad por cualquier virus en este correo electrónico o cualquier archivo adjunto, o por cualquier efecto que este correo electrónico o cualquier archivo adjunto pueda tener en su red o sistema informático. Argenta registra y almacena los correos electrónicos enviados a nosotros o a nuestros afiliados de acuerdo con nuestras políticas y procedimientos internos. Consulte www.pentec-consulting.eu para obtener información sobre Argenta y/o nuestra política de privacidad.

This email and any attached file(s), sent by Pen & Tec Consulting SLU trading as Argenta® (Argenta), are confidential and may be legally privileged. If you are not the intended recipient, any disclosure, reproduction, copying, distribution, or other dissemination or use of this communication is strictly prohibited. If you have received this transmission in error, please notify the sender and delete the email and any attachments from your system immediately. Opinions and other information in this email and any attachments which do not relate to the official business of Argenta are neither given by nor endorsed by Argenta. While Argenta uses anti-virus software, Argenta accepts no liability for any viruses in this email or any attachment, or for any effects this email or any attachment may have on your network or computer system. Argenta records and stores emails sent to us or our affiliates in keeping with our internal policies and procedures. Please see www.pentec-consulting.eu for information regarding Argenta and/or our privacy policy.

Este correo electrónico y los archivos adjuntos, enviados por Pen & Tec Consulting SLU, que opera bajo el nombre comercial de Argenta® (Argenta), son confidenciales y pueden estar protegidos por ley. Si usted no es el destinatario, cualquier divulgación, reproducción, copia, distribución u otro tipo de difusión o uso de esta comunicación está estrictamente prohibido. Si ha recibido esta transmisión por error, notifíquelo al remitente y elimine inmediatamente el correo electrónico y cualquier archivo adjunto de su sistema. Argenta no emite ni respalda las opiniones y demás información contenida en este correo electrónico y en sus anexos que no estén relacionadas con las actividades oficiales de Argenta. Aunque Argenta utiliza software antivirus, Argenta no acepta ninguna responsabilidad por cualquier virus en este correo electrónico o cualquier archivo adjunto, o por cualquier efecto que este correo electrónico o cualquier archivo adjunto pueda tener en su red o sistema informático. Argenta registra y almacena los correos electrónicos enviados a nosotros o a nuestros afiliados de acuerdo con nuestras políticas y procedimientos internos. Consulte www.pentec-consulting.eu para obtener información sobre Argenta y/o nuestra política de privacidad.

This email and any attached file(s), sent by Pen & Tec Consulting SLU trading as Argenta® (Argenta), are confidential and may be legally privileged. If you are not the intended recipient, any disclosure, reproduction, copying, distribution, or other dissemination or use of this communication is strictly prohibited. If you have received this transmission in error, please notify the sender and delete the email and any attachments from your system immediately. Opinions and other information in this email and any attachments which do not relate to the official business of Argenta are neither given by nor endorsed by Argenta. While Argenta uses anti-virus software, Argenta accepts no liability for any viruses in this email or any attachment, or for any effects this email or any attachment may have on your network or computer system. Argenta records and stores emails sent to us or our affiliates in keeping with our internal policies and procedures. Please see www.pentec-consulting.eu for information regarding Argenta and/or our privacy policy.

Este correo electrónico y los archivos adjuntos, enviados por Pen & Tec Consulting SLU, que opera bajo el nombre comercial de Argenta® (Argenta), son confidenciales y pueden estar protegidos por ley. Si usted no es el destinatario, cualquier divulgación, reproducción, copia, distribución u otro tipo de difusión o uso de esta comunicación está estrictamente prohibido. Si ha recibido esta transmisión por error, notifíquelo al remitente y elimine inmediatamente el correo electrónico y cualquier archivo adjunto de su sistema. Argenta no emite ni respalda las opiniones y demás información contenida en este correo electrónico y en sus anexos que no estén relacionadas con las actividades oficiales de Argenta. Aunque Argenta utiliza software antivirus, Argenta no acepta ninguna responsabilidad por cualquier virus en este correo electrónico o cualquier archivo adjunto, o por cualquier efecto que este correo electrónico o cualquier archivo adjunto pueda tener en su red o sistema informático. Argenta registra y almacena los correos electrónicos enviados a nosotros o a nuestros afiliados de acuerdo con nuestras políticas y procedimientos internos. Consulte www.pentec-consulting.eu para obtener información sobre Argenta y/o nuestra política de privacidad.

This email and any attached file(s), sent by Pen & Tec Consulting SLU trading as Argenta® (Argenta), are confidential and may be legally privileged. If you are not the intended recipient, any disclosure, reproduction, copying, distribution, or other dissemination or use of this communication is strictly prohibited. If you have received this transmission in error, please notify the sender and delete the email and any attachments from your system immediately. Opinions and other information in this email and any attachments which do not relate to the official business of Argenta are neither given by nor endorsed by Argenta. While Argenta uses anti-virus software, Argenta accepts no liability for any viruses in this email or any attachment, or for any effects this email or any attachment may have on your network or computer system. Argenta records and stores emails sent to us or our affiliates in keeping with our internal policies and procedures. Please see www.pentec-consulting.eu for information regarding Argenta and/or our privacy policy.

Este correo electrónico y los archivos adjuntos, enviados por Pen & Tec Consulting SLU, que opera bajo el nombre comercial de Argenta® (Argenta), son confidenciales y pueden estar protegidos por ley. Si usted no es el destinatario, cualquier divulgación, reproducción, copia, distribución u otro tipo de difusión o uso de esta comunicación está estrictamente prohibido. Si ha recibido esta transmisión por error, notifíquelo al remitente y elimine inmediatamente el correo electrónico y cualquier archivo adjunto de su sistema. Argenta no emite ni respalda las opiniones y demás información contenida en este correo electrónico y en sus anexos que no estén relacionadas con las actividades oficiales de Argenta. Aunque Argenta utiliza software antivirus, Argenta no acepta ninguna responsabilidad por cualquier virus en este correo electrónico o cualquier archivo adjunto, o por cualquier efecto que este correo electrónico o cualquier archivo adjunto pueda tener en su red o sistema informático. Argenta registra y almacena los correos electrónicos enviados a nosotros o a nuestros afiliados de acuerdo con nuestras políticas y procedimientos internos. Consulte www.pentec-consulting.eu para obtener información sobre Argenta y/o nuestra política de privacidad.

This email and any attached file(s), sent by Pen & Tec Consulting SLU trading as Argenta® (Argenta), are confidential and may be legally privileged. If you are not the intended recipient, any disclosure, reproduction, copying, distribution, or other dissemination or use of this communication is strictly prohibited. If you have received this transmission in error, please notify the sender and delete the email and any attachments from your system immediately. Opinions and other information in this email and any attachments which do not relate to the official business of Argenta are neither given by nor endorsed by Argenta. While Argenta uses anti-virus software, Argenta accepts no liability for any viruses in this email or any attachment, or for any effects this email or any attachment may have on your network or computer system. Argenta records and stores emails sent to us or our affiliates in keeping with our internal policies and procedures. Please see www.pentec-consulting.eu for information regarding Argenta and/or our privacy policy.

Este correo electrónico y los archivos adjuntos, enviados por Pen & Tec Consulting SLU, que opera bajo el nombre comercial de Argenta® (Argenta), son confidenciales y pueden estar protegidos por ley. Si usted no es el destinatario, cualquier divulgación, reproducción, copia, distribución u otro tipo de difusión o uso de esta comunicación está estrictamente prohibido. Si ha recibido esta transmisión por error, notifíquelo al remitente y elimine inmediatamente el correo electrónico y cualquier archivo adjunto de su sistema. Argenta no emite ni respalda las opiniones y demás información contenida en este correo electrónico y en sus anexos que no estén relacionadas con las actividades oficiales de Argenta. Aunque Argenta utiliza software antivirus, Argenta no acepta ninguna responsabilidad por cualquier virus en este correo electrónico o cualquier archivo adjunto, o por cualquier efecto que este correo electrónico o cualquier archivo adjunto pueda tener en su red o sistema informático. Argenta registra y almacena los correos electrónicos enviados a nosotros o a nuestros afiliados de acuerdo con nuestras políticas y procedimientos internos. Consulte www.pentec-consulting.eu para obtener información sobre Argenta y/o nuestra política de privacidad.

This email and any attached file(s), sent by Pen & Tec Consulting SLU trading as Argenta® (Argenta), are confidential and may be legally privileged. If you are not the intended recipient, any disclosure, reproduction, copying, distribution, or other dissemination or use of this communication is strictly prohibited. If you have received this transmission in error, please notify the sender and delete the email and any attachments from your system immediately. Opinions and other information in this email and any attachments which do not relate to the official business of Argenta are neither given by nor endorsed by Argenta. While Argenta uses anti-virus software, Argenta accepts no liability for any viruses in this email or any attachment, or for any effects this email or any attachment may have on your network or computer system. Argenta records and stores emails sent to us or our affiliates in keeping with our internal policies and procedures. Please see www.pentec-consulting.eu for information regarding Argenta and/or our privacy policy.

From: [Justyna Pałasińska](#)
To: [DiFranco, Stephen](#)
Subject: Re: [EXTERNAL] GRN 1122 canola concentrate status
Date: Monday, July 29, 2024 10:41:23 AM
Attachments: [image001.png](#)
[image007.png](#)
[image008.png](#)
[image009.png](#)
[image010.png](#)
[image011.png](#)
[image012.png](#)
[Outlook-Image.png](#)
[Outlook-Image.png](#)
[Outlook-Image.png](#)
[Outlook-Image.png](#)

CAUTION: This email originated from outside of the organization. Do not click links or open attachments unless you recognize the sender and know the content is safe.

Dear Steve,

I was wondering if you could share an update on the GRN 1122? Can you estimate when can we expect the response letter?

Kind regards,

Justyna Pałasińska

Regulatory Affairs Director – Human Nutrition, Argenta Barcelona



M +34 682 894 653 T +34 936 758 015

www.argentaglobal.com

La información contenida en este mensaje y/o archivo(s) adjunto(s), enviada desde Pen & Tec Consulting SLU cotiza como Argenta, es confidencial/privilegiada y está destinada a ser leída sólo por la(s) persona(s) a la(s) que va dirigida. Le recordamos que sus datos han sido incorporados en el sistema de tratamiento de Pen & Tec Consulting SLU cotiza como Argenta, y que siempre y cuando se cumplan los requisitos exigidos por la normativa, usted podrá ejercer sus derechos de acceso, rectificación, limitación de tratamiento, supresión, portabilidad y oposición/revocación, en los términos que establece la normativa vigente en materia de protección de datos, dirigiendo su petición a la dirección postal OneCoWork, Portal de l'Àngel 40, 08002, Barcelona o bien a través de correo electrónico info@pentec-consulting.eu. Si usted lee este mensaje y no es el destinatario señalado, el empleado o el agente responsable de entregar el mensaje al destinatario, o ha recibido esta comunicación por error, le informamos que está totalmente prohibida, y puede ser ilegal, cualquier divulgación, distribución o reproducción de esta comunicación, y le rogamos que nos lo notifique inmediatamente y nos devuelva el mensaje original a la dirección arriba mencionada. Gracias.

The information contained in this message and/or attached file(s), sent by Pen & Tec Consulting SLU trading as Argenta, is confidential/privileged and is intended to be read solely by the person(s) to whom it is addressed. We hereby inform you that your data will be incorporated into the processing system owned by Pen & Tec Consulting SLU, and that provided it complies with the requirements included in the law, you may exercise the rights of access, rectification, limitation of processing, deletion, portability and opposition by sending your request to the postal address OneCoWork, Portal de l'Àngel 40, 08002, Barcelona or to the email address info@pentec-consulting.eu. If you read this message and you are neither the intended recipient, employee or agent in charge of delivering the message to the recipient, or if you have received this message as the result of an error, we hereby inform you that distributing, sharing or reproducing any part of this message is totally forbidden and may be illegal. As a result, we request that you immediately inform us of the error and return this message to the address mentioned above. Thank you.

From: Justyna Pałasińska <justyna.palasincka@argentaglobal.com>

Sent: 03 July 2024 17:44

To: DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>

Subject: Re: [EXTERNAL] GRN 1122 canola concentrate status

Thank you very much for your clarification, Steve.

Following your advice: we wish to amend the notice by removing the claim that this ingredient is used as a source of dietary fiber and that we wish to add that it may be used "as an ingredient" in the food categories listed within the notice.

Please let me know if anything else is needed from our side.

Kind regards,

Justyna Pałasińska

Regulatory Affairs Director – Human Nutrition, Argenta Barcelona



M +34 682 894 653 T +34 936 758 015

www.argentaglobal.com

La información contenida en este mensaje y/o archivo(s) adjunto(s), enviada desde Pen & Tec Consulting SLU cotiza como Argenta, es confidencial/privilegiada y está destinada a ser leída sólo por la(s) persona(s) a la(s) que va dirigida. Le recordamos que sus datos han sido incorporados en el sistema de tratamiento de Pen & Tec Consulting SLU cotiza como Argenta, y que siempre y cuando se cumplan los requisitos exigidos por la normativa, usted podrá ejercer sus derechos de acceso, rectificación, limitación de tratamiento, supresión, portabilidad y oposición/revocación, en los términos que establece la normativa vigente en materia de protección de datos, dirigiendo su petición a la dirección postal OneCoWork, Portal de l'Àngel 40, 08002, Barcelona o bien a través de correo electrónico info@pentec-consulting.eu. Si usted lee este mensaje y no es el destinatario señalado, el empleado o el agente responsable de entregar el mensaje al destinatario, o ha recibido esta comunicación por error, le informamos que está totalmente prohibida, y puede ser ilegal, cualquier divulgación, distribución o reproducción de esta comunicación, y le rogamos que nos lo notifique inmediatamente y nos devuelva el mensaje original a la dirección arriba mencionada. Gracias.

The information contained in this message and/or attached file(s), sent by Pen & Tec Consulting SLU trading as Argenta, is confidential/privileged and is intended to be read solely by the person(s) to whom it is addressed. We hereby inform you that your data will be incorporated into the processing system owned by Pen & Tec Consulting SLU, and that provided it complies with the requirements included in the law, you may exercise the rights of access, rectification, limitation of processing, deletion, portability and opposition by sending your request to the postal address OneCoWork, Portal de l'Àngel 40, 08002, Barcelona or to the email address info@pentec-consulting.eu. If you read this message and you are neither the intended recipient, employee or agent in charge of delivering the message to the recipient, or if you have received this message as the result of an error, we hereby inform you that distributing, sharing or reproducing any part of this message is totally forbidden and may be illegal. As a result, we request that you immediately inform us of the error and return this message to the address mentioned above. Thank you.

From: DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>
Sent: 02 July 2024 20:49
To: Justyna Pałasińska <justyna.palasincka@argentaglobal.com>
Subject: RE: [EXTERNAL] GRN 1122 canola concentrate status

Hello Justyna,

I appreciate the quick response. Per your questions:

- The issue is only with the claim that the ingredient is a source of fiber. You may still make the other claims and claim it is a source of protein—and just add the technical effect ‘as an ingredient’. This is kind of a general, catch all term. There are different regulations addressing claims of source of protein, and this fits.
- You may keep use in all categories that are currently in the notice. This change does not require a different exposure estimate or any other change such as in use. The issue is really about what nutritional claims you can make about the ingredient, not its safety in these uses.
- You do not have to do any sort of rewrite or resubmit the notice. You can simply email me stating you wish to amend the notice by removing the claim that this ingredient is used as a source of dietary fiber and that you wish to add that it may be used “as an ingredient” in the food categories listed. In other words you are adding “as an ingredient” to the notified technical effects of the substance in food. That will be sufficient and we should be able to get this closed out shortly thereafter.

Happy to discuss if you have any other questions.

Best,

Steve

Stephen DiFranco, PhD

Regulatory Review Scientist/Chemist

Center for Food Safety and Applied Nutrition
Office of Food Additive Safety
Division of Food Ingredients
U.S. Food and Drug Administration
Tel: 240-402-2710
stephen.difranco@fda.hhs.gov



From: Justyna Pałasińska <justyna.palasincka@argentaglobal.com>
Sent: Tuesday, July 2, 2024 10:59 AM
To: DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>
Subject: Re: [EXTERNAL] GRN 1122 canola concentrate status

CAUTION: This email originated from outside of the organization. Do not click links or open attachments unless you recognize the sender and know the content is safe.

Many thanks for your swift reply, Steve.

We will update the GRAS & get the updated version to you shortly. I wanted to check a couple questions with you:

- understand the issue is with 'source of fiber' & not with other claims, e.g. 'source of protein'. Could you confirm?
- one of the intended uses is 'protein-fiber and nutritional powders'. I understand that we can keep this category, as the product is a source of protein & therefore can be used as an ingredient for this category of foods. Could you confirm?
- Is it OK for us to send the updated GRAS document by e-mail or do you require a CD-submission?

I look forward to your reply.

Kind regards,
Justyna Pałasińska
Regulatory Affairs Director – Human Nutrition, Argenta Barcelona



M +34 682 894 653 T +34 936 758 015

www.argentaglobal.com

La información contenida en este mensaje y/o archivo(s) adjunto(s), enviada desde Pen & Tec Consulting SLU cotiza como Argenta, es confidencial/privilegiada y está destinada a ser leída sólo por la(s) persona(s) a la(s) que va dirigida. Le recordamos que sus datos han sido incorporados en el sistema de tratamiento de Pen & Tec Consulting SLU cotiza como Argenta, y que siempre y cuando se cumplan los requisitos exigidos por la normativa, usted podrá ejercer sus derechos de acceso, rectificación, limitación de tratamiento, supresión, portabilidad y oposición/revocación, en los términos que establece la normativa vigente en materia de protección de datos, dirigiendo su petición a la dirección postal OneCoWork, Portal de l'Àngel 40, 08002, Barcelona o bien a través de correo electrónico info@pentec-consulting.eu. Si usted lee este mensaje y no es el destinatario señalado, el empleado o el agente responsable de entregar el mensaje al destinatario, o ha recibido esta comunicación por error, le informamos que está totalmente prohibida, y puede ser ilegal, cualquier divulgación, distribución o reproducción de esta comunicación, y le rogamos que nos lo notifique inmediatamente y nos devuelva el mensaje original a la dirección arriba mencionada. Gracias.

The information contained in this message and/or attached file(s), sent by Pen & Tec Consulting SLU trading as Argenta, is confidential/privileged and is intended to be read solely by the person(s) to whom it is addressed. We hereby inform you that your data will be incorporated into the processing system owned by Pen & Tec Consulting SLU, and that provided it complies with the requirements included in the law, you may exercise the rights of access, rectification, limitation of processing, deletion, portability and opposition by sending your request to the postal address OneCoWork, Portal de l'Àngel 40, 08002, Barcelona or to the email address info@pentec-consulting.eu. If you read this message and you are neither the intended recipient, employee or agent in charge of delivering the message to the recipient, or if you have received this message as the result of an error, we hereby inform you that distributing, sharing or reproducing any part of this message is totally forbidden and may be illegal. As a result, we request that you immediately inform us of the error and return this message to the address mentioned above. Thank you.

From: DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>
Sent: 01 July 2024 21:32
To: Justyna Pałasińska <justyna.palasinaska@argentaglobal.com>
Subject: RE: [EXTERNAL] GRN 1122 canola concentrate status

Hello Justyna,

In finalizing our response letter we ran into a bit of an issue regarding the notice's claim that the ingredient is a source of dietary fiber, as this is a legally defined area in US regulations. I got the following from our review team for your consideration:

NapiFeryn states that canola concentrate is intended to be used as a source of dietary fiber amongst other intended uses (i.e., source of protein, formulation aid, stabilizer, thickener, or texturizer). We note that FDA defines dietary fiber as "non-digestible soluble and insoluble carbohydrates (with 3 or more monomeric units), and lignin that are intrinsic and intact in plants; isolated or synthetic non-digestible carbohydrates (with 3 or more monomeric units) determined by FDA to have physiological effects that are beneficial to human health" (21 CFR 101.9(c)(6)(i)). Additional information related to dietary fiber can be found at <https://www.fda.gov/food/food-labeling-nutrition/questions-and-answers-dietary-fiber>.

During our evaluation of GRN 001122 we were not able to determine whether canola concentrate meets the definition of dietary fiber. To proceed with our evaluation of GRN 001122, we recommend that Napiferyn reconsider the description of the intended uses of canola concentrate by replacing the intended use as "a source of dietary fiber" with the use as "an ingredient".

If NapiFeryn wishes to use canola concentrate as a source of dietary fiber, we recommend that you consult with FDA's Office of Nutrition and Food Labeling (ONFL) on whether the ingredient meets the definition of dietary fiber. After ONFL provides a favorable determination, Napiferyn may choose to inform FDA about their GRAS conclusion for the use of canola concentrate as a source of dietary fiber by submitting a supplement to GRN 001122.

Again, amending the notice to state the use is simply as "an ingredient" will allow us to close out this GRAS notice while still allowing the ingredient to be used in foods. If you then wish to have the use as a source of dietary fiber included in the notice and/or displayed on the [GRAS Notice inventory](#), we can go back and amend as appropriate pending the outcome with ONFL.

Happy to discuss if this is unclear.

Thanks,

Steve

Stephen DiFranco, PhD

Regulatory Review Scientist/Chemist

Center for Food Safety and Applied Nutrition
Office of Food Additive Safety
Division of Food Ingredients
U.S. Food and Drug Administration
Tel: 240-402-2710
stephen.difranco@fda.hhs.gov



From: Justyna Pałasińska <justyna.palasinaska@argentaglobal.com>
Sent: Monday, July 1, 2024 8:16 AM
To: DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>
Subject: Re: [EXTERNAL] GRN 1122 canola concentrate status

CAUTION: This email originated from outside of the organization. Do not click links or open attachments unless you recognize the sender and know the content is safe.

Hi Steve,

I hope you are doing well.

Could you let me know when the letter is expected to receive clearance & be shared with the applicant?

Kind regards,
Justyna Pałasińska
Regulatory Affairs Director – Human Nutrition, Argenta Barcelona



M +34 682 894 653 T +34 936 758 015

www.argentaglobal.com

La información contenida en este mensaje y/o archivo(s) adjunto(s), enviada desde Pen & Tec Consulting SLU cotiza como Argenta, es confidencial/privilegiada y está destinada a ser leída sólo por la(s) persona(s) a la(s) que va dirigida. Le recordamos que sus datos han sido incorporados en el sistema de tratamiento de Pen & Tec Consulting SLU cotiza como Argenta, y que siempre y cuando se cumplan los requisitos exigidos por la normativa, usted podrá ejercer sus derechos de acceso, rectificación, limitación de tratamiento, supresión, portabilidad y oposición/revocación, en los términos que establece la normativa vigente en materia de protección de datos, dirigiendo su petición a la dirección postal OneCoWork, Portal de l'Àngel 40, 08002, Barcelona o bien a través de correo electrónico info@pentec-consulting.eu. Si usted lee este mensaje y no es el destinatario señalado, el empleado o el agente responsable de entregar el mensaje al destinatario, o ha recibido esta comunicación por error, le informamos que está totalmente prohibida, y puede ser ilegal, cualquier divulgación, distribución o reproducción de esta comunicación, y le rogamos que nos lo notifique inmediatamente y nos devuelva el mensaje original a la dirección arriba mencionada. Gracias.
The information contained in this message and/or attached file(s), sent by Pen & Tec Consulting SLU trading as Argenta, is confidential/privileged and is intended to be read solely by the person(s) to whom it is addressed. We hereby inform you that your data will be incorporated into the processing system owned by Pen & Tec Consulting SLU, and that provided it complies with the requirements included in the law, you may exercise the rights of access, rectification, limitation of processing, deletion, portability and opposition by sending your request to the postal address OneCoWork, Portal de l'Àngel 40, 08002, Barcelona or to the email address info@pentec-consulting.eu. If you read this message and you are neither the intended recipient, employee or agent in charge of delivering the message to the recipient, or if you have received this message as the result of an error, we hereby inform you that distributing, sharing or reproducing any part of this message is totally forbidden and may be illegal. As a result, we request that you immediately inform us of the error and return this message to the address mentioned above. Thank you.

From: Justyna Pałasińska <justyna.palasincka@argentaglobal.com>
Sent: 30 May 2024 16:09
To: DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>
Subject: Re: [EXTERNAL] GRN 1122 canola concentrate status

Indeed, great news, thank you Steve!

Kind regards,
Justyna Pałasińska
Regulatory Affairs Director – Human Nutrition, Argenta Barcelona



M +34 682 894 653 T +34 936 758 015

www.argentaglobal.com

La información contenida en este mensaje y/o archivo(s) adjunto(s), enviada desde Pen & Tec Consulting SLU cotiza como Argenta, es confidencial/privilegiada y está destinada a ser leída sólo por la(s) persona(s) a la(s) que va dirigida. Le recordamos que sus datos han sido incorporados en el sistema de tratamiento de Pen & Tec Consulting SLU cotiza como Argenta, y que siempre y cuando se cumplan los requisitos exigidos por la normativa, usted podrá ejercer sus derechos de acceso, rectificación, limitación de tratamiento, supresión, portabilidad y oposición/revocación, en los términos que establece la normativa vigente en materia de protección de datos, dirigiendo su petición a la dirección postal OneCoWork, Portal de l'Àngel 40, 08002, Barcelona o bien a través de correo electrónico info@pentec-consulting.eu. Si usted lee este mensaje y no es el destinatario señalado, el empleado o el agente responsable de entregar el mensaje al destinatario, o ha recibido esta comunicación por error, le informamos que está totalmente prohibida, y puede ser ilegal, cualquier divulgación, distribución o reproducción de esta comunicación, y le rogamos que nos lo notifique inmediatamente y nos devuelva el mensaje original a la dirección arriba mencionada. Gracias.
The information contained in this message and/or attached file(s), sent by Pen & Tec Consulting SLU trading as Argenta, is confidential/privileged and is intended to be read solely by the person(s) to whom it is addressed. We hereby inform you that your data will be incorporated into the processing system owned by Pen & Tec Consulting SLU, and that provided it complies with the requirements included in the law, you may exercise the rights of access, rectification, limitation of processing, deletion, portability and opposition by sending your request to the postal address OneCoWork, Portal de l'Àngel 40, 08002, Barcelona or to the email address info@pentec-consulting.eu. If you read this message and you are neither the intended recipient, employee or agent in charge of delivering the message to the recipient, or if you have received this message as the result of an error, we hereby inform you that distributing, sharing or reproducing any part of this message is totally forbidden and may be illegal. As a result, we request that you immediately inform us of the error and return this message to the address mentioned above. Thank you.

From: DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>
Sent: 30 May 2024 16:06
To: Justyna Pałasińska <justyna.palasincka@argentaglobal.com>
Subject: RE: [EXTERNAL] GRN 1122 canola concentrate status

Hi Justyna,

I finally have some good news for you—FSIS has just finished their review. I have drafted a response letter and it is currently making its way through clearance, so you should hear back soon.

Best,

Steve

Stephen DiFranco, PhD

Regulatory Review Scientist/Chemist

Center for Food Safety and Applied Nutrition
Office of Food Additive Safety
Division of Food Ingredients
U.S. Food and Drug Administration
Tel: 240-402-2710
stephen.difranco@fda.hhs.gov



From: Justyna Pałasińska <justyna.palasincka@argentaglobal.com>
Sent: Thursday, May 30, 2024 9:48 AM
To: DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>
Subject: Re: [EXTERNAL] GRN 1122 canola concentrate status

CAUTION: This email originated from outside of the organization. Do not click links or open attachments unless you recognize the sender and know the content is safe.

Dear Stephen,

I hope this e-mail finds you well. I was wondering if there is any update from FSIS on this GRN?

Kind regards,

Justyna Pałasińska

Regulatory Affairs Director – Human Nutrition, Argenta Barcelona



M +34 682 894 653 T +34 936 758 015

www.argentaglobal.com

La información contenida en este mensaje y/o archivo(s) adjunto(s), enviada desde Pen & Tec Consulting SLU cotiza como Argenta, es confidencial/privilegiada y está destinada a ser leída sólo por la(s) persona(s) a la(s) que va dirigida. Le recordamos que sus datos han sido incorporados en el sistema de tratamiento de Pen & Tec Consulting SLU cotiza como Argenta, y que siempre y cuando se cumplan los requisitos exigidos por la normativa, usted podrá ejercer sus derechos de acceso, rectificación, limitación de tratamiento, supresión, portabilidad y oposición/revocación, en los términos que establece la normativa vigente en materia de protección de datos, dirigiendo su petición a la dirección postal OneCoWork, Portal de l'Àngel 40, 08002, Barcelona o bien a través de correo electrónico info@pentec-consulting.eu. Si usted lee este mensaje y no es el destinatario señalado, el empleado o el agente responsable de entregar el mensaje al destinatario, o ha recibido esta comunicación por error, le informamos que está totalmente prohibida, y puede ser ilegal, cualquier divulgación, distribución o reproducción de esta comunicación, y le rogamos que nos lo notifique inmediatamente y nos devuelva el mensaje original a la dirección arriba mencionada. Gracias.

The information contained in this message and/or attached file(s), sent by Pen & Tec Consulting SLU trading as Argenta, is confidential/privileged and is intended to be read solely by the person(s) to whom it is addressed. We hereby inform you that your data will be incorporated into the processing system owned by Pen & Tec Consulting SLU, and that provided it complies with the requirements included in the law, you may exercise the rights of access, rectification, limitation of processing, deletion, portability and opposition by sending your request to the postal address OneCoWork, Portal de l'Àngel 40, 08002, Barcelona or to the email address info@pentec-consulting.eu. If you read this message and you are neither the intended recipient, employee or agent in charge of delivering the message to the recipient, or if you have received this message as the result of an error, we hereby inform you that distributing, sharing or reproducing any part of this message is totally forbidden and may be illegal. As a result, we request that you immediately inform us of the error and return this message to the address mentioned above. Thank you.

From: DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>
Sent: 04 April 2024 17:26
To: Justyna Pałasińska <justyna.palasincka@argentaglobal.com>
Subject: RE: [EXTERNAL] GRN 1122 canola concentrate status

Thanks Justyna,

I've passed the information to FSIS for review. Hopefully we will hear back shortly.

Best,

Steve

Stephen DiFranco, PhD

Regulatory Review Scientist/Chemist

Center for Food Safety and Applied Nutrition
Office of Food Additive Safety
Division of Food Ingredients
U.S. Food and Drug Administration
Tel: 240-402-2710
stephen.difranco@fda.hhs.gov



From: Justyna Pałasińska <justyna.palasinaska@argentaglobal.com>
Sent: Thursday, April 4, 2024 7:38 AM
To: DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>
Subject: Re: [EXTERNAL] GRN 1122 canola concentrate status

CAUTION: This email originated from outside of the organization. Do not click links or open attachments unless you recognize the sender and know the content is safe.

Dear Stephen,

Please find our reply below:

It is the applicant's understanding that OSHA OELs for heavy metals indicated by FSIS relate to the risk of exposure to heavy metals in the material under assessment via inhalation route only. The material indeed may create dust hazard if handled improperly. We note that the safety data sheet provided for the material (attached for reference) not only informs about the potential to form dust if handled improperly but also includes information on precautionary measures and personal protection and engineering controls aimed at eliminating or greatly reducing the risk of exposure to airborne particles. Proper handling of the material / adherence to these measures and controls by extension would eliminate or greatly reduce the risk of exposure to heavy metals that may be present in the material.

In case the above does not sufficiently address the potential risk of exposure to heavy metals present in the material via inhalation route, the applicant would like to inform that the bulk density of the material ranges between 0.1 and 0.3 g/cm³. A confirmation whether this information is sufficient to proceed with the calculations would be much appreciated. It would also be helpful to understand the assumptions being made by FSIS (e.g. concentration of airborne particles) when assessing whether the levels of heavy metals in the product may exceed OSHA OELs.

Kind regards,
Justyna Pałasińska
Regulatory Affairs Director – Human Nutrition, Argenta Barcelona



M +34 682 894 653 T +34 936 758 015

www.argentaglobal.com

La información contenida en este mensaje y/o archivo(s) adjunto(s), enviada desde Pen & Tec Consulting SLU cotiza como Argenta, es confidencial/privilegiada y está destinada a ser leída sólo por la(s) persona(s) a la(s) que va dirigida. Le recordamos que sus datos han sido incorporados en el sistema de tratamiento de Pen & Tec Consulting SLU cotiza como Argenta, y que siempre y cuando se cumplan los requisitos exigidos por la normativa, usted podrá ejercer sus derechos de acceso, rectificación, limitación de tratamiento, supresión, portabilidad y oposición/revocación, en los términos que establece la normativa vigente en materia de protección de datos, dirigiendo su petición a la dirección postal OneCoWork, Portal de l'Àngel 40, 08002, Barcelona o bien a través de correo electrónico info@pentec-consulting.eu. Si usted lee este mensaje y no es el destinatario señalado, el empleado o el agente responsable de entregar el mensaje al destinatario, o ha recibido esta comunicación por error, le informamos que está totalmente prohibida, y puede ser ilegal, cualquier divulgación, distribución o reproducción de esta comunicación, y le rogamos que nos lo notifique inmediatamente y nos devuelva el mensaje original a la dirección arriba mencionada. Gracias.

The information contained in this message and/or attached file(s), sent by Pen & Tec Consulting SLU trading as Argenta, is confidential/privileged and is intended to be read solely by the person(s) to whom it is addressed. We hereby inform you that your data will be incorporated into the processing system owned by Pen & Tec Consulting SLU, and that provided it complies with the requirements included in the law, you may exercise the rights of access, rectification, limitation of processing, deletion, portability and opposition by sending your request to the postal address OneCoWork, Portal de l'Àngel 40, 08002, Barcelona or to the email address info@pentec-consulting.eu. If you read this message and you are neither the intended recipient, employee or agent in charge of delivering the message to the recipient, or if you have received this message as the result of an error, we hereby inform you that distributing, sharing or reproducing any part of this message is totally forbidden and may be illegal. As a result, we request that you immediately inform us of the error and return this message to the address mentioned above. Thank you.

From: DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>
Date: Thursday, 28 March 2024 at 20:47
To: Justyna Pałasińska <justyna.palasinaska@argentaglobal.com>
Subject: RE: [EXTERNAL] GRN 1122 canola concentrate status

Hello Justyna,

I got feedback from FSIS about their review of GRN 1122. They send the following:

I have now completed the review of the documentation submitted for the approval of the above-referenced compound. I noted that it contains Lead (≤ 0.5 mg/kg), Arsenic (≤ 0.2 mg/kg), Cadmium (≤ 0.2 mg/kg), and Mercury (≤ 0.1 mg/kg). OSHA has established OEL for these substances at 0.05 mg/m³, 0.01 mg/m³, 0.01 mg/m³, 0.025 mg/m³ (depending on presentation) respectively.

To finalize my analysis, I require the composition in mg/m³ of each of these elements or the density so I may calculate their composition accurately and evaluate them against their OSHA standards.

Are you able to provide the density of the canola concentrate? I believe this is the easiest way to answer their questions. From the density and the specified ppm levels, the reviewer should be able to calculate the maximum amount by weight of each heavy metal contaminate for a given volume of canola concentrate.

Best,

Steve

Stephen DiFranco, PhD

Regulatory Review Scientist/Chemist

Center for Food Safety and Applied Nutrition
Office of Food Additive Safety
Division of Food Ingredients
U.S. Food and Drug Administration
Tel: 240-402-2710
stephen.difranco@fda.hhs.gov



From: Justyna Pałasińska <justyna.palasinaska@argentaglobal.com>

Sent: Monday, March 4, 2024 5:04 AM

To: DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>

Subject: Re: [EXTERNAL] GRN 1122 canola concentrate status

CAUTION: This email originated from outside of the organization. Do not click links or open attachments unless you recognize the sender and know the content is safe.

Many thanks for the update, Stephen. We look forward to hearing an update, hopefully soon!

Kind regards,

Justyna Pałasińska

Regulatory Affairs Director – Human Nutrition, Argenta Barcelona



M +34 682 894 653 T +34 936 758 015

www.argentaglobal.com

La información contenida en este mensaje y/o archivo(s) adjunto(s), enviada desde Pen & Tec Consulting SLU cotiza como Argenta, es confidencial/privilegiada y está destinada a ser leída sólo por la(s) persona(s) a la(s) que va dirigida. Le recordamos que sus datos han sido incorporados en el sistema de tratamiento de Pen & Tec Consulting SLU cotiza como Argenta, y que siempre y cuando se cumplan los requisitos exigidos por la normativa, usted podrá ejercer sus derechos de acceso, rectificación, limitación de tratamiento, supresión, portabilidad y oposición/revocación, en los términos que establece la normativa vigente en materia de protección de datos, dirigiendo su petición a la dirección postal Pl. Ausias March 1, 4 planta 08195, Sant Cugat del Vallès (Barcelona) o bien a través de correo electrónico info@pentec-consulting.eu. Si usted lee este mensaje y no es el destinatario señalado, el empleado o el agente responsable de entregar el mensaje al destinatario, o ha recibido esta comunicación por error, le informamos que está totalmente prohibida, y puede ser ilegal, cualquier divulgación, distribución o reproducción de esta comunicación, y le rogamos que nos lo notifique inmediatamente y nos devuelva el mensaje original a la dirección arriba mencionada. Gracias.

The information contained in this message and/or attached file(s), sent by Pen & Tec Consulting SLU trading as Argenta, is confidential/privileged and is intended to be read solely by the person(s) to whom it is addressed. We hereby inform you that your data will be incorporated into the processing system owned by Pen & Tec Consulting SLU, and that provided it complies with the requirements included in the law, you may exercise the rights of access, rectification, limitation of processing, deletion, portability and opposition by sending your request to the postal address Pl. Ausias March 1, 4 floor 08195, Sant Cugat del Valles (Barcelona) or to the email address info@pentec-consulting.eu. If you read this message and you are neither the intended recipient, employee or agent in charge of delivering the message to the recipient, or if you have received this message as the result of an error, we hereby inform you that distributing, sharing or reproducing any part of this message is totally forbidden and may be illegal. As a result, we request that you immediately inform us of the error and return this message to the address mentioned above. Thank you.

From: DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>

Date: Monday, 26 February 2024 at 17:20

To: Justyna Pałasińska <justyna.palasinaska@argentaglobal.com>

Subject: RE: [EXTERNAL] GRN 1122 canola concentrate status

You don't often get email from stephen.difranco@fda.hhs.gov. [Learn why this is important](#)

Hello Justyna,

Regarding GRN 1122; FDA has completed its review and has drafted a response letter. Unfortunately, we cannot move forward before USDA-FSIS completes their review of the uses under their jurisdiction. I have been periodically inquiring with FSIS as to the status and will get this to you as soon as possible.

We appreciate your continued patience.

Best,

Steve

Stephen DiFranco, PhD

Regulatory Review Scientist/Chemist

Center for Food Safety and Applied Nutrition
Office of Food Additive Safety
Division of Food Ingredients
U.S. Food and Drug Administration
Tel: 240-402-2710
stephen.difranco@fda.hhs.gov



From: Justyna Pałasińska <justyna.palasinaska@argentaglobal.com>
Sent: Wednesday, February 14, 2024 12:07 PM
To: Premarkt <Premarkt@fda.hhs.gov>
Cc: DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>; Ioannis Kartanos <ioannis.kartanos@argentaglobal.com>
Subject: [EXTERNAL] GRN 1122 canola concentrate status

CAUTION: This email originated from outside of the organization. Do not click links or open attachments unless you recognize the sender and know the content is safe.

Dear HHS team,

I am writing to enquire about a GRAS notice that was submitted to the FDA & filed April 19, 2023 (GRN 1122). We have been in touch with Mr Stephen DiFranco & at the beginning of December he has informed us that the FDA reviews are complete & the notice is now with USDA-FSIS.

Mr DiFranco has been very helpful through the whole process. However, we have tried to contact him several times since December without success. We were wondering if there is someone else we can get in touch with for an update on this application. We would be happy to provide any information that would help finalize the process.

I look forward to hearing from you.

Kind regards,

Justyna Pałasińska

Regulatory Affairs Director – Human Nutrition, Argenta Barcelona

M +34 682 894 653 T +34 936 758 015



La información contenida en este mensaje y/o archivo(s) adjunto(s), enviada desde Pen & Tee Consulting SLU cotiza como Argenta, es confidencial/privilegiada y está destinada a ser leída sólo por la(s) persona(s) a la(s) que va dirigida. Le recordamos que sus datos han sido incorporados en el sistema de tratamiento de Pen & Tee Consulting SLU cotiza como Argenta, y que siempre y cuando se cumplan los requisitos exigidos por la normativa, usted podrá ejercer sus derechos de acceso, rectificación, limitación de tratamiento, supresión, portabilidad y oposición/revocación, en los términos que establece la normativa vigente en materia de protección de datos, dirigiendo su petición a la dirección postal Pl. Ausias March 1, 4 planta 08195, Sant Cugat del Vallés (Barcelona) o bien a través de correo electrónico info@pentec-consulting.eu. Si usted lee este mensaje y no es el destinatario señalado, el empleado o el agente responsable de entregar el mensaje al destinatario, o ha recibido esta comunicación por error, le informamos que está totalmente prohibida, y puede ser ilegal, cualquier divulgación, distribución o reproducción de esta comunicación, y le rogamos que nos lo notifique inmediatamente y nos devuelva el mensaje original a la dirección arriba mencionada. Gracias.

The information contained in this message and/or attached file(s), sent by Pen & Tee Consulting SLU trading as Argenta, is confidential/privileged and is intended to be read solely by the person(s) to whom it is addressed. We hereby inform you that your data will be incorporated into the processing system owned by Pen & Tee Consulting SLU, and that provided it complies with the requirements included in the law, you may exercise the rights of access, rectification, limitation of processing, deletion, portability and opposition by sending your request to the postal address Pl. Ausias March 1, 4 floor 08195, Sant Cugat del Vallés (Barcelona) or to the email address info@pentec-consulting.eu. If you read this message and you are neither the intended recipient, employee or agent in charge of delivering the message to the recipient, or if you have received this message as the result of an error, we hereby inform you that distributing, sharing or reproducing any part of this message is totally forbidden and may be illegal. As a result, we request that you immediately inform us of the error and return this message to the address mentioned above. Thank you.

From: Justyna Pałasińska <justyna.palasinaska@argentaglobal.com>
Date: Wednesday, 31 January 2024 at 17:53
To: Justyna Pałasińska <justyna.palasinaska@argentaglobal.com>, DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>
Cc: Ioannis Kartanos <ioannis.kartanos@argentaglobal.com>
Subject: Re: [EXTERNAL] GRN 1122 canola concentrate - update contact person

Dear Steve,

I hope this e-mail finds you well. I was wondering if there are any updates on the finalization of this notification?

Is there any additional information that needs to be provided?

Kind regards,
Justyna Pałasińska
Regulatory Affairs Director – Human Nutrition, Argenta Barcelona



M +34 682 894 653 T +34 936 758 015

www.argentaglobal.com

La información contenida en este mensaje y/o archivo(s) adjunto(s), enviada desde Pen & Tec Consulting SLU cotiza como Argenta, es confidencial/privilegiada y está destinada a ser leída sólo por la(s) persona(s) a la(s) que va dirigida. Le recordamos que sus datos han sido incorporados en el sistema de tratamiento de Pen & Tec Consulting SLU cotiza como Argenta, y que siempre y cuando se cumplan los requisitos exigidos por la normativa, usted podrá ejercer sus derechos de acceso, rectificación, limitación de tratamiento, supresión, portabilidad y oposición/revocación, en los términos que establece la normativa vigente en materia de protección de datos, dirigiendo su petición a la dirección postal Pl. Ausias March 1, 4 planta 08195, Sant Cugat del Vallès (Barcelona) o bien a través de correo electrónico info@pentec-consulting.eu. Si usted lee este mensaje y no es el destinatario señalado, el empleado o el agente responsable de entregar el mensaje al destinatario, o ha recibido esta comunicación por error, le informamos que está totalmente prohibida, y puede ser ilegal, cualquier divulgación, distribución o reproducción de esta comunicación, y le rogamos que nos lo notifique inmediatamente y nos devuelva el mensaje original a la dirección arriba mencionada. Gracias.

The information contained in this message and/or attached file(s), sent by Pen & Tec Consulting SLU trading as Argenta, is confidential/privileged and is intended to be read solely by the person(s) to whom it is addressed. We hereby inform you that your data will be incorporated into the processing system owned by Pen & Tec Consulting SLU, and that provided it complies with the requirements included in the law, you may exercise the rights of access, rectification, limitation of processing, deletion, portability and opposition by sending your request to the postal address Pl. Ausias March 1, 4 floor 08195, Sant Cugat del Valles (Barcelona) or to the email address info@pentec-consulting.eu. If you read this message and you are neither the intended recipient, employee or agent in charge of delivering the message to the recipient, or if you have received this message as the result of an error, we hereby inform you that distributing, sharing or reproducing any part of this message is totally forbidden and may be illegal. As a result, we request that you immediately inform us of the error and return this message to the address mentioned above. Thank you.

From: Justyna Pałasińska <justyna@pentec-consulting.eu>
Date: Friday, 22 December 2023 at 13:31
To: DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>
Cc: Ioannis Kartanos <ioannis@pentec-consulting.eu>
Subject: Re: [EXTERNAL] GRN 1122 canola concentrate - update contact person

Dear Stephen,

Many thanks for confirming the change of contact person.

I'm following up on my colleague Ioannis e-mail from 12/12/2023. As he mentioned, we have already provided the answers to the questions to USDA-FSIS. Nevertheless, I have included them in a separate document.

Please let us know in case any additional information is required.

In the meantime, we wish you a Happy Holiday Season & all the best in 2024!

Kind regards,

Ing. Justyna Pałasińska

Regulatory Affairs Director – Human Nutrition | Pen & Tec Consulting
T +34 936 758 015 M +34 682 894 653 F +34 936 758 016 www.pentec-consulting.eu
Pl. Ausias March 1 | 4th floor D01 | 08195 Sant Cugat del Vallès | Barcelona | Spain

PEN + TEC
CONSULTING
PART OF THE ARGENTA GROUP

La información contenida en este mensaje y/o archivo(s) adjunto(s), enviada desde Pen & Tec Consulting SLU, es confidencial/privilegiada y está destinada a ser leída sólo por la(s) persona(s) a la(s) que va dirigida. Le recordamos que sus datos han sido incorporados en el sistema de tratamiento de Pen & Tec Consulting SLU y que siempre y cuando se cumplan los requisitos exigidos por la normativa, usted podrá ejercer sus derechos de acceso, rectificación, limitación de tratamiento, supresión, portabilidad y oposición/revocación, en los términos que establece la normativa vigente en materia de protección de datos, dirigiendo su petición a la dirección postal Pl. Ausias March 1, 4 planta 08195, Sant Cugat del Vallès (Barcelona) o bien a través de correo electrónico info@pentec-consulting.eu. Si usted lee este mensaje y no es el destinatario señalado, el empleado o el agente responsable de entregar el mensaje al destinatario, o ha recibido esta comunicación por error, le informamos que está totalmente prohibida, y puede ser ilegal, cualquier divulgación, distribución o reproducción de esta comunicación, y le rogamos que nos lo notifique inmediatamente y nos devuelva el mensaje original a la dirección arriba mencionada. Gracias.

The information contained in this message and/or attached file(s), sent by Pen & Tec Consulting SLU, is confidential/privileged and is intended to be read solely by the person(s) to whom it is addressed. We hereby inform you that your data will be incorporated into the processing system owned by Pen & Tec Consulting SLU, and that provided it complies with the requirements included in the law, you may exercise the rights of access, rectification, limitation of processing, deletion, portability and opposition by sending your request to the postal address Pl. Ausias March 1, 4 floor 08195, Sant Cugat del Valles (Barcelona) or to the email address info@pentec-consulting.eu. If you read this message and you are neither the intended recipient, employee or agent in charge of delivering the message to the recipient, or if you have received this message as the result of an error, we hereby inform you that distributing, sharing or reproducing any part of this message is totally forbidden and may be illegal. As a result, we request that you immediately inform us of the error and return this message to the address mentioned above. Thank you.

From: DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>
Date: Tuesday, 5 December 2023 at 19:05
To: Nikolaas Tilkin-Franssens <niko@pentec-consulting.eu>
Cc: Justyna Pałasińska <justyna@pentec-consulting.eu>
Subject: RE: [EXTERNAL] GRN 1122 canola concentrate - update contact person

Hello Niko and Justyna,

Just confirming the change of contact person for GRN 1122.

As for timeline, FDA reviews are complete but USDA-FSIS is requesting a few pieces of information regarding the uses of canola concentrate under USDA jurisdiction, namely:

Please provide SDS for the at use concentrations of the substance and include a description of how the use of this technology will not adversely affect the safety of FSIS inspectors. Workplace safety and health hazards include inhalation, direct skin contact (skin, eyes, mouth), and fire/explosion caused by exposure to the product, its working solution or dry mixture and potential by-products formed and/or off-gassed during the application process. The employee safety information should demonstrate how the New Technology will not "jeopardize the safety of Federal inspection personnel" as specified in the [FSIS Compliance Guideline Procedures for New Technology Notifications and Protocols, April 2015](#).

Although I'm not anticipating any issues here, FSIS workplace and employee safety must be specifically addressed. Please refer to Appendix A on page 17, Workplace Safety and Health Criteria, for clarification on what to provide in the response. For additional clarity with respect to employee safety, the following are examples of information that are typically needed by FSIS' employee safety and health group;

1. Potential workplace exposures that could result from inhalation and direct contact during use of the substance/technology. This information is required in addition to a Safety Data Sheet (SDS) to determine accurate hazard potential and recommended exposure control measures for IPP work areas in accordance with Occupational Safety and Health Administration (OSHA) regulations: 29 CFR 1910.1200, Hazard Communication, 29 CFR 1910.132, Personal Protective Equipment, and 29 CFR 1910.1000, Air Contaminants. The information should be included as a specific section in each of the protocols.
2. If the SDS workplace hazards/precautions do not apply to the type of exposure that would be expected for the FSIS IPP, please have the submitter provide specific information (per the April 2015 FSIS Compliance Guideline Procedures) for the actual type of exposures expected.
3. If no IPP workplace exposures are expected and no control measures are required, please have the submitter state this and provide the reasons why (e.g., such as the substance "as used" [for all concentrations] is not hazardous by inhalation or direct contact and/or IPP would not be exposed to the substance based on the system design, operation and/or control measures that will be in place).
4. Please also indicate how will FSIS IPP be informed of the above information so that it is clear that the information contained in the SDS for the concentrate does not apply to their actual workplace exposure.
5. Are there any potential hazards from chemical mixing or low pH as a result of discharges of the various solutions to floor drains? Are dedicated drain lines or any other enclosures required?
6. With respect to potential airborne exposures to FSIS IPP in the use/application areas, does the submitter have air sampling results taken during the use of the various concentrations of the technology in the listed mixture?

Suitability data;

The intended use of this product in FSIS meat and poultry products is apparently as a binder/extender. The suitability support provided in Appendix 6 does sufficiently support no significant difference in yield and other organoleptic qualities when used as a partial replacement for another binder in a processed meat and poultry product, such as sausage.

However, **additional suitability support is needed:**

- No suitability data was provided for **whole muscle meat and poultry products at the maximum proposed use level**. We would need to see similar data as provided in Appendix 6 for:
 - Whole muscle red meat control containing no other binders, extenders, or moisture retention agents, as compared to a whole muscle red meat product containing 15% isolated canola product.
 - Whole muscle poultry control containing no other binders, extenders, or moisture retention agents as compared to a whole muscle poultry product containing 15% isolated canola product.

Your responses can be emailed directly to me and I will distribute to the necessary staff inside FDA and USDA.

Thanks,

Steve

Stephen DiFranco, PhD

Regulatory Review Scientist/Chemist

Center for Food Safety and Applied Nutrition

Office of Food Additive Safety

Division of Food Ingredients

U.S. Food and Drug Administration

Tel: 240-402-2710

stephen.difranco@fda.hhs.gov



From: Nikolaas Tilkin-Franssens <niko@pentec-consulting.eu>

Sent: Monday, December 4, 2023 4:36 AM

To: DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>

Cc: Justyna Pałasińska <justyna@pentec-consulting.eu>

Subject: [EXTERNAL] GRN 1122 canola concentrate - update contact person

CAUTION: This email originated from outside of the organization. Do not click links or open attachments unless you recognize the sender and know the content is safe.

Hi Mr. DiFranco,

Hope this email finds you well.

Due to a change in position, I will no longer be the contact person for the GRAS Notice 1122 (Canola Protein Concentrate). Could you please update your records to ascertain that Justyna Pałasińska, in copy to this email, is informed of any relevant updates?

Could you kindly confirm receipt of this email for our records?

And if possible, let us know if there is any estimate on the timeline re. finalization of the review of this GRAS Notice.

Many thanks for your great and flexible support on this application.

Kind regards,

Niko

Nikolaas Tilkin-Franssens

Regulatory Affairs Manager | Pen & Tec Consulting

T +34 936 758 015 M +34 649 840 417 F +34 936 758 016 www.pentec-consulting.eu

Pl. Ausias March 1 | 4th floor D01 | 08195 Sant Cugat del Vallès | Barcelona | Spain

PEN + TEC
CONSULTING

PART OF THE ARGENTA GROUP

La información contenida en este mensaje y/o archivo(s) adjunto(s), enviada desde Pen & Tec Consulting SLU, es confidencial/privilegiada y está destinada a ser leída sólo por la(s) persona(s) a la(s) que va dirigida. Le recordamos que sus datos han sido incorporados en el sistema de tratamiento de Pen & Tec Consulting SLU y que siempre y cuando se cumplan los requisitos exigidos por la normativa, usted podrá ejercer sus derechos de acceso, rectificación, limitación de tratamiento, supresión, portabilidad y oposición/revocación, en los términos que establece la normativa vigente en materia de protección de datos, dirigiendo su petición a la dirección postal Pl. Ausias March 1, 4 planta 08195, Sant Cugat del Vallès (Barcelona) o bien a través de correo electrónico info@pentec-consulting.eu. Si usted lee este mensaje y no es el destinatario señalado, el empleado o el agente responsable de entregar el mensaje al destinatario, o ha recibido esta comunicación por error, le informamos que está totalmente prohibida, y puede ser ilegal, cualquier divulgación, distribución o reproducción de esta comunicación, y le rogamos que nos lo notifique inmediatamente y nos devuelva el mensaje original a la dirección arriba mencionada. Gracias.

The information contained in this message and/or attached file(s), sent by Pen & Tec Consulting SLU, is confidential/privileged and is intended to be read solely by the person(s) to whom it is addressed. We hereby inform you that your data will be incorporated into the processing system owned by Pen & Tec Consulting SLU, and that provided it complies with the requirements included in the law, you may exercise the rights of access, rectification, limitation of processing, deletion, portability and opposition by sending your request to the postal address Pl. Ausias March 1, 4 floor 08195, Sant Cugat del Valles (Barcelona) or to the email address info@pentec-consulting.eu. If you read this message and you are neither the intended recipient, employee or agent in charge of delivering the message to the recipient, or if you have received this message as the result of an error, we hereby inform you that distributing, sharing or reproducing any part of this message is totally forbidden and may be illegal. As a result, we request that you immediately inform us of the error and return this message to the address mentioned above. Thank you.

From: DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>

Date: Monday, 17 July 2023 at 17:01

To: Nikolaas Tilkin-Franssens <niko@pentec-consulting.eu>

Subject: RE: [EXTERNAL] Re: GRN 1122 canola concentrate items for clarification - Reply

Hello Niko,

No problem—I'll distribute this to the team for review.

Best,

Steve

Stephen DiFranco, PhD

Regulatory Review Scientist/Chemist

Center for Food Safety and Applied Nutrition

Office of Food Additive Safety

Division of Food Ingredients

U.S. Food and Drug Administration

Tel: 240-402-2710

stephen.difranco@fda.hhs.gov



From: Nikolaas Tilkin-Franssens <niko@pentec-consulting.eu>
Sent: Monday, July 17, 2023 10:35 AM
To: DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>
Subject: [EXTERNAL] Re: GRN 1122 canola concentrate items for clarification - Reply

CAUTION: This email originated from outside of the organization. Do not click links or open attachments unless you recognize the sender and know the content is safe.

Hi Stephen,

Apologies for this inconvenience.

We noticed that the reply to question 9 refers to Canola protein isolate (as per GRN 1103). I have updated the answer for it to be mentioning Canola protein concentrate (GRN 1122).

We hope this can be taken into consideration.

Kind regards,

Nikolaas Tilkin-Franssens

Regulatory Affairs Manager | Pen & Tec Consulting

T +34 936 758 015 M +34 649 840 417 F +34 936 758 016 www.pentec-consulting.eu

Pl. Ausias March 1 | 4th floor D01 | 08195 Sant Cugat del Vallès | Barcelona | Spain

PEN + TEC
CONSULTING
PART OF THE ARGENTA GROUP

La información contenida en este mensaje y/o archivo(s) adjunto(s), enviada desde Pen & Tec Consulting SLU, es confidencial/privilegiada y está destinada a ser leída sólo por la(s) persona(s) a la(s) que va dirigida. Le recordamos que sus datos han sido incorporados en el sistema de tratamiento de Pen & Tec Consulting SLU y que siempre y cuando se cumplan los requisitos exigidos por la normativa, usted podrá ejercer sus derechos de acceso, rectificación, limitación de tratamiento, supresión, portabilidad y oposición/revocación, en los términos que establece la normativa vigente en materia de protección de datos, dirigiendo su petición a la dirección postal Pl. Ausias March 1, 4 planta 08195, Sant Cugat del Vallès (Barcelona) o bien a través de correo electrónico info@pentec-consulting.eu. Si usted lee este mensaje y no es el destinatario señalado, el empleado o el agente responsable de entregar el mensaje al destinatario, o ha recibido esta comunicación por error, le informamos que está totalmente prohibida, y puede ser ilegal, cualquier divulgación, distribución o reproducción de esta comunicación, y le rogamos que nos lo notifique inmediatamente y nos devuelva el mensaje original a la dirección arriba mencionada. Gracias.

The information contained in this message and/or attached file(s), sent by Pen & Tec Consulting SLU, is confidential/privileged and is intended to be read solely by the person(s) to whom it is addressed. We hereby inform you that your data will be incorporated into the processing system owned by Pen & Tec Consulting SLU, and that provided it complies with the requirements included in the law, you may exercise the rights of access, rectification, limitation of processing, deletion, portability and opposition by sending your request to the postal address Pl. Ausias March 1, 4 floor 08195, Sant Cugat del Valles (Barcelona) or to the email address info@pentec-consulting.eu. If you read this message and you are neither the intended recipient, employee or agent in charge of delivering the message to the recipient, or if you have received this message as the result of an error, we hereby inform you that distributing, sharing or reproducing any part of this message is totally forbidden and may be illegal. As a result, we request that you immediately inform us of the error and return this message to the address mentioned above. Thank you.

From: Nikolaas Tilkin-Franssens <niko@pentec-consulting.eu>
Date: Tuesday, 11 July 2023 at 17:03
To: DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>
Cc: Justyna Pałasińska <justyna@pentec-consulting.eu>
Subject: Re: GRN 1122 canola concentrate items for clarification - Reply

Dear Stephen,

Thank you for reaching out with the questions for clarification. We have worked closely with Napiferyn to close the doubts.

Kindly find attached a Word file including the Questions&Answers, a report on the requested literature review, a SDS sheet as requested by the USDA-FSIS, and a report on the suitability assessment.

We remain available for any further questions or updates.

Thanks for taking the application in further consideration, best regards,

Nikolaas Tilkin-Franssens

Regulatory Affairs Manager | Pen & Tec Consulting

T +34 936 758 015 M +34 649 840 417 F +34 936 758 016 www.pentec-consulting.eu

Pl. Ausias March 1 | 4th floor D01 | 08195 Sant Cugat del Vallès | Barcelona | Spain

PEN + TEC
CONSULTING
PART OF THE ARGENTA GROUP

La información contenida en este mensaje y/o archivo(s) adjunto(s), enviada desde Pen & Tec Consulting SLU, es confidencial/privilegiada y está destinada a ser leída sólo por la(s) persona(s) a la(s) que va dirigida. Le recordamos que sus datos han sido incorporados en el sistema de tratamiento de Pen & Tec Consulting SLU y que siempre y cuando se cumplan los requisitos exigidos

por la normativa, usted podrá ejercer sus derechos de acceso, rectificación, limitación de tratamiento, supresión, portabilidad y oposición/revocación, en los términos que establece la normativa vigente en materia de protección de datos, dirigiendo su petición a la dirección postal Pl. Ausias March 1, 4 planta 08195, Sant Cugat del Vallès (Barcelona) o bien a través de correo electrónico info@pentec-consulting.eu. Si usted lee este mensaje y no es el destinatario señalado, el empleado o el agente responsable de entregar el mensaje al destinatario, o ha recibido esta comunicación por error, le informamos que está totalmente prohibida, y puede ser ilegal, cualquier divulgación, distribución o reproducción de esta comunicación, y le rogamos que nos lo notifique inmediatamente y nos devuelva el mensaje original a la dirección arriba mencionada. Gracias.

The information contained in this message and/or attached file(s), sent by Pen & Tec Consulting SLU, is confidential/privileged and is intended to be read solely by the person(s) to whom it is addressed. We hereby inform you that your data will be incorporated into the processing system owned by Pen & Tec Consulting SLU, and that provided it complies with the requirements included in the law, you may exercise the rights of access, rectification, limitation of processing, deletion, portability and opposition by sending your request to the postal address Pl. Ausias March 1, 4 floor 08195, Sant Cugat del Vallès (Barcelona) or to the email address info@pentec-consulting.eu. If you read this message and you are neither the intended recipient, employee or agent in charge of delivering the message to the recipient, or if you have received this message as the result of an error, we hereby inform you that distributing, sharing or reproducing any part of this message is totally forbidden and may be illegal. As a result, we request that you immediately inform us of the error and return this message to the address mentioned above. Thank you.

From: DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>

Date: Wednesday, 28 June 2023 at 17:41

To: Nicoleta Pasecinic <nicoleta@pentec-consulting.eu>

Cc: Nikolaas Tilkin-Franssens <niko@pentec-consulting.eu>

Subject: [EXTERNAL]: GRN 1122 canola concentrate items for clarification

CAUTION: This email originated from outside of the organization. Do not click links or open attachments unless you recognize the sender and know the content is safe.

Hello Ms. Pasecinic,

After evaluating NapiFeryn's GRAS Notice No. GRN 1122 on canola concentrate we noted a few issues that should be addressed. Please respond to the following points for clarification:

1. On p. 9, NapiFeryn states that the major storage proteins in canola seed are cruciferins and napins, and that canola concentrate consists of 30-45% protein and 40-70% dietary fiber. Please provide the typical cruciferin content and napin content in canola concentrate.
2. Please confirm that all raw materials and processing aids used in the manufacturing process are used in accordance with the U.S. regulations, are GRAS for their respective uses or are the subject of an effective food contact notification. For the record, we note that the food additive regulations cited in Table 4 (p. 15) for ascorbic acid (21 CFR 182.8013), ethanol (21 CFR 184.1293), and ethyl acetate (21 CFR 173.228) do not appear to be applicable to your intended uses of these substances.
3. In Table 6 (p. 18-19), NapiFeryn provides the results from the batch analyses for heavy metals. We would like to bring to your attention a relevant FDA's "[Closer to Zero](#)" initiative that focuses on reducing the levels of heavy metals in foods and recommend that you lower the specification limits for heavy metal to better reflect the batch analyses results and to be as low as possible.
4. In Table 10 (p. 22), NapiFeryn provides batch analyses data for residual solvents and processing aids. In addition, in Table 21 (p. 50), you provided the results from the batch analyses for erucic acid in your canola concentrate ranging from 0.37% to < 0.1%.
Please include limits for residual ethanol, ethyl acetate, and sulphur dioxide as well as a limit for erucic acid in the specifications for canola concentrate and specify the analytical methods used to test for these parameters.
In addition, please provide an updated Tables 5 and 6 (p. 16-19) to include the additional specification parameters mentioned above, corresponding analytical methods, and batch analyses.
5. Please state that all analytical methods used to test batches were validated and are fit for their respective purpose.
6. Please state that canola concentrate is not intended for use in infant formula or in foods where standards of identity preclude its use.
7. In Table 15 (p.), NapiFeryn provides the results of the batch analyses for total plate count in the raw material (rapeseed press cake). Please address the significant variation in the results (from <10 to 28,000 CFU/g) and discuss whether this will impact safety of the final ingredient.
8. On p. 19, NapiFeryn states that the levels of mycotoxins in canola concentrate are below the limit of quantitation (LOQ) and provide the results from the analyses of five batches to support your statement. Please clarify whether you expect mycotoxins to be present in canola concentrate manufactured in accordance with good manufacturing practices.
9. In Part 1.4 (p. 6) and Part 3.1 (p. 33), NapiFeryn states that the intended use of canola concentrate is as a source of protein and/or fiber, thickener, or texturizer. However, we note that on p. 33 you also state the intended use of canola concentrate is as a flavoring agent or binder in various comminuted or whole muscle meat and poultry products. In addition, in Appendix 3 (p. 5) you state that canola concentrate may also be used "to create a flavored salt" or as "a flavor enhancer like monosodium glutamate". Please confirm these additional uses of canola concentrate are within the scope of GRN 001122.
10. On p. 10, the notifier describes the protein composition of canola concentrate, being primarily cruciferins, napin, oleosin, and squalene monooxygenase. However, the pivotal safety data provided appear to only be relevant to the cruciferin and napin fractions of the canola concentrate. Please provide a brief narrative to confirm the safety of oleosin and squalene monooxygenase exposure from the intended uses.
11. On p. 31-32 of the notice, the notifier clearly establishes that canola concentrate is intended to be substitutive to protein and fiber

consumption and will not contribute to additional exposure to protein or fiber in general. Please elaborate on this conclusion, and clarify if the intended uses of canola concentrate are additive or substitutive to other canola protein products currently on the market (i.e., GRNs 327, 386, and 683)?

12. On p. 37, the notifier concludes exposure to canola concentrate from the intended uses is safe since the EDI reported is “still much lower (approximately 7- to 22-fold lower) than the no-observed-adverse-effect level (NOAEL) values established” for cruciferin- and napin-rich protein isolates in male rats following a 13-week oral exposure regimen (Mejia *et al.*, 2009a & 2009b). We note that an uncertainty factor, or margin of safety (MOS), of 100 (10 for interindividual variability × 10 for interspecies variability) is normally used when assessing safety of a food ingredient by comparing estimated human exposure levels to the NOAEL from animal toxicology data. Therefore, it is not clear why MOS that is ~5-10-fold lower can be concluded as safe without proper justification. Additionally, we note that potential thyrotoxic effects were observed at the highest doses in these two rat studies, as well as for rapeseed products in general tested in other species, as cited in Table 20 of the GRAS notice. This effect was mostly attributed to the presence of glucosinolate; however, we note that since the level of glucosinolate was low or absent in both the test articles from Mejia *et al.* and the article of commerce, the rationale used by the study authors to conclude that the observed NOAEL was not in fact the LOAEL may be questionable. Regardless, it appears that the provided safety narrative lacks sufficient basis to conclude MOS of 7-22 is adequate to reach the conclusion of “reasonable certainty of no harm.” Based on generally available data and information, please provide additional narrative to explain your rationale for your GRAS conclusion.
13. We note that when discussing the absorption, distribution, metabolism, and excretion of canola concentrate (p. 49), the notifier reports unpublished data from an EU Novel Foods application for “defatted rapeseed powder” to support their conclusion. Similarly, genotoxicity conclusions are made using unpublished data from an EFSA Panel conclusion on defatted rapeseed powder. Given other data and information have been used in prior GRAS notices for canola ingredients (e.g., GRN 327), please confirm that the EFSA Panel and EU Novel Foods conclusions are only considered as corroborative, not pivotal, to the safety determination of canola concentrate at its intended use level?
14. On p. 40, the notifier discusses the allergenicity potential of canola concentrate being determined via a “bioinformatics approach” and concludes that canola concentrate “may elicit possible allergenic effects.” Additionally, on p. 59 the notifier reiterates that the bioinformatics analysis indicated “possible allergenic effects” of canola concentrate, but no further discussion is provided. While data from an allergen online database search is provided as part of Appendix 4, no discussion of these data are included in the current GRAS notice. Please briefly detail the “possible allergenic effects” of canola concentrate similar to previous notices (e.g., GRN 683), and discuss why they would not be expected to pose a safety concern from the intended use.
15. We note that a recent study on rapeseed protein isolate was published (Xiong *et al.*, 2022).
 - a. Please discuss if this study presents additional safety concerns for the article of commerce or contradicts the current GRAS conclusion.
 - b. Please also perform an updated literature review from 2021 to present and discuss if any additional studies relevant to the safety of canola concentrate were identified that would contradict the current GRAS conclusion.

References cited:

Xiong Z, Fu Y, Yao J, Zhang N, He R, Ju X, Wang Z. Removal of anti-nutritional factors of rapeseed protein isolate (RPI) and toxicity assessment of RPI. *Food Funct.* 2022 Jan 24;13(2):664-674. doi: 10.1039/d1fo03217h. PMID: 34933325.

Additionally, we received the following questions from USDA FSIS regarding their review of the uses of GRN 1122 concerning products within their purview. Please respond to the following and we will pass your responses along to them.

Please provide Safety Data Sheet (SDS) for the at use concentrations of the substance and include a description of how the use of this technology will not adversely affect the safety of FSIS inspectors. Workplace safety and health hazards include inhalation, direct skin contact (skin, eyes, mouth), and fire/explosion caused by exposure to the product, its working solution or dry mixture and potential by-products formed and/or off-gassed during the application process. The employee safety information should demonstrate how the New Technology will not “jeopardize the safety of Federal inspection personnel” as specified in the [FSIS Compliance Guideline Procedures for New Technology Notifications and Protocols, April 2015](#). FSIS workplace and employee safety must be specifically addressed. Please refer to Appendix A on p. 17, Workplace Safety and Health Criteria, for clarification on what to provide in the response. For additional clarity with respect to employee safety, the following are examples of information that are typically needed by FSIS’ employee safety and health group;

1. Potential workplace exposures that could result from inhalation and direct contact during use of the substance/technology. This information is required in addition to a SDS to determine accurate hazard potential and recommended exposure control measures for IPP work areas in accordance with Occupational Safety and Health Administration (OSHA) regulations: 29 CFR 1910.1200, Hazard Communication, 29 CFR 1910.132, Personal Protective Equipment, and 29 CFR 1910.1000, Air Contaminants. The information should be included as a specific section in each of the protocols.
2. If the SDS workplace hazards/precautions do not apply to the type of exposure that would be expected for the FSIS IPP, please have the submitter provide specific information (per the April 2015 FSIS Compliance Guideline Procedures) for the actual type of exposures expected.
3. If no IPP workplace exposures are expected and no control measures are required, please have the submitter state this and provide the reasons why (e.g., such as the substance “as used” [for all concentrations] is not hazardous by inhalation or direct contact and/or IPP would not be exposed to the substance based on the system design, operation and/or control measures that will be in place).

4. Please also indicate how will FSIS IPP be informed of the above information so that it is clear that the information contained in the SDS for the concentrate does not apply to their actual workplace exposure.
5. Are there any potential hazards from chemical mixing or low pH as a result of discharges of the various solutions to floor drains? Are dedicated drain lines or any other enclosures required?
6. With respect to potential airborne exposures to FSIS IPP in the use/application areas, does the submitter have air sampling results taken during the use of the various concentrations of the technology in the listed mixture?
7. The intended use of this product in FSIS meat and poultry products is apparently as a binder/extender. The suitability support provided in Appendix 6 does sufficiently support no significant difference in yield and other organoleptic qualities when used as a partial replacement for another binder in a processed meat and poultry product, such as sausage.

However, **additional suitability support is needed:**

- a. No suitability data was provided for **whole muscle meat and poultry products at the maximum proposed use level**. We would need to see similar data as provided in Appendix 6 for:

Whole muscle red meat control containing no other binders, extenders, or moisture retention agents, as compared to a whole muscle red meat product containing 15% isolated canola product.

Whole muscle poultry control containing no other binders, extenders, or moisture retention agents as compared to a whole muscle poultry product containing 15% isolated canola product.

Responses may be sent in an email or in a separate document. We respectfully request a response within 10 business days. If you are unable to complete the response within that time frame, please contact me to discuss further options.

If you have any additional questions or concerns, please don't hesitate to contact me at stephen.difranco@fda.hhs.gov or by phone at 240.402.2710.

Best,
Steve

Stephen DiFranco, PhD

Regulatory Review Scientist/Chemist

Center for Food Safety and Applied Nutrition

Office of Food Additive Safety

Division of Food Ingredients

U.S. Food and Drug Administration

Tel: 240-402-2710

stephen.difranco@fda.hhs.gov



CAUTION: This email, including any attachments, is confidential. If you are not the intended recipient, please notify the sender and delete the email and any attachments from your system. In addition, you must not use, distribute or reproduce this email or any attachments. Opinions and other information in this email and any attachments which do not relate to the official business of Argenta are neither given by nor endorsed by Argenta. While Argenta uses anti-virus software, Argenta accepts no liability for any viruses in this email or any attachment, or for any effects this email or any attachment may have on your network or computer system.

CAUTION: This email, including any attachments, is confidential. If you are not the intended recipient, please notify the sender and delete the email and any attachments from your system. In addition, you must not use, distribute or reproduce this email or any attachments. Opinions and other information in this email and any attachments which do not relate to the official business of Argenta are neither given by nor endorsed by Argenta. While Argenta uses anti-virus software, Argenta accepts no liability for any viruses in this email or any attachment, or for any effects this email or any attachment may have on your network or computer system.

Este correo electrónico y los archivos adjuntos, enviados por Pen & Tec Consulting SLU, que opera bajo el nombre comercial de Argenta® (Argenta), son confidenciales y pueden estar protegidos por ley. Si usted no es el destinatario, cualquier divulgación, reproducción, copia, distribución u otro tipo de difusión o uso de esta comunicación está estrictamente prohibido. Si ha recibido esta transmisión por error, notifíquelo al remitente y elimine inmediatamente el correo electrónico y cualquier archivo adjunto de su sistema. Argenta no emite ni respalda las opiniones y demás información contenida en este correo electrónico y en sus anexos que no estén relacionadas con las actividades oficiales de Argenta. Aunque Argenta utiliza software antivirus, Argenta no acepta ninguna responsabilidad por cualquier virus en este correo electrónico o cualquier archivo adjunto, o por cualquier efecto que este correo electrónico o cualquier archivo adjunto pueda tener en su red o sistema informático. Argenta registra y almacena los correos electrónicos enviados a nosotros o a nuestros afiliados de acuerdo con nuestras políticas y procedimientos internos. Consulte www.pentec-consulting.eu para obtener información sobre Argenta y/o nuestra política de privacidad.

This email and any attached file(s), sent by Pen & Tec Consulting SLU trading as Argenta® (Argenta), are confidential and may be legally privileged. If you are not the intended recipient, any disclosure, reproduction, copying, distribution, or other dissemination or use of this communication is strictly prohibited. If you have received this transmission in error, please notify the sender and delete the email and any attachments from your system immediately. Opinions and other information in this email and any attachments which do not relate to the official business of Argenta are neither given by nor endorsed by Argenta. While Argenta uses anti-virus software, Argenta accepts no liability for any viruses in this email or any attachment, or for any effects this email or any attachment may have on your network or computer system. Argenta records and stores emails sent to us or our affiliates in keeping with our internal policies and procedures. Please see www.pentec-consulting.eu for information regarding Argenta and/or our privacy policy.

Este correo electrónico y los archivos adjuntos, enviados por Pen & Tec Consulting SLU, que opera bajo el nombre comercial de Argenta® (Argenta), son confidenciales y pueden estar protegidos por ley. Si usted no es el destinatario, cualquier divulgación, reproducción, copia, distribución u otro tipo de difusión o uso de esta comunicación está estrictamente prohibido. Si ha recibido esta

From: [Justyna Pałasińska](#)
To: [DiFranco, Stephen](#)
Subject: Re: [EXTERNAL] GRN 1122 canola concentrate status
Date: Wednesday, July 31, 2024 11:29:17 AM

CAUTION: This email originated from outside of the organization. Do not click links or open attachments unless you recognize the sender and know the content is safe.

Many thanks for the good news, Steve! & for all your patience & assistance.

A small comment - we noticed a minor typo - the text states NepiFeryn (p.4). Would it be possible to correct it in the published version?

We also noticed a small inconsistency in the 'sister notice' for canola isolate (GRN 1103, attached for reference). Pages 2&3 refer to spray drying, while Napiferyn did not refer to this specifically in their notice & would like to keep the exact drying method open. Would it be possible to remove the reference to 'spray' in the published version?

Kind regards,
Justyna Pałasińska
Regulatory Affairs Director – Human Nutrition, Argenta Barcelona



M +34 682 894 653 T +34 936 758 015

www.argentaglobal.com



La información contenida en este mensaje y/o archivo(s) adjunto(s), enviada desde Pen & Tec Consulting SLU cotiza como Argenta, es confidencial/privilegiada y está destinada a ser leída sólo por la(s) persona(s) a la(s) que va dirigida. Le recordamos que sus datos han sido incorporados en el sistema de tratamiento de Pen & Tec Consulting SLU cotiza como Argenta, y que siempre y cuando se cumplan los requisitos exigidos por la normativa, usted podrá ejercer sus derechos de acceso, rectificación, limitación de tratamiento, supresión, portabilidad y oposición/revocación, en los términos que establece la normativa vigente en materia de protección de datos, dirigiendo su petición a la dirección postal OneCoWork, Portal de l'Àngel 40, 08002, Barcelona o bien a través de correo electrónico info@pentec-consulting.eu. Si usted lee este mensaje y no es el destinatario señalado, el empleado o el agente responsable de entregar el mensaje al destinatario, o ha recibido esta comunicación por error, le informamos que está totalmente prohibida, y puede ser ilegal, cualquier divulgación, distribución o reproducción de esta comunicación, y le rogamos que nos lo notifique inmediatamente y nos devuelva el mensaje original a la dirección arriba mencionada. Gracias.

The information contained in this message and/or attached file(s), sent by Pen & Tec Consulting SLU trading as Argenta, is confidential/privileged and is intended to be read solely by the person(s) to whom it is addressed. We hereby inform you that your data will be incorporated into the processing system owned by Pen & Tec Consulting SLU, and that provided it complies with the requirements included in the law, you may exercise the rights of access, rectification, limitation of processing, deletion, portability and opposition by sending your request to the postal address OneCoWork, Portal de l'Àngel 40, 08002, Barcelona or to the email address info@pentec-consulting.eu. If you read this message and you are neither the intended recipient, employee or agent in charge of delivering the message to the recipient, or if you have received this message as the result of an error, we hereby inform you that distributing, sharing or reproducing any part of this message is totally forbidden and may be illegal. As a result, we request that you immediately inform us of the error and return this message to the address mentioned above. Thank you.

From: DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>
Sent: 30 July 2024 18:57
To: Justyna Pałasińska <justyna.palasincka@argentaglobal.com>
Subject: RE: [EXTERNAL] GRN 1122 canola concentrate status

Hello Justyna,

Please see the attached letter regarding GRN 1122. We appreciate your patience on this one.

Best,

Steve

Stephen DiFranco, PhD
Regulatory Review Scientist/Chemist

Center for Food Safety and Applied Nutrition
Office of Food Additive Safety
Division of Food Ingredients
U.S. Food and Drug Administration
Tel: 240-402-2710
stephen.difranco@fda.hhs.gov



From: Justyna Pałasińska <justyna.palasincka@argentaglobal.com>
Sent: Monday, July 29, 2024 10:41 AM
To: DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>
Subject: Re: [EXTERNAL] GRN 1122 canola concentrate status

CAUTION: This email originated from outside of the organization. Do not click links or open attachments unless you recognize the sender and know the content is safe.

Dear Steve,

I was wondering if you could share an update on the GRN 1122? Can you estimate when can we expect the response letter?

Kind regards,
Justyna Pałasińska
Regulatory Affairs Director – Human Nutrition, Argenta Barcelona



M +34 682 894 653 T +34 936 758 015

www.argentaglobal.com

Image



La información contenida en este mensaje y/o archivo(s) adjunto(s), enviada desde Pen & Tec Consulting SLU cotiza como Argenta, es confidencial/privilegiada y está destinada a ser leída sólo por la(s) persona(s) a la(s) que va dirigida. Le recordamos que sus datos han sido incorporados en el sistema de tratamiento de Pen & Tec Consulting SLU cotiza como Argenta, y que siempre y cuando se cumplan los requisitos exigidos por la normativa, usted podrá ejercer sus derechos de acceso, rectificación, limitación de tratamiento, supresión, portabilidad y oposición/revocación, en los términos que establece la normativa vigente en materia de protección de datos, dirigiendo su petición a la dirección postal OneCoWork, Portal de l'Àngel 40, 08002, Barcelona o bien a través de correo electrónico info@pentec-consulting.eu. Si usted lee este mensaje y no es el destinatario señalado, el empleado o el agente responsable de entregar el mensaje al destinatario, o ha recibido esta comunicación por error, le informamos que está totalmente prohibida, y puede ser ilegal, cualquier divulgación, distribución o reproducción de esta comunicación, y le rogamos que nos lo notifique inmediatamente y nos devuelva el mensaje original a la dirección arriba mencionada. Gracias.
The information contained in this message and/or attached file(s), sent by Pen & Tec Consulting SLU trading as Argenta, is confidential/privileged and is intended to be read solely by the person(s) to whom it is addressed. We hereby inform you that your data will be incorporated into the processing system owned by Pen & Tec Consulting SLU, and that provided it complies with the requirements included in the law, you may exercise the rights of access, rectification, limitation of processing, deletion, portability and opposition by sending your request to the postal address OneCoWork, Portal de l'Àngel 40, 08002, Barcelona or to the email address info@pentec-consulting.eu. If you read this message and you are neither the intended recipient, employee or agent in charge of delivering the message to the recipient, or if you have received this message as the result of an error, we hereby inform you that distributing, sharing or reproducing any part of this message is totally forbidden and may be illegal. As a result, we request that you immediately inform us of the error and return this message to the address mentioned above. Thank you.

From: Justyna Pałasińska <justyna.palasinaska@argentaglobal.com>

Sent: 03 July 2024 17:44

To: DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>

Subject: Re: [EXTERNAL] GRN 1122 canola concentrate status

Thank you very much for your clarification, Steve.

Following your advice: we wish to amend the notice by removing the claim that this ingredient is used as a source of dietary fiber and that we wish to add that it may be used "as an ingredient" in the food categories listed within the notice.

Please let me know if anything else is needed from our side.

Kind regards,
Justyna Pałasińska
Regulatory Affairs Director – Human Nutrition, Argenta Barcelona



M +34 682 894 653 T +34 936 758 015

www.argentaglobal.com

Image



La información contenida en este mensaje y/o archivo(s) adjunto(s), enviada desde Pen & Tec Consulting SLU cotiza como Argenta, es confidencial/privilegiada y está destinada a ser leída sólo por la(s) persona(s) a la(s) que va dirigida. Le recordamos que sus datos han sido incorporados en el sistema de tratamiento de Pen & Tec Consulting SLU cotiza como Argenta, y que siempre y cuando se cumplan los requisitos exigidos por la normativa, usted podrá ejercer sus derechos de acceso, rectificación, limitación de tratamiento, supresión, portabilidad y oposición/revocación, en los términos que establece la normativa vigente en materia de protección de datos, dirigiendo su petición a la dirección postal OneCoWork, Portal de l'Àngel 40, 08002, Barcelona o bien a través de correo electrónico info@pentec-consulting.eu. Si usted lee este mensaje y no es el destinatario señalado, el empleado o el agente responsable de entregar el mensaje al destinatario, o ha recibido esta comunicación por error, le informamos que está totalmente prohibida, y puede ser ilegal, cualquier divulgación, distribución o reproducción de esta comunicación, y le rogamos que nos lo notifique inmediatamente y nos devuelva el mensaje original a la dirección arriba mencionada. Gracias.
The information contained in this message and/or attached file(s), sent by Pen & Tec Consulting SLU trading as Argenta, is confidential/privileged and is intended to be read solely by the person(s) to whom it is addressed. We hereby inform you that your data will be incorporated into the processing system owned by Pen & Tec Consulting SLU, and that provided it complies with the requirements included in the law, you may exercise the rights of access, rectification, limitation of processing, deletion, portability and opposition by sending your request to the postal address OneCoWork, Portal de l'Àngel 40, 08002, Barcelona or to the email address info@pentec-consulting.eu. If you read this message and you are neither the intended recipient, employee or agent in charge of delivering the message to the recipient, or if you have received this message as the result of an error, we hereby inform you that distributing, sharing or reproducing any part of this message is totally forbidden and may be illegal. As a result, we request that you immediately inform us of the error and return this message to the address mentioned above. Thank you.

From: DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>

Sent: 02 July 2024 20:49

To: Justyna Pałasińska <justyna.palasinaska@argentaglobal.com>

Subject: RE: [EXTERNAL] GRN 1122 canola concentrate status

Hello Justyna,

I appreciate the quick response. Per your questions:

- The issue is only with the claim that the ingredient is a source of fiber. You may still make the other claims and claim it is a source of protein—and just add the technical effect "as an ingredient". This is kind of a general, catch all term. There are different regulations addressing claims of source of protein, and this fits.
- You may keep use in all categories that are currently in the notice. This change does not require a different exposure estimate or any

other change such as in use. The issue is really about what nutritional claims you can make about the ingredient, not its safety in these uses.

- You do not have to do any sort of rewrite or resubmit the notice. You can simply email me stating you wish to amend the notice by removing the claim that this ingredient is used as a source of dietary fiber and that you wish to add that it may be used “as an ingredient” in the food categories listed. In other words you are adding “as an ingredient” to the notified technical effects of the substance in food. That will be sufficient and we should be able to get this closed out shortly thereafter.

Happy to discuss if you have any other questions.

Best,

Steve

Stephen DiFranco, PhD

Regulatory Review Scientist/Chemist

Center for Food Safety and Applied Nutrition

Office of Food Additive Safety

Division of Food Ingredients

U.S. Food and Drug Administration

Tel: 240-402-2710

stephen.difranco@fda.hhs.gov



From: Justyna Pałasińska <justyna.palasincka@argentaglobal.com>

Sent: Tuesday, July 2, 2024 10:59 AM

To: DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>

Subject: Re: [EXTERNAL] GRN 1122 canola concentrate status

CAUTION: This email originated from outside of the organization. Do not click links or open attachments unless you recognize the sender and know the content is safe.

Many thanks for your swift reply, Steve.

We will update the GRAS & get the updated version to you shortly. I wanted to check a couple questions with you:

- understand the issue is with 'source of fiber' & not with other claims, e.g. 'source of protein'. Could you confirm?
- one of the intended uses is 'protein-fiber and nutritional powders'. I understand that we can keep this category, as the product is a source of protein & therefore can be used as an ingredient for this category of foods. Could you confirm?
- Is it OK for us to send the updated GRAS document by e-mail or do you require a CD-submission?

I look forward to your reply.

Kind regards,

Justyna Pałasińska

Regulatory Affairs Director – Human Nutrition, Argenta Barcelona



M +34 682 894 653 T +34 936 758 015

www.argentaglobal.com

Image



La información contenida en este mensaje y/o archivo(s) adjunto(s), enviada desde Pen & Tec Consulting SLU cotiza como Argenta, es confidencial/privilegiada y está destinada a ser leída sólo por la(s) persona(s) a la(s) que va dirigida. Le recordamos que sus datos han sido incorporados en el sistema de tratamiento de Pen & Tec Consulting SLU cotiza como Argenta, y que siempre y cuando se cumplan los requisitos exigidos por la normativa, usted podrá ejercer sus derechos de acceso, rectificación, limitación de tratamiento, supresión, portabilidad y oposición/revocación, en los términos que establece la normativa vigente en materia de protección de datos, dirigiendo su petición a la dirección postal OneCoWork, Portal de l'Àngel 40, 08002, Barcelona o bien a través de correo electrónico info@pentec-consulting.eu. Si usted lee este mensaje y no es el destinatario señalado, el empleado o el agente responsable de entregar el mensaje al destinatario, o ha recibido esta comunicación por error, le informamos que está totalmente prohibida, y puede ser ilegal, cualquier divulgación, distribución o reproducción de esta comunicación, y le rogamos que nos lo notifique inmediatamente y nos devuelva el mensaje original a la dirección arriba mencionada. Gracias.

The information contained in this message and/or attached file(s), sent by Pen & Tec Consulting SLU trading as Argenta, is confidential/privileged and is intended to be read solely by the person(s) to whom it is addressed. We hereby inform you that your data will be incorporated into the processing system owned by Pen & Tec Consulting SLU, and that provided it complies with the requirements included in the law, you may exercise the rights of access, rectification, limitation of processing, deletion, portability and opposition by sending your request to the postal address OneCoWork, Portal de l'Àngel 40, 08002, Barcelona or to the email address info@pentec-consulting.eu. If you read this message and you are neither the intended recipient, employee or agent in charge of delivering the message to the recipient, or if you have received this message as the result of an error, we hereby inform you that distributing, sharing or reproducing any part of this message is totally forbidden and may be illegal. As a result, we request that you immediately inform us of the error and return this message to the address mentioned above. Thank you.

From: DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>

Sent: 01 July 2024 21:32

To: Justyna Pałasińska <justyna.palasincka@argentaglobal.com>

Subject: RE: [EXTERNAL] GRN 1122 canola concentrate status

Hello Justyna,

In finalizing our response letter we ran into a bit of an issue regarding the notice's claim that the ingredient is a source of dietary fiber, as this is a legally defined area in US regulations. I got the following from our review team for your consideration:

NapiFeryn states that canola concentrate is intended to be used as a source of dietary fiber amongst other intended uses (i.e., source of protein, formulation aid, stabilizer, thickener, or texturizer). We note that FDA defines dietary fiber as "non-digestible soluble and insoluble carbohydrates (with 3 or more monomeric units), and lignin that are intrinsic and intact in plants; isolated or synthetic non-digestible carbohydrates (with 3 or more monomeric units) determined by FDA to have physiological effects that are beneficial to human health" (21 CFR 101.9(c)(6)(i)). Additional information related to dietary fiber can be found at <https://www.fda.gov/food/food-labeling-nutrition/questions-and-answers-dietary-fiber>.

During our evaluation of GRN 001122 we were not able to determine whether canola concentrate meets the definition of dietary fiber. To proceed with our evaluation of GRN 001122, we recommend that Napiferyn reconsider the description of the intended uses of canola concentrate by replacing the intended use as "a source of dietary fiber" with the use as "an ingredient".

If NapiFeryn wishes to use canola concentrate as a source of dietary fiber, we recommend that you consult with FDA's Office of Nutrition and Food Labeling (ONFL) on whether the ingredient meets the definition of dietary fiber. After ONFL provides a favorable determination, Napiferyn may choose to inform FDA about their GRAS conclusion for the use of canola concentrate as a source of dietary fiber by submitting a supplement to GRN 001122.

Again, amending the notice to state the use is simply as "an ingredient" will allow us to close out this GRAS notice while still allowing the ingredient to be used in foods. If you then wish to have the use as a source of dietary fiber included in the notice and/or displayed on the [GRAS Notice inventory](#), we can go back and amend as appropriate pending the outcome with ONFL.

Happy to discuss if this is unclear.

Thanks,

Steve

Stephen DiFranco, PhD

Regulatory Review Scientist/Chemist

Center for Food Safety and Applied Nutrition
Office of Food Additive Safety
Division of Food Ingredients
U.S. Food and Drug Administration
Tel: 240-402-2710
stephen.difranco@fda.hhs.gov



From: Justyna Pałasińska <justyna.palasincka@argentaglobal.com>

Sent: Monday, July 1, 2024 8:16 AM

To: DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>

Subject: Re: [EXTERNAL] GRN 1122 canola concentrate status

CAUTION: This email originated from outside of the organization. Do not click links or open attachments unless you recognize the sender and know the content is safe.

Hi Steve,

I hope you are doing well.

Could you let me know when the letter is expected to receive clearance & be shared with the applicant?

Kind regards,

Justyna Pałasińska

Regulatory Affairs Director – Human Nutrition, Argenta Barcelona



M +34 682 894 653 T +34 936 758 015

www.argentaglobal.com

Image



La información contenida en este mensaje y/o archivo(s) adjunto(s), enviada desde Pen & Tec Consulting SLU cotiza como Argenta, es confidencial/privilegiada y está destinada a ser leída sólo por la(s) persona(s) a la(s) que va dirigida. Le recordamos que sus datos han sido incorporados en el sistema de tratamiento de Pen & Tec Consulting SLU cotiza como Argenta, y que siempre y cuando se cumplan los requisitos exigidos por la normativa, usted podrá ejercer sus derechos de acceso, rectificación, limitación de tratamiento, supresión, portabilidad y oposición/revocación, en los términos que establece la normativa vigente en materia de protección de datos, dirigiendo su petición a la dirección postal OneCoWork, Portal de l'Àngel 40, 08002, Barcelona o bien a través de correo electrónico info@pentec-consulting.eu. Si usted lee este mensaje y no es el destinatario señalado, el empleado o el agente responsable de entregar el mensaje al destinatario, o ha recibido esta comunicación por error, le informamos que está totalmente prohibida, y puede ser ilegal, cualquier divulgación, distribución o reproducción de esta comunicación, y le rogamos que nos lo notifique inmediatamente y nos devuelva el mensaje original a la dirección arriba mencionada. Gracias.

The information contained in this message and/or attached file(s), sent by Pen & Tec Consulting SLU trading as Argenta, is confidential/privileged and is intended to be read solely by the person(s) to whom it is addressed. We hereby inform you that your data will be incorporated into the processing system owned by Pen & Tec Consulting SLU, and that provided it complies with the requirements included in the law, you may exercise the rights of access, rectification, limitation of processing, deletion, portability and opposition by sending your request to the postal address OneCoWork, Portal de l'Àngel 40, 08002, Barcelona or to the email address info@pentec-consulting.eu. If you read this message and you are neither the intended recipient, employee or agent in charge of delivering the message to the recipient, or if you have received this message as the result of an error, we hereby inform you that distributing, sharing or reproducing any part of this message is totally forbidden and may be illegal. As a result, we request that you immediately inform us of the error and return this message to the address mentioned above. Thank you.

From: Justyna Pałasińska <justyna.palasincka@argentaglobal.com>
Sent: 30 May 2024 16:09
To: DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>
Subject: Re: [EXTERNAL] GRN 1122 canola concentrate status

Indeed, great news, thank you Steve!

Kind regards,
Justyna Pałasińska
Regulatory Affairs Director – Human Nutrition, Argenta Barcelona



M +34 682 894 653 T +34 936 758 015

www.argentaglobal.com

Image



La información contenida en este mensaje y/o archivo(s) adjunto(s), enviada desde Pen & Tec Consulting SLU cotiza como Argenta, es confidencial/privilegiada y está destinada a ser leída sólo por la(s) persona(s) a la(s) que va dirigida. Le recordamos que sus datos han sido incorporados en el sistema de tratamiento de Pen & Tec Consulting SLU cotiza como Argenta, y que siempre y cuando se cumplan los requisitos exigidos por la normativa, usted podrá ejercer sus derechos de acceso, rectificación, limitación de tratamiento, supresión, portabilidad y oposición/revocación, en los términos que establece la normativa vigente en materia de protección de datos, dirigiendo su petición a la dirección postal OneCoWork, Portal de l'Àngel 40, 08002, Barcelona o bien a través de correo electrónico info@pentec-consulting.eu. Si usted lee este mensaje y no es el destinatario señalado, el empleado o el agente responsable de entregar el mensaje al destinatario, o ha recibido esta comunicación por error, le informamos que está totalmente prohibida, y puede ser ilegal, cualquier divulgación, distribución o reproducción de esta comunicación, y le rogamos que nos lo notifique inmediatamente y nos devuelva el mensaje original a la dirección arriba mencionada. Gracias.

The information contained in this message and/or attached file(s), sent by Pen & Tec Consulting SLU trading as Argenta, is confidential/privileged and is intended to be read solely by the person(s) to whom it is addressed. We hereby inform you that your data will be incorporated into the processing system owned by Pen & Tec Consulting SLU, and that provided it complies with the requirements included in the law, you may exercise the rights of access, rectification, limitation of processing, deletion, portability and opposition by sending your request to the postal address OneCoWork, Portal de l'Àngel 40, 08002, Barcelona or to the email address info@pentec-consulting.eu. If you read this message and you are neither the intended recipient, employee or agent in charge of delivering the message to the recipient, or if you have received this message as the result of an error, we hereby inform you that distributing, sharing or reproducing any part of this message is totally forbidden and may be illegal. As a result, we request that you immediately inform us of the error and return this message to the address mentioned above. Thank you.

From: DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>
Sent: 30 May 2024 16:06
To: Justyna Pałasińska <justyna.palasincka@argentaglobal.com>
Subject: RE: [EXTERNAL] GRN 1122 canola concentrate status

Hi Justyna,

I finally have some good news for you—FSIS has just finished their review. I have drafted a response letter and it is currently making its way through clearance, so you should hear back soon.

Best,

Steve

Stephen DiFranco, PhD
Regulatory Review Scientist/Chemist

Center for Food Safety and Applied Nutrition
Office of Food Additive Safety
Division of Food Ingredients
U.S. Food and Drug Administration
Tel: 240-402-2710
stephen.difranco@fda.hhs.gov



From: Justyna Pałasińska <justyna.palasincka@argentaglobal.com>

Sent: Thursday, May 30, 2024 9:48 AM
To: DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>
Subject: Re: [EXTERNAL] GRN 1122 canola concentrate status

CAUTION: This email originated from outside of the organization. Do not click links or open attachments unless you recognize the sender and know the content is safe.

Dear Stephen,

I hope this e-mail finds you well. I was wondering if there is any update from FSIS on this GRN?

Kind regards,
Justyna Pałasińska
Regulatory Affairs Director – Human Nutrition, Argenta Barcelona



M +34 682 894 653 T +34 936 758 015

www.argentaglobal.com

Image



La información contenida en este mensaje y/o archivo(s) adjunto(s), enviada desde Pen & Tec Consulting SLU cotiza como Argenta, es confidencial/privilegiada y está destinada a ser leída sólo por la(s) persona(s) a la(s) que va dirigida. Le recordamos que sus datos han sido incorporados en el sistema de tratamiento de Pen & Tec Consulting SLU cotiza como Argenta, y que siempre y cuando se cumplan los requisitos exigidos por la normativa, usted podrá ejercer sus derechos de acceso, rectificación, limitación de tratamiento, supresión, portabilidad y oposición/revocación, en los términos que establece la normativa vigente en materia de protección de datos, dirigiendo su petición a la dirección postal OneCoWork, Portal de l'Àngel 40, 08002, Barcelona o bien a través de correo electrónico info@pentec-consulting.eu. Si usted lee este mensaje y no es el destinatario señalado, el empleado o el agente responsable de entregar el mensaje al destinatario, o ha recibido esta comunicación por error, le informamos que está totalmente prohibida, y puede ser ilegal, cualquier divulgación, distribución o reproducción de esta comunicación, y le rogamos que nos lo notifique inmediatamente y nos devuelva el mensaje original a la dirección arriba mencionada. Gracias.

The information contained in this message and/or attached file(s), sent by Pen & Tec Consulting SLU trading as Argenta, is confidential/privileged and is intended to be read solely by the person(s) to whom it is addressed. We hereby inform you that your data will be incorporated into the processing system owned by Pen & Tec Consulting SLU, and that provided it complies with the requirements included in the law, you may exercise the rights of access, rectification, limitation of processing, deletion, portability and opposition by sending your request to the postal address OneCoWork, Portal de l'Àngel 40, 08002, Barcelona or to the email address info@pentec-consulting.eu. If you read this message and you are neither the intended recipient, employee or agent in charge of delivering the message to the recipient, or if you have received this message as the result of an error, we hereby inform you that distributing, sharing or reproducing any part of this message is totally forbidden and may be illegal. As a result, we request that you immediately inform us of the error and return this message to the address mentioned above. Thank you.

From: DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>
Sent: 04 April 2024 17:26
To: Justyna Pałasińska <justyna.palasinaska@argentaglobal.com>
Subject: RE: [EXTERNAL] GRN 1122 canola concentrate status

Thanks Justyna,

I've passed the information to FSIS for review. Hopefully we will hear back shortly.

Best,

Steve

Stephen DiFranco, PhD
Regulatory Review Scientist/Chemist

Center for Food Safety and Applied Nutrition
Office of Food Additive Safety
Division of Food Ingredients
U.S. Food and Drug Administration
Tel: 240-402-2710
stephen.difranco@fda.hhs.gov



From: Justyna Pałasińska <justyna.palasinaska@argentaglobal.com>
Sent: Thursday, April 4, 2024 7:38 AM
To: DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>
Subject: Re: [EXTERNAL] GRN 1122 canola concentrate status

CAUTION: This email originated from outside of the organization. Do not click links or open attachments unless you recognize the sender and know the content is safe.

Dear Stephen,

Please find our reply below:

It is the applicant's understanding that OSHA OELs for heavy metals indicated by FSIS relate to the risk of exposure to heavy metals in the material under assessment via inhalation route only. The material indeed may create dust hazard if handled improperly. We note that the safety data sheet provided for the material (attached for reference) not only informs about the potential to form dust if handled improperly but also includes information on precautionary measures and personal protection and engineering controls aimed at eliminating or greatly reducing the risk of exposure to airborne particles. Proper handling of the material / adherence to these measures and controls by extension would eliminate or greatly reduce the risk of exposure to heavy metals that may be present in the material.

In case the above does not sufficiently address the potential risk of exposure to heavy metals present in the material via inhalation route, the applicant would like to inform that the bulk density of the material ranges between 0.1 and 0.3 g/cm³. A confirmation whether this information is sufficient to proceed with the calculations would be much appreciated. It would also be helpful to understand the assumptions being made by FSIS (e.g. concentration of airborne particles) when assessing whether the levels of heavy metals in the product may exceed OSHA OELs.

Kind regards,

Justyna Pałasińska

Regulatory Affairs Director – Human Nutrition, Argenta Barcelona



M +34 682 894 653 T +34 936 758 015

www.argentaglobal.com

Image



La información contenida en este mensaje y/o archivo(s) adjunto(s), enviada desde Pen & Tec Consulting SLU cotiza como Argenta, es confidencial/privilegiada y está destinada a ser leída sólo por la(s) persona(s) a la(s) que va dirigida. Le recordamos que sus datos han sido incorporados en el sistema de tratamiento de Pen & Tec Consulting SLU cotiza como Argenta, y que siempre y cuando se cumplan los requisitos exigidos por la normativa, usted podrá ejercer sus derechos de acceso, rectificación, limitación de tratamiento, supresión, portabilidad y oposición/revocación, en los términos que establece la normativa vigente en materia de protección de datos, dirigiendo su petición a la dirección postal OneCoWork, Portal de l'Àngel 40, 08002, Barcelona o bien a través de correo electrónico info@pentec-consulting.eu. Si usted lee este mensaje y no es el destinatario señalado, el empleado o el agente responsable de entregar el mensaje al destinatario, o ha recibido esta comunicación por error, le informamos que está totalmente prohibida, y puede ser ilegal, cualquier divulgación, distribución o reproducción de esta comunicación, y le rogamos que nos lo notifique inmediatamente y nos devuelva el mensaje original a la dirección arriba mencionada. Gracias.

The information contained in this message and/or attached file(s), sent by Pen & Tec Consulting SLU trading as Argenta, is confidential/privileged and is intended to be read solely by the person(s) to whom it is addressed. We hereby inform you that your data will be incorporated into the processing system owned by Pen & Tec Consulting SLU, and that provided it complies with the requirements included in the law, you may exercise the rights of access, rectification, limitation of processing, deletion, portability and opposition by sending your request to the postal address OneCoWork, Portal de l'Àngel 40, 08002, Barcelona or to the email address info@pentec-consulting.eu. If you read this message and you are neither the intended recipient, employee or agent in charge of delivering the message to the recipient, or if you have received this message as the result of an error, we hereby inform you that distributing, sharing or reproducing any part of this message is totally forbidden and may be illegal. As a result, we request that you immediately inform us of the error and return this message to the address mentioned above. Thank you.

From: DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>

Date: Thursday, 28 March 2024 at 20:47

To: Justyna Pałasińska <justyna.palasinaska@argentaglobal.com>

Subject: RE: [EXTERNAL] GRN 1122 canola concentrate status

Hello Justyna,

I got feedback from FSIS about their review of GRN 1122. They send the following:

I have now completed the review of the documentation submitted for the approval of the above-referenced compound. I noted that it contains Lead (≤ 0.5 mg/kg), Arsenic (≤ 0.2 mg/kg), Cadmium (≤ 0.2 mg/kg), and Mercury (≤ 0.1 mg/kg). OSHA has established OEL for these substances at 0.05 mg/m³, 0.01 mg/m³, 0.01 mg/m³, 0.025 mg/m³ (depending on presentation) respectively.

To finalize my analysis, I require the composition in mg/m³ of each of these elements or the density so I may calculate their composition accurately and evaluate them against their OSHA standards.

Are you able to provide the density of the canola concentrate? I believe this is the easiest way to answer their questions. From the density and the specified ppm levels, the reviewer should be able to calculate the maximum amount by weight of each heavy metal contaminate for a given volume of canola concentrate.

Best,

Steve

Stephen DiFranco, PhD

Regulatory Review Scientist/Chemist

Center for Food Safety and Applied Nutrition

Office of Food Additive Safety

Division of Food Ingredients

U.S. Food and Drug Administration

Tel: 240-402-2710

stephen.difranco@fda.hhs.gov





From: Justyna Pałasińska <justyna.palasinaska@argentaglobal.com>
Sent: Monday, March 4, 2024 5:04 AM
To: DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>
Subject: Re: [EXTERNAL] GRN 1122 canola concentrate status

CAUTION: This email originated from outside of the organization. Do not click links or open attachments unless you recognize the sender and know the content is safe.

Many thanks for the update, Stephen. We look forward to hearing an update, hopefully soon!

Kind regards,
Justyna Pałasińska
Regulatory Affairs Director – Human Nutrition, Argenta Barcelona



M +34 682 894 653 T +34 936 758 015

www.argentaglobal.com

Image



La información contenida en este mensaje y/o archivo(s) adjunto(s), enviada desde Pen & Tec Consulting SLU cotiza como Argenta, es confidencial/privilegiada y está destinada a ser leída sólo por la(s) persona(s) a la(s) que va dirigida. Le recordamos que sus datos han sido incorporados en el sistema de tratamiento de Pen & Tec Consulting SLU cotiza como Argenta, y que siempre y cuando se cumplan los requisitos exigidos por la normativa, usted podrá ejercer sus derechos de acceso, rectificación, limitación de tratamiento, supresión, portabilidad y oposición/revocación, en los términos que establece la normativa vigente en materia de protección de datos, dirigiendo su petición a la dirección postal Pl. Ausias March 1, 4 planta 08195, Sant Cugat del Valles (Barcelona) o bien a través de correo electrónico info@pentec-consulting.eu. Si usted lee este mensaje y no es el destinatario señalado, el empleado o el agente responsable de entregar el mensaje al destinatario, o ha recibido esta comunicación por error, le informamos que está totalmente prohibida, y puede ser ilegal, cualquier divulgación, distribución o reproducción de esta comunicación, y le rogamos que nos lo notifique inmediatamente y nos devuelva el mensaje original a la dirección arriba mencionada. Gracias.

The information contained in this message and/or attached file(s), sent by Pen & Tec Consulting SLU trading as Argenta, is confidential/privileged and is intended to be read solely by the person(s) to whom it is addressed. We hereby inform you that your data will be incorporated into the processing system owned by Pen & Tec Consulting SLU, and that provided it complies with the requirements included in the law, you may exercise the rights of access, rectification, limitation of processing, deletion, portability and opposition by sending your request to the postal address Pl. Ausias March 1, 4 floor 08195, Sant Cugat del Valles (Barcelona) or to the email address info@pentec-consulting.eu. If you read this message and you are neither the intended recipient, employee or agent in charge of delivering the message to the recipient, or if you have received this message as the result of an error, we hereby inform you that distributing, sharing or reproducing any part of this message is totally forbidden and may be illegal. As a result, we request that you immediately inform us of the error and return this message to the address mentioned above. Thank you.

From: DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>
Date: Monday, 26 February 2024 at 17:20
To: Justyna Pałasińska <justyna.palasinaska@argentaglobal.com>
Subject: RE: [EXTERNAL] GRN 1122 canola concentrate status

You don't often get email from stephen.difranco@fda.hhs.gov. [Learn why this is important](#)

Hello Justyna,

Regarding GRN 1122; FDA has completed its review and has drafted a response letter. Unfortunately, we cannot move forward before USDA-FSIS completes their review of the uses under their jurisdiction. I have been periodically inquiring with FSIS as to the status and will get this to you as soon as possible.

We appreciate your continued patience.

Best,

Steve

Stephen DiFranco, PhD
Regulatory Review Scientist/Chemist

Center for Food Safety and Applied Nutrition
Office of Food Additive Safety
Division of Food Ingredients
U.S. Food and Drug Administration
Tel: 240-402-2710
stephen.difranco@fda.hhs.gov



From: Justyna Pałasińska <justyna.palasinaska@argentaglobal.com>

Sent: Wednesday, February 14, 2024 12:07 PM

To: Premarkt <Premarkt@fda.hhs.gov>

Cc: DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>; Ioannis Kartanos <ioannis.kartanos@argentaglobal.com>

Subject: [EXTERNAL] GRN 1122 canola concentrate status

CAUTION: This email originated from outside of the organization. Do not click links or open attachments unless you recognize the sender and know the content is safe.

Dear HHS team,

I am writing to enquire about a GRAS notice that was submitted to the FDA & filed April 19, 2023 (GRN 1122). We have been in touch with Mr Stephen DiFranco & at the beginning of December he has informed us that the FDA reviews are complete & the notice is now with USDA-FSIS.

Mr DiFranco has been very helpful through the whole process. However, we have tried to contact him several times since December without success. We were wondering if there is someone else we can get in touch with for an update on this application. We would be happy to provide any information that would help finalize the process.

I look forward to hearing from you.

Kind regards,

Justyna Pałasińska

Regulatory Affairs Director – Human Nutrition, Argenta Barcelona



M +34 682 894 653 T +34 936 758 015

www.argentaglobal.com

Image



La información contenida en este mensaje y/o archivo(s) adjunto(s), enviada desde Pen & Tec Consulting SLU cotiza como Argenta, es confidencial/privilegiada y está destinada a ser leída sólo por la(s) persona(s) a la(s) que va dirigida. Le recordamos que sus datos han sido incorporados en el sistema de tratamiento de Pen & Tec Consulting SLU cotiza como Argenta, y que siempre y cuando se cumplan los requisitos exigidos por la normativa, usted podrá ejercer sus derechos de acceso, rectificación, limitación de tratamiento, supresión, portabilidad y oposición/revocación, en los términos que establece la normativa vigente en materia de protección de datos, dirigiendo su petición a la dirección postal Pl. Ausias March 1, 4 planta 08195, Sant Cugat del Vallès (Barcelona) o bien a través de correo electrónico info@pentec-consulting.eu. Si usted lee este mensaje y no es el destinatario señalado, el empleado o el agente responsable de entregar el mensaje al destinatario, o ha recibido esta comunicación por error, le informamos que está totalmente prohibida, y puede ser ilegal, cualquier divulgación, distribución o reproducción de esta comunicación, y le rogamos que nos lo notifique inmediatamente y nos devuelva el mensaje original a la dirección arriba mencionada. Gracias.

The information contained in this message and/or attached file(s), sent by Pen & Tec Consulting SLU trading as Argenta, is confidential/privileged and is intended to be read solely by the person(s) to whom it is addressed. We hereby inform you that your data will be incorporated into the processing system owned by Pen & Tec Consulting SLU, and that provided it complies with the requirements included in the law, you may exercise the rights of access, rectification, limitation of processing, deletion, portability and opposition by sending your request to the postal address Pl. Ausias March 1, 4 floor 08195, Sant Cugat del Valles (Barcelona) or to the email address info@pentec-consulting.eu. If you read this message and you are neither the intended recipient, employee or agent in charge of delivering the message to the recipient, or if you have received this message as the result of an error, we hereby inform you that distributing, sharing or reproducing any part of this message is totally forbidden and may be illegal. As a result, we request that you immediately inform us of the error and return this message to the address mentioned above. Thank you.

From: Justyna Pałasińska <justyna.palasinaska@argentaglobal.com>

Date: Wednesday, 31 January 2024 at 17:53

To: Justyna Pałasińska <justyna.palasinaska@argentaglobal.com>, DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>

Cc: Ioannis Kartanos <ioannis.kartanos@argentaglobal.com>

Subject: Re: [EXTERNAL] GRN 1122 canola concentrate - update contact person

Dear Steve,

I hope this e-mail finds you well. I was wondering if there are any updates on the finalization of this notification?

Is there any additional information that needs to be provided?

Kind regards,

Justyna Pałasińska

Regulatory Affairs Director – Human Nutrition, Argenta Barcelona



M +34 682 894 653 T +34 936 758 015

www.argentaglobal.com

Image



La información contenida en este mensaje y/o archivo(s) adjunto(s), enviada desde Pen & Tec Consulting SLU cotiza como Argenta, es confidencial/privilegiada y está destinada a ser leída sólo por la(s) persona(s) a la(s) que va dirigida. Le recordamos que sus datos han sido incorporados en el sistema de tratamiento de Pen & Tec Consulting SLU cotiza como Argenta, y que siempre y cuando se cumplan los requisitos exigidos por la normativa, usted podrá ejercer sus derechos de acceso, rectificación, limitación de tratamiento, supresión, portabilidad y oposición/revocación, en los términos que establece la normativa vigente en materia de protección de datos, dirigiendo su petición a la dirección postal Pl. Ausias March 1, 4 planta 08195, Sant Cugat del Vallès (Barcelona) o bien a través de correo electrónico info@pentec-consulting.eu. Si usted lee este mensaje y no es el destinatario señalado, el empleado o el agente responsable de entregar el mensaje al destinatario, o ha recibido esta comunicación por error, le informamos que está totalmente prohibida, y puede ser ilegal, cualquier divulgación, distribución o reproducción de esta comunicación, y le rogamos que nos lo notifique inmediatamente y nos devuelva el mensaje original a la dirección arriba mencionada. Gracias.

The information contained in this message and/or attached file(s), sent by Pen & Tec Consulting SLU trading as Argenta, is confidential/privileged and is intended to be read solely by the person(s) to whom it is addressed. We hereby inform you that your data will be incorporated into the processing system owned by Pen & Tec Consulting SLU, and that provided it complies with the requirements included in the law, you may exercise the rights of access, rectification, limitation of processing, deletion, portability and opposition by sending your request to the postal address Pl. Ausias March 1, 4 floor 08195, Sant Cugat del Valles (Barcelona) or to the email address info@pentec-consulting.eu. If you read this message and you are neither the intended recipient, employee or agent in charge of delivering the message to the recipient, or if you have received this message as the result of an error, we hereby inform you that distributing, sharing or reproducing any part of this message is totally forbidden and may be illegal. As a result, we request that you

immediately inform us of the error and return this message to the address mentioned above. Thank you.

From: Justyna Pałasińska <justyna@pentec-consulting.eu>
Date: Friday, 22 December 2023 at 13:31
To: DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>
Cc: Ioannis Kartanos <ioannis@pentec-consulting.eu>
Subject: Re: [EXTERNAL] GRN 1122 canola concentrate - update contact person

Dear Stephen,

Many thanks for confirming the change of contact person.

I'm following up on my colleague Ioannis e-mail from 12/12/2023. As he mentioned, we have already provided the answers to the questions to USDA-FSIS. Nevertheless, I have included them in a separate document.

Please let us know in case any additional information is required.

In the meantime, we wish you a Happy Holiday Season & all the best in 2024!

Kind regards,

Ing. Justyna Pałasińska

Regulatory Affairs Director – Human Nutrition | Pen & Tec Consulting
T +34 936 758 015 M +34 682 894 653 F +34 936 758 016 www.pentec-consulting.eu
Pl. Ausias March 1 | 4th floor D01 | 08195 Sant Cugat del Vallès | Barcelona | Spain



La información contenida en este mensaje y/o archivo(s) adjunto(s), enviada desde Pen & Tec Consulting SLU, es confidencial/privilegiada y está destinada a ser leída sólo por la(s) persona(s) a la(s) que va dirigida. Le recordamos que sus datos han sido incorporados en el sistema de tratamiento de Pen & Tec Consulting SLU y que siempre y cuando se cumplan los requisitos exigidos por la normativa, usted podrá ejercer sus derechos de acceso, rectificación, limitación de tratamiento, supresión, portabilidad y oposición/revocación, en los términos que establece la normativa vigente en materia de protección de datos, dirigiendo su petición a la dirección postal Pl. Ausias March 1, 4 planta 08195, Sant Cugat del Vallès (Barcelona) o bien a través de correo electrónico info@pentec-consulting.eu. Si usted lee este mensaje y no es el destinatario señalado, el empleado o el agente responsable de entregar el mensaje al destinatario, o ha recibido esta comunicación por error, le informamos que está totalmente prohibida, y puede ser ilegal, cualquier divulgación, distribución o reproducción de esta comunicación, y le rogamos que nos lo notifique inmediatamente y nos devuelva el mensaje original a la dirección arriba mencionada. Gracias.

The information contained in this message and/or attached file(s), sent by Pen & Tec Consulting SLU, is confidential/privileged and is intended to be read solely by the person(s) to whom it is addressed. We hereby inform you that your data will be incorporated into the processing system owned by Pen & Tec Consulting SLU, and that provided it complies with the requirements included in the law, you may exercise the rights of access, rectification, limitation of processing, deletion, portability and opposition by sending your request to the postal address Pl. Ausias March 1, 4 floor 08195, Sant Cugat del Valles (Barcelona) or to the email address info@pentec-consulting.eu. If you read this message and you are neither the intended recipient, employee or agent in charge of delivering the message to the recipient, or if you have received this message as the result of an error, we hereby inform you that distributing, sharing or reproducing any part of this message is totally forbidden and may be illegal. As a result, we request that you immediately inform us of the error and return this message to the address mentioned above. Thank you.

From: DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>
Date: Tuesday, 5 December 2023 at 19:05
To: Nikolaas Tilkin-Franssens <niko@pentec-consulting.eu>
Cc: Justyna Pałasińska <justyna@pentec-consulting.eu>
Subject: RE: [EXTERNAL] GRN 1122 canola concentrate - update contact person

Hello Niko and Justyna,

Just confirming the change of contact person for GRN 1122.

As for timeline, FDA reviews are complete but USDA-FSIS is requesting a few pieces of information regarding the uses of canola concentrate under USDA jurisdiction, namely:

Please provide SDS for the at use concentrations of the substance and include a description of how the use of this technology will not adversely affect the safety of FSIS inspectors. Workplace safety and health hazards include inhalation, direct skin contact (skin, eyes, mouth), and fire/explosion caused by exposure to the product, its working solution or dry mixture and potential by-products formed and/or off-gassed during the application process. The employee safety information should demonstrate how the New Technology will not "jeopardize the safety of Federal inspection personnel" as specified in the [FSIS Compliance Guideline Procedures for New Technology Notifications and Protocols, April 2015](#).

Although I'm not anticipating any issues here, FSIS workplace and employee safety must be specifically addressed. Please refer to Appendix A on page 17, Workplace Safety and Health Criteria, for clarification on what to provide in the response. For additional clarity with respect to employee safety, the following are examples of information that are typically needed by FSIS' employee safety and health group;

1. Potential workplace exposures that could result from inhalation and direct contact during use of the substance/technology. This information is required in addition

to a Safety Data Sheet (SDS) to determine accurate hazard potential and recommended exposure control measures for IPP work areas in accordance with Occupational Safety and Health Administration (OSHA) regulations: 29 CFR 1910.1200, Hazard Communication, 29 CFR 1910.132, Personal Protective Equipment, and 29 CFR 1910.1000, Air Contaminants. The information should be included as a specific section in each of the protocols.

2. If the SDS workplace hazards/precautions do not apply to the type of exposure that would be expected for the FSIS IPP, please have the submitter provide specific information (per the April 2015 FSIS Compliance Guideline Procedures) for the actual type of exposures expected.
3. If no IPP workplace exposures are expected and no control measures are required, please have the submitter state this and provide the reasons why (e.g., such as the substance "as used" [for all concentrations] is not hazardous by inhalation or direct contact and/or IPP would not be exposed to the substance based on the system design, operation and/or control measures that will be in place).
4. Please also indicate how will FSIS IPP be informed of the above information so that it is clear that the information contained in the SDS for the concentrate does not apply to their actual workplace exposure.
5. Are there any potential hazards from chemical mixing or low pH as a result of discharges of the various solutions to floor drains? Are dedicated drain lines or any other enclosures required?
6. With respect to potential airborne exposures to FSIS IPP in the use/application areas, does the submitter have air sampling results taken during the use of the various concentrations of the technology in the listed mixture?

Suitability data;

The intended use of this product in FSIS meat and poultry products is apparently as a binder/extender. The suitability support provided in Appendix 6 does sufficiently support no significant difference in yield and other organoleptic qualities when used as a partial replacement for another binder in a processed meat and poultry product, such as sausage.

However, **additional suitability support is needed:**

- No suitability data was provided for **whole muscle meat and poultry products at the maximum proposed use level**. We would need to see similar data as provided in Appendix 6 for:
 - Whole muscle red meat control containing no other binders, extenders, or moisture retention agents, as compared to a whole muscle red meat product containing 15% isolated canola product.
 - Whole muscle poultry control containing no other binders, extenders, or moisture retention agents as compared to a whole muscle poultry product containing 15% isolated canola product.

Your responses can be emailed directly to me and I will distribute to the necessary staff inside FDA and USDA.

Thanks,

Steve

Stephen DiFranco, PhD

Regulatory Review Scientist/Chemist

Center for Food Safety and Applied Nutrition
Office of Food Additive Safety
Division of Food Ingredients
U.S. Food and Drug Administration
Tel: 240-402-2710
stephen.difranco@fda.hhs.gov



From: Nikolaas Tilkin-Franssens <niko@pentec-consulting.eu>
Sent: Monday, December 4, 2023 4:36 AM
To: DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>
Cc: Justyna Pałasińska <justyna@pentec-consulting.eu>
Subject: [EXTERNAL] GRN 1122 canola concentrate - update contact person

CAUTION: This email originated from outside of the organization. Do not click links or open attachments unless you recognize the sender and know the content is safe.

Hi Mr. DiFranco,

Hope this email finds you well.

Due to a change in position, I will no longer be the contact person for the GRAS Notice 1122 (Canola Protein Concentrate). Could you please update your records to ascertain that Justyna Pałasińska, in copy to this email, is informed of any relevant updates?

Could you kindly confirm receipt of this email for our records?

And if possible, let us know if there is any estimate on the timeline re. finalization of the review of this GRAS Notice.

Many thanks for your great and flexible support on this application.

Kind regards,

Niko

Nikolaas Tilkin-Franssens

Regulatory Affairs Manager | Pen & Tec Consulting

T +34 936 758 015 M +34 649 840 417 F +34 936 758 016 www.pentec-consulting.eu

Pl. Ausias March 1 | 4th floor D01 | 08195 Sant Cugat del Vallès | Barcelona | Spain



La información contenida en este mensaje y/o archivo(s) adjunto(s), enviada desde Pen & Tec Consulting SLU, es confidencial/privilegiada y está destinada a ser leída sólo por la(s) persona(s) a la(s) que va dirigida. Le recordamos que sus datos han sido incorporados en el sistema de tratamiento de Pen & Tec Consulting SLU y que siempre y cuando se cumplan los requisitos exigidos por la normativa, usted podrá ejercer sus derechos de acceso, rectificación, limitación de tratamiento, supresión, portabilidad y oposición/revocación, en los términos que establece la normativa vigente en materia de protección de datos, dirigiendo su petición a la dirección postal Pl. Ausias March 1, 4 planta 08195, Sant Cugat del Vallès (Barcelona) o bien a través de correo electrónico info@pentec-consulting.eu. Si usted lee este mensaje y no es el destinatario señalado, el empleado o el agente responsable de entregar el mensaje al destinatario, o ha recibido esta comunicación por error, le informamos que está totalmente prohibida, y puede ser ilegal, cualquier divulgación, distribución o reproducción de esta comunicación, y le rogamos que nos lo notifique inmediatamente y nos devuelva el mensaje original a la dirección arriba mencionada. Gracias.

The information contained in this message and/or attached file(s), sent by Pen & Tec Consulting SLU, is confidential/privileged and is intended to be read solely by the person(s) to whom it is addressed. We hereby inform you that your data will be incorporated into the processing system owned by Pen & Tec Consulting SLU, and that provided it complies with the requirements included in the law, you may exercise the rights of access, rectification, limitation of processing, deletion, portability and opposition by sending your request to the postal address Pl. Ausias March 1, 4 floor 08195, Sant Cugat del Valles (Barcelona) or to the email address info@pentec-consulting.eu. If you read this message and you are neither the intended recipient, employee or agent in charge of delivering the message to the recipient, or if you have received this message as the result of an error, we hereby inform you that distributing, sharing or reproducing any part of this message is totally forbidden and may be illegal. As a result, we request that you immediately inform us of the error and return this message to the address mentioned above. Thank you.

From: DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>

Date: Monday, 17 July 2023 at 17:01

To: Nikolaas Tilkin-Franssens <niko@pentec-consulting.eu>

Subject: RE: [EXTERNAL] Re: GRN 1122 canola concentrate items for clarification - Reply

Hello Niko,

No problem—Ill distribute this to the team for review.

Best,

Steve

Stephen DiFranco, PhD

Regulatory Review Scientist/Chemist

Center for Food Safety and Applied Nutrition

Office of Food Additive Safety

Division of Food Ingredients

U.S. Food and Drug Administration

Tel: 240-402-2710

stephen.difranco@fda.hhs.gov



From: Nikolaas Tilkin-Franssens <niko@pentec-consulting.eu>

Sent: Monday, July 17, 2023 10:35 AM

To: DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>

Subject: [EXTERNAL] Re: GRN 1122 canola concentrate items for clarification - Reply

CAUTION: This email originated from outside of the organization. Do not click links or open attachments unless you recognize the sender and know the content is safe.

Hi Stephen,

Apologies for this inconvenience.

We noticed that the reply to question 9 refers to Canola protein isolate (as per GRN 1103). I have updated the answer for it to be mentioning Canola protein concentrate (GRN 1122).

We hope this can be taken into consideration.

Kind regards,

Nikolaas Tilkin-Franssens

Regulatory Affairs Manager | Pen & Tec Consulting

T +34 936 758 015 M +34 649 840 417 F +34 936 758 016 www.pentec-consulting.eu

Pl. Ausias March 1 | 4th floor D01 | 08195 Sant Cugat del Vallès | Barcelona | Spain



La información contenida en este mensaje y/o archivo(s) adjunto(s), enviada desde Pen & Tec Consulting SLU, es confidencial/privilegiada y está destinada a ser leída sólo por la(s) persona(s) a la(s) que va dirigida. Le recordamos que sus datos han sido incorporados en el sistema de tratamiento de Pen & Tec Consulting SLU y que siempre y cuando se cumplan los requisitos exigidos por la normativa, usted podrá ejercer sus derechos de acceso, rectificación, limitación de tratamiento, supresión, portabilidad y oposición/revocación, en los términos que establece la normativa vigente en materia de protección de datos, dirigiendo su petición a la dirección postal Pl. Ausias March 1, 4 planta 08195, Sant Cugat del Vallès (Barcelona) o bien a través de correo electrónico info@pentec-consulting.eu. Si usted lee este mensaje y no es el destinatario señalado, el empleado o el agente responsable de entregar el mensaje al destinatario, o ha recibido esta comunicación por error, le informamos que está totalmente prohibida, y puede ser ilegal, cualquier divulgación, distribución o reproducción de esta comunicación, y le rogamos que nos lo notifique inmediatamente y nos devuelva el mensaje original a la dirección arriba mencionada. Gracias.

The information contained in this message and/or attached file(s), sent by Pen & Tec Consulting SLU, is confidential/privileged and is intended to be read solely by the person(s) to whom it is addressed. We hereby inform you that your data will be incorporated into the processing system owned by Pen & Tec Consulting SLU, and that provided it complies with the requirements included in the law, you may exercise the rights of access, rectification, limitation of processing, deletion, portability and opposition by sending your request to the postal address Pl. Ausias March 1, 4 floor 08195, Sant Cugat del Valles (Barcelona) or to the email address info@pentec-consulting.eu. If you read this message and you are neither the intended recipient, employee or agent in charge of delivering the message to the recipient, or if you have received this message as the result of an error, we hereby inform you that distributing, sharing or reproducing any part of this message is totally forbidden and may be illegal. As a result, we request that you immediately inform us of the error and return this message to the address mentioned above. Thank you.

From: Nikolaas Tilkin-Franssens <niko@pentec-consulting.eu>

Date: Tuesday, 11 July 2023 at 17:03

To: DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>

Cc: Justyna Pałasińska <justyna@pentec-consulting.eu>

Subject: Re: GRN 1122 canola concentrate items for clarification - Reply

Dear Stephen,

Thank you for reaching out with the questions for clarification.
We have worked closely with Napiferyn to close the doubts.

Kindly find attached a Word file including the Questions&Answers, a report on the requested literature review, a SDS sheet as requested by the USDA-FSIS, and a report on the suitability assessment.

We remain available for any further questions or updates.

Thanks for taking the application in further consideration,
best regards,

Nikolaas Tilkin-Franssens

Regulatory Affairs Manager | Pen & Tec Consulting

T +34 936 758 015 M +34 649 840 417 F +34 936 758 016 www.pentec-consulting.eu

Pl. Ausias March 1 | 4th floor D01 | 08195 Sant Cugat del Vallès | Barcelona | Spain



La información contenida en este mensaje y/o archivo(s) adjunto(s), enviada desde Pen & Tec Consulting SLU, es confidencial/privilegiada y está destinada a ser leída sólo por la(s) persona(s) a la(s) que va dirigida. Le recordamos que sus datos han sido incorporados en el sistema de tratamiento de Pen & Tec Consulting SLU y que siempre y cuando se cumplan los requisitos exigidos por la normativa, usted podrá ejercer sus derechos de acceso, rectificación, limitación de tratamiento, supresión, portabilidad y oposición/revocación, en los términos que establece la normativa vigente en materia de protección de datos, dirigiendo su petición a la dirección postal Pl. Ausias March 1, 4 planta 08195, Sant Cugat del Vallès (Barcelona) o bien a través de correo electrónico info@pentec-consulting.eu. Si usted lee este mensaje y no es el destinatario señalado, el empleado o el agente responsable de entregar el mensaje al destinatario, o ha recibido esta comunicación por error, le informamos que está totalmente prohibida, y puede ser ilegal, cualquier divulgación, distribución o reproducción de esta comunicación, y le rogamos que nos lo notifique inmediatamente y nos devuelva el mensaje original a la dirección arriba mencionada. Gracias.

The information contained in this message and/or attached file(s), sent by Pen & Tec Consulting SLU, is confidential/privileged and is intended to be read solely by the person(s) to whom it is addressed. We hereby inform you that your data will be incorporated into the processing system owned by Pen & Tec Consulting SLU, and that provided it complies with the requirements included in the law, you may exercise the rights of access, rectification, limitation of processing, deletion, portability and opposition by sending your request to the postal address Pl. Ausias March 1, 4 floor 08195, Sant Cugat del Valles (Barcelona) or to the email address info@pentec-consulting.eu. If you read this message and you are neither the intended recipient, employee or agent in charge of delivering the message to the recipient, or if you have received this message as the result of an error, we hereby inform you that distributing, sharing or reproducing any part of this message is totally forbidden and may be illegal. As a result, we request that you immediately inform us of the error and return this message to the address mentioned above. Thank you.

From: DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>

Date: Wednesday, 28 June 2023 at 17:41

To: Nicoleta Pasecinic <nicoleta@pentec-consulting.eu>

Cc: Nikolaas Tilkin-Franssens <niko@pentec-consulting.eu>

Subject: [EXTERNAL]: GRN 1122 canola concentrate items for clarification

CAUTION: This email originated from outside of the organization. Do not click links or open attachments unless you recognize the sender and know the content is safe.

Hello Ms. Pasecinic,

After evaluating NapiFeryn's GRAS Notice No. GRN 1122 on canola concentrate we noted a few issues that should be addressed. Please respond to the following points for clarification:

1. On p. 9, NapiFeryn states that the major storage proteins in canola seed are cruciferins and napins, and that canola concentrate consists of 30-45% protein and 40-70% dietary fiber. Please provide the typical cruciferin content and napin content in canola concentrate.
2. Please confirm that all raw materials and processing aids used in the manufacturing process are used in accordance with the U.S. regulations, are GRAS for their respective uses or are the subject of an effective food contact notification. For the record, we note that the food additive regulations cited in Table 4 (p. 15) for ascorbic acid (21 CFR 182.8013), ethanol (21 CFR 184.1293), and ethyl acetate (21 CFR 173.228) do not appear to be applicable to your intended uses of these substances.
3. In Table 6 (p. 18-19), NapiFeryn provides the results from the batch analyses for heavy metals. We would like to bring to your attention a relevant FDA's "[Closer to Zero](#)" initiative that focuses on reducing the levels of heavy metals in foods and recommend that you lower the specification limits for heavy metal to better reflect the batch analyses results and to be as low as possible.
4. In Table 10 (p. 22), NapiFeryn provides batch analyses data for residual solvents and processing aids. In addition, in Table 21 (p. 50), you provided the results from the batch analyses for erucic acid in your canola concentrate ranging from 0.37% to < 0.1%.
Please include limits for residual ethanol, ethyl acetate, and sulphur dioxide as well as a limit for erucic acid in the specifications for canola concentrate and specify the analytical methods used to test for these parameters.
In addition, please provide an updated Tables 5 and 6 (p. 16-19) to include the additional specification parameters mentioned above, corresponding analytical methods, and batch analyses.
5. Please state that all analytical methods used to test batches were validated and are fit for their respective purpose.
6. Please state that canola concentrate is not intended for use in infant formula or in foods where standards of identity preclude its use.
7. In Table 15 (p.), NapiFeryn provides the results of the batch analyses for total plate count in the raw material (rapeseed press cake). Please address the significant variation in the results (from <10 to 28,000 CFU/g) and discuss whether this will impact safety of the final ingredient.
8. On p. 19, NapiFeryn states that the levels of mycotoxins in canola concentrate are below the limit of quantitation (LOQ) and provide the results from the analyses of five batches to support your statement. Please clarify whether you expect mycotoxins to be present in canola concentrate manufactured in accordance with good manufacturing practices.
9. In Part 1.4 (p. 6) and Part 3.1 (p. 33), NapiFeryn states that the intended use of canola concentrate is as a source of protein and/or fiber, thickener, or texturizer. However, we note that on p. 33 you also state the intended use of canola concentrate is as a flavoring agent or binder in various comminuted or whole muscle meat and poultry products. In addition, in Appendix 3 (p. 5) you state that canola concentrate may also be used "to create a flavored salt" or as "a flavor enhancer like monosodium glutamate". Please confirm these additional uses of canola concentrate are within the scope of GRN 001122.
10. On p. 10, the notifier describes the protein composition of canola concentrate, being primarily cruciferins, napin, oleosin, and squalene monooxygenase. However, the pivotal safety data provided appear to only be relevant to the cruciferin and napin fractions of the canola concentrate. Please provide a brief narrative to confirm the safety of oleosin and squalene monooxygenase exposure from the intended uses.
11. On p. 31-32 of the notice, the notifier clearly establishes that canola concentrate is intended to be substitutive to protein and fiber consumption and will not contribute to additional exposure to protein or fiber in general. Please elaborate on this conclusion, and clarify if the intended uses of canola concentrate are additive or substitutive to other canola protein products currently on the market (i.e., GRNs 327, 386, and 683)?
12. On p. 37, the notifier concludes exposure to canola concentrate from the intended uses is safe since the EDI reported is "still much lower (approximately 7- to 22-fold lower) than the no-observed-adverse-effect level (NOAEL) values established" for cruciferin- and napin-rich protein isolates in male rats following a 13-week oral exposure regimen (Mejia *et al.*, 2009a & 2009b). We note that an uncertainty factor, or margin of safety (MOS), of 100 (10 for interindividual variability × 10 for interspecies variability) is normally used when assessing safety of a food ingredient by comparing estimated human exposure levels to the NOAEL from animal toxicology data. Therefore, it is not clear why MOS that is ~5-10-fold lower can be concluded as safe without proper justification. Additionally, we note that potential thyrotoxic effects were observed at the highest doses in these two rat studies, as well as for rapeseed products in general tested in other species, as cited in Table 20 of the GRAS notice. This effect was mostly attributed to the presence of glucosinolate; however, we note that since the level of glucosinolate was low or absent in both the test articles from Mejia *et al.* and the article of commerce, the rationale used by the study authors to conclude that the observed NOAEL was not in fact the LOAEL may be questionable. Regardless, it appears that the provided safety narrative lacks sufficient basis to conclude MOS of 7-22 is adequate to reach the conclusion of "reasonable certainty of no harm." Based on generally available data and information, please provide additional narrative

to explain your rationale for your GRAS conclusion.

13. We note that when discussing the absorption, distribution, metabolism, and excretion of canola concentrate (p. 49), the notifier reports unpublished data from an EU Novel Foods application for “defatted rapeseed powder” to support their conclusion. Similarly, genotoxicity conclusions are made using unpublished data from an EFSA Panel conclusion on defatted rapeseed powder. Given other data and information have been used in prior GRAS notices for canola ingredients (e.g., GRN 327), please confirm that the EFSA Panel and EU Novel Foods conclusions are only considered as corroborative, not pivotal, to the safety determination of canola concentrate at its intended use level?
14. On p. 40, the notifier discusses the allergenicity potential of canola concentrate being determined via a “bioinformatics approach” and concludes that canola concentrate “may elicit possible allergenic effects.” Additionally, on p. 59 the notifier reiterates that the bioinformatics analysis indicated “possible allergenic effects” of canola concentrate, but no further discussion is provided. While data from an allergen online database search is provided as part of Appendix 4, no discussion of these data are included in the current GRAS notice. Please briefly detail the “possible allergenic effects” of canola concentrate similar to previous notices (e.g., GRN 683), and discuss why they would not be expected to pose a safety concern from the intended use.
15. We note that a recent study on rapeseed protein isolate was published (Xiong et al., 2022).
 1. Please discuss if this study presents additional safety concerns for the article of commerce or contradicts the current GRAS conclusion.
 2. Please also perform an updated literature review from 2021 to present and discuss if any additional studies relevant to the safety of canola concentrate were identified that would contradict the current GRAS conclusion.

References cited:

Xiong Z, Fu Y, Yao J, Zhang N, He R, Ju X, Wang Z. Removal of anti-nutritional factors of rapeseed protein isolate (RPI) and toxicity assessment of RPI. *Food Funct.* 2022 Jan 24;13(2):664-674. doi: 10.1039/d1fo03217h. PMID: 34933325.

Additionally, we received the following questions from USDA FSIS regarding their review of the uses of GRN 1122 concerning products within their purview. Please respond to the following and we will pass your responses along to them.

Please provide Safety Data Sheet (SDS) for the at use concentrations of the substance and include a description of how the use of this technology will not adversely affect the safety of FSIS inspectors. Workplace safety and health hazards include inhalation, direct skin contact (skin, eyes, mouth), and fire/explosion caused by exposure to the product, its working solution or dry mixture and potential by-products formed and/or off-gassed during the application process. The employee safety information should demonstrate how the New Technology will not “jeopardize the safety of Federal inspection personnel” as specified in the [FSIS Compliance Guideline Procedures for New Technology Notifications and Protocols, April 2015](#). FSIS workplace and employee safety must be specifically addressed. Please refer to Appendix A on p. 17, Workplace Safety and Health Criteria, for clarification on what to provide in the response. For additional clarity with respect to employee safety, the following are examples of information that are typically needed by FSIS’ employee safety and health group;

1. Potential workplace exposures that could result from inhalation and direct contact during use of the substance/technology. This information is required in addition to a SDS to determine accurate hazard potential and recommended exposure control measures for IPP work areas in accordance with Occupational Safety and Health Administration (OSHA) regulations: 29 CFR 1910.1200, Hazard Communication, 29 CFR 1910.132, Personal Protective Equipment, and 29 CFR 1910.1000, Air Contaminants. The information should be included as a specific section in each of the protocols.
2. If the SDS workplace hazards/precautions do not apply to the type of exposure that would be expected for the FSIS IPP, please have the submitter provide specific information (per the April 2015 FSIS Compliance Guideline Procedures) for the actual type of exposures expected.
3. If no IPP workplace exposures are expected and no control measures are required, please have the submitter state this and provide the reasons why (e.g., such as the substance “as used” [for all concentrations] is not hazardous by inhalation or direct contact and/or IPP would not be exposed to the substance based on the system design, operation and/or control measures that will be in place).
4. Please also indicate how will FSIS IPP be informed of the above information so that it is clear that the information contained in the SDS for the concentrate does not apply to their actual workplace exposure.
5. Are there any potential hazards from chemical mixing or low pH as a result of discharges of the various solutions to floor drains? Are dedicated drain lines or any other enclosures required?
6. With respect to potential airborne exposures to FSIS IPP in the use/application areas, does the submitter have air sampling results taken during the use of the various concentrations of the technology in the listed mixture?
7. The intended use of this product in FSIS meat and poultry products is apparently as a binder/extender. The suitability support provided in Appendix 6 does sufficiently support no significant difference in yield and other organoleptic qualities when used as a partial replacement for another binder in a processed meat and poultry product, such as sausage.

However, **additional suitability support is needed:**

1. No suitability data was provided for **whole muscle meat and poultry products at the maximum proposed use level**. We would need to see similar data as provided in Appendix 6 for:
 - Whole muscle red meat control containing no other binders, extenders, or moisture retention agents, as compared to a whole muscle red meat product containing 15% isolated canola product.
 - Whole muscle poultry control containing no other binders, extenders, or moisture retention agents as compared to a whole

muscle poultry product containing 15% isolated canola product.

Responses may be sent in an email or in a separate document. We respectfully request a response within 10 business days. If you are unable to complete the response within that time frame, please contact me to discuss further options.

If you have any additional questions or concerns, please don't hesitate to contact me at stephen.difranco@fda.hhs.gov or by phone at 240.402.2710.

Best,
Steve

Stephen DiFranco, PhD

Regulatory Review Scientist/Chemist

Center for Food Safety and Applied Nutrition

Office of Food Additive Safety

Division of Food Ingredients

U.S. Food and Drug Administration

Tel: 240-402-2710

stephen.difranco@fda.hhs.gov



CAUTION: This email, including any attachments, is confidential. If you are not the intended recipient, please notify the sender and delete the email and any attachments from your system. In addition, you must not use, distribute or reproduce this email or any attachments. Opinions and other information in this email and any attachments which do not relate to the official business of Argenta are neither given by nor endorsed by Argenta. While Argenta uses anti-virus software, Argenta accepts no liability for any viruses in this email or any attachment, or for any effects this email or any attachment may have on your network or computer system.

CAUTION: This email, including any attachments, is confidential. If you are not the intended recipient, please notify the sender and delete the email and any attachments from your system. In addition, you must not use, distribute or reproduce this email or any attachments. Opinions and other information in this email and any attachments which do not relate to the official business of Argenta are neither given by nor endorsed by Argenta. While Argenta uses anti-virus software, Argenta accepts no liability for any viruses in this email or any attachment, or for any effects this email or any attachment may have on your network or computer system.

Este correo electrónico y los archivos adjuntos, enviados por Pen & Tec Consulting SLU, que opera bajo el nombre comercial de Argenta® (Argenta), son confidenciales y pueden estar protegidos por ley. Si usted no es el destinatario, cualquier divulgación, reproducción, copia, distribución u otro tipo de difusión o uso de esta comunicación está estrictamente prohibido. Si ha recibido esta transmisión por error, notifíquelo al remitente y elimine inmediatamente el correo electrónico y cualquier archivo adjunto de su sistema. Argenta no emite ni respalda las opiniones y demás información contenida en este correo electrónico y en sus anexos que no estén relacionadas con las actividades oficiales de Argenta. Aunque Argenta utiliza software antivirus, Argenta no acepta ninguna responsabilidad por cualquier virus en este correo electrónico o cualquier archivo adjunto, o por cualquier efecto que este correo electrónico o cualquier archivo adjunto pueda tener en su red o sistema informático. Argenta registra y almacena los correos electrónicos enviados a nosotros o a nuestros afiliados de acuerdo con nuestras políticas y procedimientos internos. Consulte www.pentec-consulting.eu para obtener información sobre Argenta y/o nuestra política de privacidad.

This email and any attached file(s), sent by Pen & Tec Consulting SLU trading as Argenta® (Argenta), are confidential and may be legally privileged. If you are not the intended recipient, any disclosure, reproduction, copying, distribution, or other dissemination or use of this communication is strictly prohibited. If you have received this transmission in error, please notify the sender and delete the email and any attachments from your system immediately. Opinions and other information in this email and any attachments which do not relate to the official business of Argenta are neither given by nor endorsed by Argenta. While Argenta uses anti-virus software, Argenta accepts no liability for any viruses in this email or any attachment, or for any effects this email or any attachment may have on your network or computer system. Argenta records and stores emails sent to us or our affiliates in keeping with our internal policies and procedures. Please see www.pentec-consulting.eu for information regarding Argenta and/or our privacy policy.

Este correo electrónico y los archivos adjuntos, enviados por Pen & Tec Consulting SLU, que opera bajo el nombre comercial de Argenta® (Argenta), son confidenciales y pueden estar protegidos por ley. Si usted no es el destinatario, cualquier divulgación, reproducción, copia, distribución u otro tipo de difusión o uso de esta comunicación está estrictamente prohibido. Si ha recibido esta transmisión por error, notifíquelo al remitente y elimine inmediatamente el correo electrónico y cualquier archivo adjunto de su sistema. Argenta no emite ni respalda las opiniones y demás información contenida en este correo electrónico y en sus anexos que no estén relacionadas con las actividades oficiales de Argenta. Aunque Argenta utiliza software antivirus, Argenta no acepta ninguna responsabilidad por cualquier virus en este correo electrónico o cualquier archivo adjunto, o por cualquier efecto que este correo electrónico o cualquier archivo adjunto pueda tener en su red o sistema informático. Argenta registra y almacena los correos electrónicos enviados a nosotros o a nuestros afiliados de acuerdo con nuestras políticas y procedimientos internos. Consulte www.pentec-consulting.eu para obtener información sobre Argenta y/o nuestra política de privacidad.

This email and any attached file(s), sent by Pen & Tec Consulting SLU trading as Argenta® (Argenta), are confidential and may be legally privileged. If you are not the intended recipient, any disclosure, reproduction, copying, distribution, or other dissemination or use of this communication is strictly prohibited. If you have received this transmission in error, please notify the sender and delete the email and any attachments from your system immediately. Opinions and other information in this email and any attachments which do not relate to the official business of Argenta are neither given by nor endorsed by Argenta. While Argenta uses anti-virus software, Argenta accepts no liability for any viruses in this email or any attachment, or for any effects this email or any attachment may have on your network or computer system. Argenta records and stores emails sent to us or our affiliates in keeping with our internal policies and procedures. Please see www.pentec-consulting.eu for information regarding Argenta and/or our privacy policy.

Este correo electrónico y los archivos adjuntos, enviados por Pen & Tec Consulting SLU, que opera bajo el nombre comercial de Argenta® (Argenta), son confidenciales y pueden estar protegidos por ley. Si usted no es el destinatario, cualquier divulgación, reproducción, copia, distribución u otro tipo de difusión o uso de esta comunicación está estrictamente prohibido. Si ha recibido esta transmisión por error, notifíquelo al remitente y elimine inmediatamente el correo electrónico y cualquier archivo adjunto de su sistema. Argenta no emite ni respalda las opiniones y demás información contenida en este correo electrónico y en sus anexos que no estén relacionadas con las actividades oficiales de Argenta. Aunque Argenta utiliza software antivirus, Argenta no acepta ninguna responsabilidad por cualquier virus en este correo electrónico o cualquier archivo adjunto, o por cualquier efecto que este correo electrónico o cualquier archivo adjunto pueda tener en su red o sistema informático. Argenta registra y almacena los correos electrónicos enviados a nosotros o a nuestros afiliados de acuerdo con nuestras políticas y procedimientos internos. Consulte www.pentec-consulting.eu para obtener información sobre Argenta y/o nuestra política de privacidad.

This email and any attached file(s), sent by Pen & Tec Consulting SLU trading as Argenta® (Argenta), are confidential and may be legally privileged. If you are not the intended recipient, any

From: [Justyna Pałasińska](#)
To: [DiFranco, Stephen](#)
Subject: Re: [EXTERNAL] GRN 1122 canola concentrate status
Date: Thursday, August 8, 2024 9:39:31 AM
Attachments: [image005.png](#)
[Outlook-Image.png](#)
[Outlook-Image.png](#)

CAUTION: This email originated from outside of the organization. Do not click links or open attachments unless you recognize the sender and know the content is safe.

Many thanks, Steve.

I have confirmed with the applicant that they agree with your proposal.

On another note, would you be able to estimate when the GRN will be published in the Inventory?

Thanks again for all your support.

Kind regards,
Justyna Pałasińska
Regulatory Affairs Director – Human Nutrition, Argenta Barcelona



M +34 682 894 653 T +34 936 758 015



La información contenida en este mensaje y/o archivo(s) adjunto(s), enviada desde Pen & Tec Consulting SLU cotiza como Argenta, es confidencial/privilegiada y está destinada a ser leída sólo por la(s) persona(s) a la(s) que va dirigida. Le recordamos que sus datos han sido incorporados en el sistema de tratamiento de Pen & Tec Consulting SLU cotiza como Argenta, y que siempre y cuando se cumplan los requisitos exigidos por la normativa, usted podrá ejercer sus derechos de acceso, rectificación, limitación de tratamiento, supresión, portabilidad y oposición/revocación, en los términos que establece la normativa vigente en materia de protección de datos, dirigiendo su petición a la dirección postal OneCoWork, Portal de l'Àngel 40, 08002, Barcelona o bien a través de correo electrónico info@pentec-consulting.eu. Si usted lee este mensaje y no es el destinatario señalado, el empleado o el agente responsable de entregar el mensaje al destinatario, o ha recibido esta comunicación por error, le informamos que está totalmente prohibida, y puede ser ilegal, cualquier divulgación, distribución o reproducción de esta comunicación, y le rogamos que nos lo notifique inmediatamente y nos devuelva el mensaje original a la dirección arriba mencionada. Gracias.

The information contained in this message and/or attached file(s), sent by Pen & Tec Consulting SLU trading as Argenta, is confidential/privileged and is intended to be read solely by the person(s) to whom it is addressed. We hereby inform you that your data will be incorporated into the processing system owned by Pen & Tec Consulting SLU, and that provided it complies with the requirements included in the law, you may exercise the rights of access, rectification, limitation of processing, deletion, portability and opposition by sending your request to the postal address OneCoWork, Portal de l'Àngel 40, 08002, Barcelona or to the email address info@pentec-consulting.eu. If you read this message and you are neither the intended recipient, employee or agent in charge of delivering the message to the recipient, or if you have received this message as the result of an error, we hereby inform you that distributing, sharing or reproducing any part of this message is totally forbidden and may be illegal. As a result, we request that you immediately inform us of the error and return this message to the address mentioned above. Thank you.

From: DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>
Sent: 02 August 2024 6:49
To: Justyna Pałasińska <justyna.palasinaska@argentaglobal.com>
Subject: RE: [EXTERNAL] GRN 1122 canola concentrate status

Hi Justyna,

I wanted to follow up on your request to removing “spray” drying from our official response letter. That term appears twice in our response letter (below)

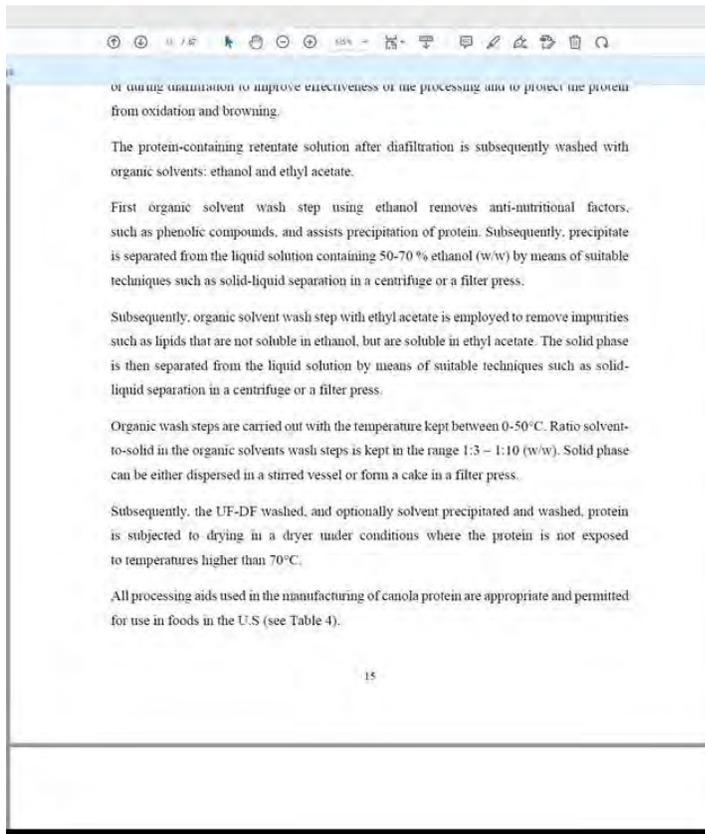
NapiFeryn describes the manufacturing process for canola protein isolate that begins with an aqueous extraction of cold-pressed rapeseed cake to yield an aqueous extract and a solid residue slurry. The aqueous crude extract containing the protein fraction is filtered and centrifuged. Processing aids may be added to aid in the clarification process. The clarified extract is subjected to ultrafiltration and diafiltration to concentrate the protein and remove carbohydrates and anti-nutritional factors. Processing aids may be added to the extract prior to or during diafiltration to improve the effectiveness of the process and to protect the protein from oxidation and browning. The concentrate is spray dried to obtain the final canola protein isolate. NapiFeryn states that optionally the concentrate may be treated with ethanol to precipitate the protein fraction and remove residual anti-nutritional factors. The precipitated solid protein fraction is

² NapiFeryn states that rapeseed press cake is sourced solely from low-erucic acid rapeseed varieties.

Page 3 – Mr. Tilkin-Franssens

separated and may be subjected to further washes with ethanol or ethyl acetate prior to spray drying. NapiFeryn states that canola protein isolate is manufactured according to current good manufacturing practices using food grade raw materials and processing aids that are appropriate for use in the manufacture of food in the U.S.

You are correct in that the original notice does not specify the method of drying only stating on page 15 of the notice that the “...protein is subjected to drying in a dryer....” (below).



In a follow up email (below) you provided the following clarification describing a route “If spray drying is employed...” The amendment goes on to talk about alternate processing in which the product “may be subjected to further solvent washes with ethanol or ethyl acetate, to be finally subjected to drying.” I believe this may be how “spray drying” was incorporated into the letter even though that term does not appear in the original notice—but in a clarifying amendment to the

notice.

In the passage from the amendment the first method of drying is clearly stated as “spray drying”. I believe our reviewer took that the “*finally subjected to drying*” after the additional solvent wash steps also to mean “spray drying”.

In terms of our response letter, I believe it most accurately reflects what was described in the amendment if we leave the first occurrence of “spray drying” in the letter. It looks that in the second occurrence of “spray drying” in the letter, the method of drying was not specified, and we would be amenable to changing this simply to “drying”.

Is this the change Napiferyn had in mind? Please let me know and I can work to get a correction to the letter out.

Thanks,

Steve

Pro (32-bit)

From: [Nikolaas Tikin-Franssens](#)
To: [DiFranco, Stephen](#)
Subject: Re: [EXTERNAL]: GRN 1103 Items for clarification - Reply
Date: Monday, August 28, 2023 4:47:59 AM
Attachments: [image001.png](#)
[image007.png](#)
[image008.png](#)

CAUTION: This email originated from outside of the organization. Do not click links or open attachments unless you recognize the sender and know the content is safe.

Hi Steve,

In this email I provide the set of answers for Canola protein isolate (GRN 1103).

1. In a response to Question 8 (amendment dated June 28, 2023), you state that the results from the batch analyses in Table 7 (page 19) are for canola protein isolate that was subjected to solvent wash and that if the solvent wash step is not employed then there is no need to analyze for solvent residues. We would like to clarify our Question 8. In this question, we requested that you clarify whether you expect higher levels of the impurities (or any additional impurities) to be present in the final ingredient that is not subjected to the solvent precipitation and wash steps compared to the ingredient that is subjected to the solvent precipitation and wash steps. Please provide this information to sufficiently address Question 8.

Answer: Yes, we would expect slightly higher levels of some impurities. Solvent wash steps are used to remove impurities such as lipids and remove anti-nutritional factors, such as phenolic compounds.

Solvent wash steps are optional and if employed, they are subsequent to ultrafiltration step, in which all impurities specified in the specification are being washed out to the required levels during the diafiltration step. After this mandatory step is completed, the process to obtain protein isolate may take two mutually exclusive routes: ethanol wash step or spray drying (solvent-free route). If spray drying is employed, the process of obtaining protein isolate is not different from the ones already disclosed in the GRN327, GRN386, GRN683. If the ethanol wash step is employed, the protein is isolated from the concentrated retentate after ultrafiltration by the effect of addition of ethanol to the solution/suspension of protein in water. Because of effectuated change in the polarity of the resulting mixture as compared to water, protein is precipitating as an amorphous solid phase. Worth to notice is that supernatant may still contain some minute residues of impurities that have not been washed out in the ultrafiltration step. In particular, the Applicant has found out that some phenolic compounds such as sinapic acid and its derivatives (Kaempferol 3-O-(2''-O-Sinapoyl)-β-sophoroside) that may render bitter taste notes to the protein isolate¹ are effectively separated from the protein isolate if the ethanolic wash step is employed. Subsequently after ethanolic wash the solid liquid separation step is employed to obtain solid cake (ca 20-30% dry mass) which may be subjected to further solvent washes with ethanol or ethyl acetate, to be finally subjected to drying. Employing ethyl acetate wash brings the advantage of removal of the residues of fats and lipids, if present in the protein isolated in the ethanolic wash step. Additionally, replacing high boiling point solvents (ethanol-water mixture after ethanolic step) with low-boiling point ethyl acetate enables lowering of the production costs associated with the drying of the final isolate.

References:
1: Christoph Hald, Corinna Dawid, Ralf Tressel, and Thomas Hofmann Journal of Agricultural and Food Chemistry 2019 67 (1), 372-378. DOI: 10.1021/acs.jafc.8b06260.

Stephen DiFranco, PhD
Regulatory Review Scientist/Chemist

Center for Food Safety and Applied Nutrition
Office of Food Additive Safety

Division of Food Ingredients
U.S. Food and Drug Administration
Tel: 240-402-2710
stephen.difranco@fda.hhs.gov



From: Justyna Pałasińska <justyna.palasincka@argentaglobal.com>
Sent: Wednesday, July 31, 2024 11:29 AM
To: DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>
Subject: Re: [EXTERNAL] GRN 1122 canola concentrate status

CAUTION: This email originated from outside of the organization. Do not click links or open attachments unless you recognize the sender and know the content is safe.

Many thanks for the good news, Steve! & for all your patience & assistance.

A small comment - we noticed a minor typo - the text states NepiFeryn (p.4). Would it be possible to correct it in the published version?

We also noticed a small inconsistency in the 'sister notice' for canola isolate (GRN 1103, attached for reference). Pages 2&3 refer to spray drying, while Napiferyn did not refer to this specifically in their notice & would like to keep the exact drying method open. Would it be possible to remove the reference to 'spray' in the published version?

Kind regards,
Justyna Pałasińska
Regulatory Affairs Director – Human Nutrition, Argenta Barcelona



M +34 682 894 653 T +34 936 758 015

www.argentaglobal.com

Image



La información contenida en este mensaje y/o archivo(s) adjunto(s), enviada desde Pen & Tec Consulting SLU cotiza como Argenta, es confidencial/privilegiada y está destinada a ser leída sólo por la(s) persona(s) a la(s) que va dirigida. Le recordamos que sus datos han sido incorporados en el sistema de tratamiento de Pen & Tec Consulting SLU cotiza como Argenta, y que siempre y cuando se cumplan los requisitos exigidos por la normativa, usted podrá ejercer sus derechos de acceso, rectificación, limitación de tratamiento, supresión, portabilidad y oposición/revocación, en los términos que establece la normativa vigente en materia de protección de datos, dirigiendo su petición a la dirección postal OneCoWork, Portal de l'Àngel 40, 08002, Barcelona o bien a través de correo electrónico info@pentec-consulting.eu. Si usted lee este mensaje y no es el destinatario señalado, el empleado o el agente responsable de entregar el mensaje al destinatario, o ha recibido esta comunicación por error, le informamos que está totalmente prohibida, y puede ser ilegal, cualquier divulgación, distribución o reproducción de esta comunicación, y le rogamos que nos lo notifique inmediatamente y nos devuelva el mensaje original a la dirección arriba mencionada. Gracias.
The information contained in this message and/or attached file(s), sent by Pen & Tec Consulting SLU trading as Argenta, is confidential/privileged and is intended to be read solely by the person(s) to whom it is addressed. We hereby inform you that your data will be incorporated into the processing system owned by Pen & Tec Consulting SLU, and that provided it complies with the requirements included in the law, you may exercise the rights of access, rectification, limitation of processing, deletion, portability and opposition by sending your request to the postal address OneCoWork, Portal de l'Àngel 40, 08002, Barcelona or to the email address info@pentec-consulting.eu. If you read this message and you are neither the intended recipient, employee or agent in charge of delivering the message to the recipient, or if you have received this message as the result of an error, we hereby inform you that distributing, sharing or reproducing any part of this message is totally forbidden and may be illegal. As a result, we request that you immediately inform us of the error and return this message to the address mentioned above. Thank you.

From: DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>
Sent: 30 July 2024 18:57
To: Justyna Pałasińska <justyna.palasincka@argentaglobal.com>
Subject: RE: [EXTERNAL] GRN 1122 canola concentrate status

Hello Justyna,

Please see the attached letter regarding GRN 1122. We appreciate your patience on this one.

Best,

Steve

Stephen DiFranco, PhD
Regulatory Review Scientist/Chemist

Center for Food Safety and Applied Nutrition
Office of Food Additive Safety
Division of Food Ingredients
U.S. Food and Drug Administration
Tel: 240-402-2710
stephen.difranco@fda.hhs.gov





From: Justyna Pałasińska <justyna.palasincka@argentaglobal.com>
Sent: Monday, July 29, 2024 10:41 AM
To: DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>
Subject: Re: [EXTERNAL] GRN 1122 canola concentrate status

CAUTION: This email originated from outside of the organization. Do not click links or open attachments unless you recognize the sender and know the content is safe.

Dear Steve,

I was wondering if you could share an update on the GRN 1122? Can you estimate when can we expect the response letter?

Kind regards,

Justyna Pałasińska

Regulatory Affairs Director – Human Nutrition, Argenta Barcelona



M +34 682 894 653 T +34 936 758 015

www.argentaglobal.com

Image



La información contenida en este mensaje y/o archivo(s) adjunto(s), enviada desde Pen & Tec Consulting SLU cotiza como Argenta, es confidencial/privilegiada y está destinada a ser leída sólo por la(s) persona(s) a la(s) que va dirigida. Le recordamos que sus datos han sido incorporados en el sistema de tratamiento de Pen & Tec Consulting SLU cotiza como Argenta, y que siempre y cuando se cumplan los requisitos exigidos por la normativa, usted podrá ejercer sus derechos de acceso, rectificación, limitación de tratamiento, supresión, portabilidad y oposición/revocación, en los términos que establece la normativa vigente en materia de protección de datos, dirigiendo su petición a la dirección postal OneCoWork, Portal de l'Àngel 40, 08002, Barcelona o bien a través de correo electrónico info@pentec-consulting.eu. Si usted lee este mensaje y no es el destinatario señalado, el empleado o el agente responsable de entregar el mensaje al destinatario, o ha recibido esta comunicación por error, le informamos que está totalmente prohibida, y puede ser ilegal, cualquier divulgación, distribución o reproducción de esta comunicación, y le rogamos que nos lo notifique inmediatamente y nos devuelva el mensaje original a la dirección arriba mencionada. Gracias.
The information contained in this message and/or attached file(s), sent by Pen & Tec Consulting SLU trading as Argenta, is confidential/privileged and is intended to be read solely by the person(s) to whom it is addressed. We hereby inform you that your data will be incorporated into the processing system owned by Pen & Tec Consulting SLU, and that provided it complies with the requirements included in the law, you may exercise the rights of access, rectification, limitation of processing, deletion, portability and opposition by sending your request to the postal address OneCoWork, Portal de l'Àngel 40, 08002, Barcelona or to the email address info@pentec-consulting.eu. If you read this message and you are neither the intended recipient, employee or agent in charge of delivering the message to the recipient, or if you have received this message as the result of an error, we hereby inform you that distributing, sharing or reproducing any part of this message is totally forbidden and may be illegal. As a result, we request that you immediately inform us of the error and return this message to the address mentioned above. Thank you.

From: Justyna Pałasińska <justyna.palasincka@argentaglobal.com>
Sent: 03 July 2024 17:44
To: DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>
Subject: Re: [EXTERNAL] GRN 1122 canola concentrate status

Thank you very much for your clarification, Steve.

Following your advice: we wish to amend the notice by removing the claim that this ingredient is used as a source of dietary fiber and that we wish to add that it may be used "as an ingredient" in the food categories listed within the notice.

Please let me know if anything else is needed from our side.

Kind regards,

Justyna Pałasińska

Regulatory Affairs Director – Human Nutrition, Argenta Barcelona



M +34 682 894 653 T +34 936 758 015

www.argentaglobal.com

Image



La información contenida en este mensaje y/o archivo(s) adjunto(s), enviada desde Pen & Tec Consulting SLU cotiza como Argenta, es confidencial/privilegiada y está destinada a ser leída sólo por la(s) persona(s) a la(s) que va dirigida. Le recordamos que sus datos han sido incorporados en el sistema de tratamiento de Pen & Tec Consulting SLU cotiza como Argenta, y que siempre y cuando se cumplan los requisitos exigidos por la normativa, usted podrá ejercer sus derechos de acceso, rectificación, limitación de tratamiento, supresión, portabilidad y oposición/revocación, en los términos que establece la normativa vigente en materia de protección de datos, dirigiendo su petición a la dirección postal OneCoWork, Portal de l'Àngel 40, 08002, Barcelona o bien a través de correo electrónico info@pentec-consulting.eu. Si usted lee este mensaje y no es el destinatario señalado, el empleado o el agente responsable de entregar el mensaje al destinatario, o ha recibido esta comunicación por error, le informamos que está totalmente prohibida, y puede ser ilegal, cualquier divulgación, distribución o reproducción de esta comunicación, y le rogamos que nos lo notifique inmediatamente y nos devuelva el mensaje original a la dirección arriba mencionada. Gracias.
The information contained in this message and/or attached file(s), sent by Pen & Tec Consulting SLU trading as Argenta, is confidential/privileged and is intended to be read solely by the person(s) to whom it is addressed. We hereby inform you that your data will be incorporated into the processing system owned by Pen & Tec Consulting SLU, and that provided it complies with the requirements included in the law, you may exercise the rights of access, rectification, limitation of processing, deletion, portability and opposition by sending your request to the postal address OneCoWork, Portal de l'Àngel 40, 08002, Barcelona or to the email address info@pentec-consulting.eu. If you read this message and you are neither the intended recipient, employee or agent in charge of delivering the message to the recipient, or if you have received this message as the result of an error, we hereby inform you that distributing, sharing or reproducing any part of this message is totally forbidden and may be illegal. As a result, we request that you immediately inform us of the error and return this message to the address mentioned above. Thank you.

From: DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>
Sent: 02 July 2024 20:49
To: Justyna Pałasińska <justyna.palasincka@argentaglobal.com>
Subject: RE: [EXTERNAL] GRN 1122 canola concentrate status

Hello Justyna,

I appreciate the quick response. Per your questions:

- The issue is only with the claim that the ingredient is a source of fiber. You may still make the other claims and claim it is a source of protein—and just add the technical effect ‘as an ingredient’. This is kind of a general, catch all term. There are different regulations addressing claims of source of protein, and this fits.
- You may keep use in all categories that are currently in the notice. This change does not require a different exposure estimate or any other change such as in use. The issue is really about what nutritional claims you can make about the ingredient, not its safety in these uses.
- You do not have to do any sort of rewrite or resubmit the notice. You can simply email me stating you wish to amend the notice by removing the claim that this ingredient is used as a source of dietary fiber and that you wish to add that it may be used “as an ingredient” in the food categories listed. In other words you are adding “as an ingredient” to the notified technical effects of the substance in food. That will be sufficient and we should be able to get this closed out shortly thereafter.

Happy to discuss if you have any other questions.

Best,

Steve

Stephen DiFranco, PhD

Regulatory Review Scientist/Chemist

Center for Food Safety and Applied Nutrition
Office of Food Additive Safety
Division of Food Ingredients
U.S. Food and Drug Administration
Tel: 240-402-2710
stephen.difranco@fda.hhs.gov



From: Justyna Pałasińska <justyna.palasincka@argentaglobal.com>

Sent: Tuesday, July 2, 2024 10:59 AM

To: DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>

Subject: Re: [EXTERNAL] GRN 1122 canola concentrate status

CAUTION: This email originated from outside of the organization. Do not click links or open attachments unless you recognize the sender and know the content is safe.

Many thanks for your swift reply, Steve.

We will update the GRAS & get the updated version to you shortly. I wanted to check a couple questions with you:

- understand the issue is with 'source of fiber' & not with other claims, e.g. 'source of protein'. Could you confirm?
- one of the intended uses is 'protein-fiber and nutritional powders'. I understand that we can keep this category, as the product is a source of protein & therefore can be used as an ingredient for this category of foods. Could you confirm?
- Is it OK for us to send the updated GRAS document by e-mail or do you require a CD-submission?

I look forward to your reply.

Kind regards,

Justyna Pałasińska

Regulatory Affairs Director – Human Nutrition, Argenta Barcelona



M +34 682 894 653 T +34 936 758 015

www.argentaglobal.com

Image



La información contenida en este mensaje y/o archivo(s) adjunto(s), enviada desde Pen & Tec Consulting SLU cotiza como Argenta, es confidencial/privilegiada y está destinada a ser leída sólo por la(s) persona(s) a la(s) que va dirigida. Le recordamos que sus datos han sido incorporados en el sistema de tratamiento de Pen & Tec Consulting SLU cotiza como Argenta, y que siempre y cuando se cumplan los requisitos exigidos por la normativa, usted podrá ejercer sus derechos de acceso, rectificación, limitación de tratamiento, supresión, portabilidad y oposición/revocación, en los términos que establece la normativa vigente en materia de protección de datos, dirigiendo su petición a la dirección postal OneCoWork, Portal de l'Àngel 40, 08002, Barcelona o bien a través de correo electrónico info@pentec-consulting.eu. Si usted lee este mensaje y no es el destinatario señalado, el empleado o el agente responsable de entregar el mensaje al destinatario, o ha recibido esta comunicación por error, le informamos que está totalmente prohibida, y puede ser ilegal, cualquier divulgación, distribución o reproducción de esta comunicación, y le rogamos que nos lo notifique inmediatamente y nos devuelva el mensaje original a la dirección arriba mencionada. Gracias.
The information contained in this message and/or attached file(s), sent by Pen & Tec Consulting SLU trading as Argenta, is confidential/privileged and is intended to be read solely by the person(s) to whom it is addressed. We hereby inform you that your data will be incorporated into the processing system owned by Pen & Tec Consulting SLU, and that provided it complies with the requirements included in the law, you may exercise the rights of access, rectification, limitation of processing, deletion, portability and opposition by sending your request to the postal address OneCoWork, Portal de l'Àngel 40, 08002, Barcelona or to the email address info@pentec-consulting.eu. If you read this message and you are neither the intended recipient, employee or agent in charge of delivering the message to the recipient, or if you have received this message as the result of an error, we hereby inform you that distributing, sharing or reproducing any part of this message is totally forbidden and may be illegal. As a result, we request that you immediately inform us of the error and return this message to the address mentioned above. Thank you.

From: DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>
Sent: 01 July 2024 21:32
To: Justyna Pałasińska <justyna.palasinaska@argentaglobal.com>
Subject: RE: [EXTERNAL] GRN 1122 canola concentrate status

Hello Justyna,

In finalizing our response letter we ran into a bit of an issue regarding the notice's claim that the ingredient is a source of dietary fiber, as this is a legally defined area in US regulations. I got the following from our review team for your consideration:

NapiFeryn states that canola concentrate is intended to be used as a source of dietary fiber amongst other intended uses (i.e., source of protein, formulation aid, stabilizer, thickener, or texturizer). We note that FDA defines dietary fiber as "non-digestible soluble and insoluble carbohydrates (with 3 or more monomeric units), and lignin that are intrinsic and intact in plants; isolated or synthetic non-digestible carbohydrates (with 3 or more monomeric units) determined by FDA to have physiological effects that are beneficial to human health" (21 CFR 101.9(c)(6)(i)). Additional information related to dietary fiber can be found at <https://www.fda.gov/food/food-labeling-nutrition/questions-and-answers-dietary-fiber>.

During our evaluation of GRN 001122 we were not able to determine whether canola concentrate meets the definition of dietary fiber. To proceed with our evaluation of GRN 001122, we recommend that Napiferyn reconsider the description of the intended uses of canola concentrate by replacing the intended use as "a source of dietary fiber" with the use as "an ingredient".

If NapiFeryn wishes to use canola concentrate as a source of dietary fiber, we recommend that you consult with FDA's Office of Nutrition and Food Labeling (ONFL) on whether the ingredient meets the definition of dietary fiber. After ONFL provides a favorable determination, Napiferyn may choose to inform FDA about their GRAS conclusion for the use of canola concentrate as a source of dietary fiber by submitting a supplement to GRN 001122.

Again, amending the notice to state the use is simply as "an ingredient" will allow us to close out this GRAS notice while still allowing the ingredient to be used in foods. If you then wish to have the use as a source of dietary fiber included in the notice and/or displayed on the [GRAS Notice inventory](#), we can go back and amend as appropriate pending the outcome with ONFL.

Happy to discuss if this is unclear.

Thanks,

Steve

Stephen DiFranco, PhD

Regulatory Review Scientist/Chemist

Center for Food Safety and Applied Nutrition
Office of Food Additive Safety
Division of Food Ingredients
U.S. Food and Drug Administration
Tel: 240-402-2710
stephen.difranco@fda.hhs.gov



From: Justyna Pałasińska <justyna.palasinaska@argentaglobal.com>
Sent: Monday, July 1, 2024 8:16 AM
To: DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>
Subject: Re: [EXTERNAL] GRN 1122 canola concentrate status

CAUTION: This email originated from outside of the organization. Do not click links or open attachments unless you recognize the sender and know the content is safe.

Hi Steve,

I hope you are doing well.

Could you let me know when the letter is expected to receive clearance & be shared with the applicant?

Kind regards,

Justyna Pałasińska

Regulatory Affairs Director – Human Nutrition, Argenta Barcelona

M +34 682 894 653 T +34 936 758 015

www.argentaglobal.com

Image



La información contenida en este mensaje y/o archivo(s) adjunto(s), enviada desde Pen & Tec Consulting SLU cotiza como Argenta, es confidencial/privilegiada y está destinada a ser leída sólo por la(s) persona(s) a la(s) que va dirigida. Le recordamos que sus datos han sido incorporados en el sistema de tratamiento de Pen & Tec Consulting SLU cotiza como Argenta, y que siempre y cuando se cumplan los requisitos exigidos por la normativa, usted podrá ejercer sus derechos de acceso, rectificación, limitación de tratamiento, supresión, portabilidad y oposición/revocación, en los términos que establece la normativa vigente en materia de protección de datos, dirigiendo su petición a la dirección postal OneCoWork, Portal de l'Àngel 40, 08002, Barcelona o bien a través de correo electrónico info@pentec-consulting.eu. Si usted lee este mensaje y no es el destinatario señalado, el empleado o el agente responsable de entregar el mensaje al destinatario, o ha recibido esta comunicación por error, le informamos que está totalmente prohibida, y puede ser ilegal, cualquier divulgación, distribución o reproducción de esta comunicación, y le rogamos que nos lo notifique inmediatamente y nos devuelva el mensaje original a la dirección arriba mencionada. Gracias.
The information contained in this message and/or attached file(s), sent by Pen & Tec Consulting SLU trading as Argenta, is confidential/privileged and is intended to be read solely by the person(s) to whom it is addressed. We hereby inform you that your data will be incorporated into the processing system owned by Pen & Tec Consulting SLU, and that provided it complies with the requirements included in the law, you may exercise the rights of access, rectification, limitation of processing, deletion, portability and opposition by sending your request to the postal address OneCoWork, Portal de l'Àngel 40, 08002, Barcelona or to the email address info@pentec-consulting.eu. If you read this message and you are neither the intended recipient, employee or agent in charge of delivering the message to the recipient, or if you have received this message as the result of an error, we hereby inform you that distributing, sharing or reproducing any part of this message is totally forbidden and may be illegal. As a result, we request that you immediately inform us of the error and return this message to the address mentioned above. Thank you.

From: Justyna Pałasińska <justyna.palasinaska@argentaglobal.com>

Sent: 30 May 2024 16:09

To: DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>

Subject: Re: [EXTERNAL] GRN 1122 canola concentrate status

Indeed, great news, thank you Steve!

Kind regards,

Justyna Pałasińska

Regulatory Affairs Director – Human Nutrition, Argenta Barcelona



M +34 682 894 653 T +34 936 758 015

www.argentaglobal.com

Image



La información contenida en este mensaje y/o archivo(s) adjunto(s), enviada desde Pen & Tec Consulting SLU cotiza como Argenta, es confidencial/privilegiada y está destinada a ser leída sólo por la(s) persona(s) a la(s) que va dirigida. Le recordamos que sus datos han sido incorporados en el sistema de tratamiento de Pen & Tec Consulting SLU cotiza como Argenta, y que siempre y cuando se cumplan los requisitos exigidos por la normativa, usted podrá ejercer sus derechos de acceso, rectificación, limitación de tratamiento, supresión, portabilidad y oposición/revocación, en los términos que establece la normativa vigente en materia de protección de datos, dirigiendo su petición a la dirección postal OneCoWork, Portal de l'Àngel 40, 08002, Barcelona o bien a través de correo electrónico info@pentec-consulting.eu. Si usted lee este mensaje y no es el destinatario señalado, el empleado o el agente responsable de entregar el mensaje al destinatario, o ha recibido esta comunicación por error, le informamos que está totalmente prohibida, y puede ser ilegal, cualquier divulgación, distribución o reproducción de esta comunicación, y le rogamos que nos lo notifique inmediatamente y nos devuelva el mensaje original a la dirección arriba mencionada. Gracias.
The information contained in this message and/or attached file(s), sent by Pen & Tec Consulting SLU trading as Argenta, is confidential/privileged and is intended to be read solely by the person(s) to whom it is addressed. We hereby inform you that your data will be incorporated into the processing system owned by Pen & Tec Consulting SLU, and that provided it complies with the requirements included in the law, you may exercise the rights of access, rectification, limitation of processing, deletion, portability and opposition by sending your request to the postal address OneCoWork, Portal de l'Àngel 40, 08002, Barcelona or to the email address info@pentec-consulting.eu. If you read this message and you are neither the intended recipient, employee or agent in charge of delivering the message to the recipient, or if you have received this message as the result of an error, we hereby inform you that distributing, sharing or reproducing any part of this message is totally forbidden and may be illegal. As a result, we request that you immediately inform us of the error and return this message to the address mentioned above. Thank you.

From: DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>

Sent: 30 May 2024 16:06

To: Justyna Pałasińska <justyna.palasinaska@argentaglobal.com>

Subject: RE: [EXTERNAL] GRN 1122 canola concentrate status

Hi Justyna,

I finally have some good news for you—FSIS has just finished their review. I have drafted a response letter and it is currently making its way through clearance, so you should hear back soon.

Best,

Steve

Stephen DiFranco, PhD

Regulatory Review Scientist/Chemist

Center for Food Safety and Applied Nutrition

Office of Food Additive Safety

Division of Food Ingredients

U.S. Food and Drug Administration

Tel: 240-402-2710

stephen.difranco@fda.hhs.gov



From: Justyna Pałasińska <justyna.palasinaska@argentaglobal.com>
Sent: Thursday, May 30, 2024 9:48 AM
To: DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>
Subject: Re: [EXTERNAL] GRN 1122 canola concentrate status

CAUTION: This email originated from outside of the organization. Do not click links or open attachments unless you recognize the sender and know the content is safe.

Dear Stephen,

I hope this e-mail finds you well. I was wondering if there is any update from FSIS on this GRN?

Kind regards,
Justyna Pałasińska
Regulatory Affairs Director – Human Nutrition, Argenta Barcelona



M +34 682 894 653 T +34 936 758 015

www.argentaglobal.com

Image



La información contenida en este mensaje y/o archivo(s) adjunto(s), enviada desde Pen & Tec Consulting SLU cotiza como Argenta, es confidencial/privilegiada y está destinada a ser leída sólo por la(s) persona(s) a la(s) que va dirigida. Le recordamos que sus datos han sido incorporados en el sistema de tratamiento de Pen & Tec Consulting SLU cotiza como Argenta, y que siempre y cuando se cumplan los requisitos exigidos por la normativa, usted podrá ejercer sus derechos de acceso, rectificación, limitación de tratamiento, supresión, portabilidad y oposición/revocación, en los términos que establece la normativa vigente en materia de protección de datos, dirigiendo su petición a la dirección postal OneCoWork, Portal de l'Àngel 40, 08002, Barcelona o bien a través de correo electrónico info@pentec-consulting.eu. Si usted lee este mensaje y no es el destinatario señalado, el empleado o el agente responsable de entregar el mensaje al destinatario, o ha recibido esta comunicación por error, le informamos que está totalmente prohibida, y puede ser ilegal, cualquier divulgación, distribución o reproducción de esta comunicación, y le rogamos que nos lo notifique inmediatamente y nos devuelva el mensaje original a la dirección arriba mencionada. Gracias.

The information contained in this message and/or attached file(s), sent by Pen & Tec Consulting SLU trading as Argenta, is confidential/privileged and is intended to be read solely by the person(s) to whom it is addressed. We hereby inform you that your data will be incorporated into the processing system owned by Pen & Tec Consulting SLU, and that provided it complies with the requirements included in the law, you may exercise the rights of access, rectification, limitation of processing, deletion, portability and opposition by sending your request to the postal address OneCoWork, Portal de l'Àngel 40, 08002, Barcelona or to the email address info@pentec-consulting.eu. If you read this message and you are neither the intended recipient, employee or agent in charge of delivering the message to the recipient, or if you have received this message as the result of an error, we hereby inform you that distributing, sharing or reproducing any part of this message is totally forbidden and may be illegal. As a result, we request that you immediately inform us of the error and return this message to the address mentioned above. Thank you.

From: DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>
Sent: 04 April 2024 17:26
To: Justyna Pałasińska <justyna.palasinaska@argentaglobal.com>
Subject: RE: [EXTERNAL] GRN 1122 canola concentrate status

Thanks Justyna,

I've passed the information to FSIS for review. Hopefully we will hear back shortly.

Best,

Steve

Stephen DiFranco, PhD
Regulatory Review Scientist/Chemist

Center for Food Safety and Applied Nutrition
Office of Food Additive Safety
Division of Food Ingredients
U.S. Food and Drug Administration
Tel: 240-402-2710
stephen.difranco@fda.hhs.gov



From: Justyna Pałasińska <justyna.palasinaska@argentaglobal.com>
Sent: Thursday, April 4, 2024 7:38 AM
To: DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>
Subject: Re: [EXTERNAL] GRN 1122 canola concentrate status

CAUTION: This email originated from outside of the organization. Do not click links or open attachments unless you recognize the sender and know the content is safe.

Dear Stephen,

Please find our reply below:

It is the applicant's understanding that OSHA OELs for heavy metals indicated by FSIS relate to the risk of exposure to heavy metals in the material under assessment via inhalation route only. The material indeed may create dust hazard if handled improperly. We note that the safety data sheet provided for the material (attached for reference) not only informs about the potential to form dust if handled improperly but also includes information on precautionary measures and personal protection and engineering controls aimed at eliminating or greatly reducing the risk of exposure to airborne particles. Proper handling of the material / adherence to these measures and controls by extension would eliminate or greatly reduce the risk of exposure to heavy metals that may be present in the material.

In case the above does not sufficiently address the potential risk of exposure to heavy metals present in the material via inhalation route, the applicant would like to inform that the bulk density of the material ranges between 0.1 and 0.3 g/cm³. A confirmation whether this information is sufficient to proceed with the calculations would be much appreciated. It would also be helpful to understand the assumptions being made by FSIS (e.g. concentration of airborne particles) when assessing whether the levels of heavy metals in the product may exceed OSHA OELs.

Kind regards,
Justyna Pałasińska
Regulatory Affairs Director – Human Nutrition, Argenta Barcelona



M +34 682 894 653 T +34 936 758 015

www.argentaglobal.com

Image



La información contenida en este mensaje y/o archivo(s) adjunto(s), enviada desde Pen & Tec Consulting SLU cotiza como Argenta, es confidencial/privilegiada y está destinada a ser leída sólo por la(s) persona(s) a la(s) que va dirigida. Le recordamos que sus datos han sido incorporados en el sistema de tratamiento de Pen & Tec Consulting SLU cotiza como Argenta, y que siempre y cuando se cumplan los requisitos exigidos por la normativa, usted podrá ejercer sus derechos de acceso, rectificación, limitación de tratamiento, supresión, portabilidad y oposición/revocación, en los términos que establece la normativa vigente en materia de protección de datos, dirigiendo su petición a la dirección postal OneCoWork, Portal de l'Àngel 40, 08002, Barcelona o bien a través de correo electrónico info@pentec-consulting.eu. Si usted lee este mensaje y no es el destinatario señalado, el empleado o el agente responsable de entregar el mensaje al destinatario, o ha recibido esta comunicación por error, le informamos que está totalmente prohibida, y puede ser ilegal, cualquier divulgación, distribución o reproducción de esta comunicación, y le rogamos que nos lo notifique inmediatamente y nos devuelva el mensaje original a la dirección arriba mencionada. Gracias.
The information contained in this message and/or attached file(s), sent by Pen & Tec Consulting SLU trading as Argenta, is confidential/privileged and is intended to be read solely by the person(s) to whom it is addressed. We hereby inform you that your data will be incorporated into the processing system owned by Pen & Tec Consulting SLU, and that provided it complies with the requirements included in the law, you may exercise the rights of access, rectification, limitation of processing, deletion, portability and opposition by sending your request to the postal address OneCoWork, Portal de l'Àngel 40, 08002, Barcelona or to the email address info@pentec-consulting.eu. If you read this message and you are neither the intended recipient, employee or agent in charge of delivering the message to the recipient, or if you have received this message as the result of an error, we hereby inform you that distributing, sharing or reproducing any part of this message is totally forbidden and may be illegal. As a result, we request that you immediately inform us of the error and return this message to the address mentioned above. Thank you.

From: DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>
Date: Thursday, 28 March 2024 at 20:47
To: Justyna Pałasińska <justyna.palasinaska@argentaglobal.com>
Subject: RE: [EXTERNAL] GRN 1122 canola concentrate status
Hello Justyna,

I got feedback from FSIS about their review of GRN 1122. They send the following:

I have now completed the review of the documentation submitted for the approval of the above-referenced compound. I noted that it contains Lead (≤ 0.5 mg/kg), Arsenic (≤ 0.2 mg/kg), Cadmium (≤ 0.2 mg/kg), and Mercury (≤ 0.1 mg/kg). OSHA has established OEL for these substances at 0.05 mg/m³, 0.01 mg/m³, 0.01 mg/m³, 0.025 mg/m³ (depending on presentation) respectively.

To finalize my analysis, I require the composition in mg/m³ of each of these elements or the density so I may calculate their composition accurately and evaluate them against their OSHA standards.

Are you able to provide the density of the canola concentrate? I believe this is the easiest way to answer their questions. From the density and the specified ppm levels, the reviewer should be able to calculate the maximum amount by weight of each heavy metal contaminate for a given volume of canola concentrate.

Best,

Steve

Stephen DiFranco, PhD
Regulatory Review Scientist/Chemist

Center for Food Safety and Applied Nutrition
Office of Food Additive Safety
Division of Food Ingredients
U.S. Food and Drug Administration
Tel: 240-402-2710
stephen.difranco@fda.hhs.gov



From: Justyna Pałasińska <justyna.palasinaska@argentaglobal.com>

Sent: Monday, March 4, 2024 5:04 AM
To: DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>
Subject: Re: [EXTERNAL] GRN 1122 canola concentrate status

CAUTION: This email originated from outside of the organization. Do not click links or open attachments unless you recognize the sender and know the content is safe.

Many thanks for the update, Stephen. We look forward to hearing an update, hopefully soon!

Kind regards,
Justyna Pałasińska
Regulatory Affairs Director – Human Nutrition, Argenta Barcelona



M +34 682 894 653 T +34 936 758 015

www.argentaglobal.com

Image



La información contenida en este mensaje y/o archivo(s) adjunto(s), enviada desde Pen & Tec Consulting SLU cotiza como Argenta, es confidencial/privilegiada y está destinada a ser leída sólo por la(s) persona(s) a la(s) que va dirigida. Le recordamos que sus datos han sido incorporados en el sistema de tratamiento de Pen & Tec Consulting SLU cotiza como Argenta, y que siempre y cuando se cumplan los requisitos exigidos por la normativa, usted podrá ejercer sus derechos de acceso, rectificación, limitación de tratamiento, supresión, portabilidad y oposición/revocación, en los términos que establece la normativa vigente en materia de protección de datos, dirigiendo su petición a la dirección postal Pl. Ausias March 1, 4 planta 08195, Sant Cugat del Vallès (Barcelona) o bien a través de correo electrónico info@pentec-consulting.eu. Si usted lee este mensaje y no es el destinatario señalado, el empleado o el agente responsable de entregar el mensaje al destinatario, o ha recibido esta comunicación por error, le informamos que está totalmente prohibida, y puede ser ilegal, cualquier divulgación, distribución o reproducción de esta comunicación, y le rogamos que nos lo notifique inmediatamente y nos devuelva el mensaje original a la dirección arriba mencionada. Gracias.

The information contained in this message and/or attached file(s), sent by Pen & Tec Consulting SLU trading as Argenta, is confidential/privileged and is intended to be read solely by the person(s) to whom it is addressed. We hereby inform you that your data will be incorporated into the processing system owned by Pen & Tec Consulting SLU, and that provided it complies with the requirements included in the law, you may exercise the rights of access, rectification, limitation of processing, deletion, portability and opposition by sending your request to the postal address Pl. Ausias March 1, 4 floor 08195, Sant Cugat del Vallès (Barcelona) or to the email address info@pentec-consulting.eu. If you read this message and you are neither the intended recipient, employee or agent in charge of delivering the message to the recipient, or if you have received this message as the result of an error, we hereby inform you that distributing, sharing or reproducing any part of this message is totally forbidden and may be illegal. As a result, we request that you immediately inform us of the error and return this message to the address mentioned above. Thank you.

From: DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>
Date: Monday, 26 February 2024 at 17:20
To: Justyna Pałasińska <justyna.palasinaska@argentaglobal.com>
Subject: RE: [EXTERNAL] GRN 1122 canola concentrate status

Hello Justyna,

Regarding GRN 1122; FDA has completed its review and has drafted a response letter. Unfortunately, we cannot move forward before USDA-FSIS completes their review of the uses under their jurisdiction. I have been periodically inquiring with FSIS as to the status and will get this to you as soon as possible.

We appreciate your continued patience.

Best,

Steve

Stephen DiFranco, PhD

Regulatory Review Scientist/Chemist

Center for Food Safety and Applied Nutrition
Office of Food Additive Safety
Division of Food Ingredients
U.S. Food and Drug Administration
Tel: 240-402-2710
stephen.difranco@fda.hhs.gov



From: Justyna Pałasińska <justyna.palasinaska@argentaglobal.com>
Sent: Wednesday, February 14, 2024 12:07 PM
To: Premarkt <Premarkt@fda.hhs.gov>
Cc: DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>; Ioannis Kartanos <ioannis.kartanos@argentaglobal.com>
Subject: [EXTERNAL] GRN 1122 canola concentrate status

CAUTION: This email originated from outside of the organization. Do not click links or open attachments unless you recognize the sender and know the content is safe.

Dear HHS team,

I am writing to enquire about a GRAS notice that was submitted to the FDA & filed April 19, 2023 (GRN 1122). We have been in touch with Mr Stephen DiFranco & at the beginning of December he has informed us that the FDA reviews are complete & the notice is now with USDA-FSIS.

Mr DiFranco has been very helpful through the whole process. However, we have tried to contact him several times since December without success. We were wondering if there is someone else we can get in touch with for an update on this application. We would be happy to provide any information that would help finalize the process.

I look forward to hearing from you.

Kind regards,

Justyna Pałasińska

Regulatory Affairs Director – Human Nutrition, Argenta Barcelona



M +34 682 894 653 T +34 936 758 015

www.argentaglobal.com

Image



La información contenida en este mensaje y/o archivo(s) adjunto(s), enviada desde Pen & Tec Consulting SLU cotiza como Argenta, es confidencial/privilegiada y está destinada a ser leída sólo por la(s) persona(s) a la(s) que va dirigida. Le recordamos que sus datos han sido incorporados en el sistema de tratamiento de Pen & Tec Consulting SLU cotiza como Argenta, y que siempre y cuando se cumplan los requisitos exigidos por la normativa, usted podrá ejercer sus derechos de acceso, rectificación, limitación de tratamiento, supresión, portabilidad y oposición/revocación, en los términos que establece la normativa vigente en materia de protección de datos, dirigiendo su petición a la dirección postal Pl. Ausias March 1, 4 planta 08195, Sant Cugat del Vallès (Barcelona) o bien a través de correo electrónico info@pentec-consulting.eu. Si usted lee este mensaje y no es el destinatario señalado, el empleado o el agente responsable de entregar el mensaje al destinatario, o ha recibido esta comunicación por error, le informamos que está totalmente prohibida, y puede ser ilegal, cualquier divulgación, distribución o reproducción de esta comunicación, y le rogamos que nos lo notifique inmediatamente y nos devuelva el mensaje original a la dirección arriba mencionada. Gracias. The information contained in this message and/or attached file(s), sent by Pen & Tec Consulting SLU trading as Argenta, is confidential/privileged and is intended to be read solely by the person(s) to whom it is addressed. We hereby inform you that your data will be incorporated into the processing system owned by Pen & Tec Consulting SLU, and that provided it complies with the requirements included in the law, you may exercise the rights of access, rectification, limitation of processing, deletion, portability and opposition by sending your request to the postal address Pl. Ausias March 1, 4 floor 08195, Sant Cugat del Valles (Barcelona) or to the email address info@pentec-consulting.eu. If you read this message and you are neither the intended recipient, employee or agent in charge of delivering the message to the recipient, or if you have received this message as the result of an error, we hereby inform you that distributing, sharing or reproducing any part of this message is totally forbidden and may be illegal. As a result, we request that you immediately inform us of the error and return this message to the address mentioned above. Thank you.

From: Justyna Pałasińska <justyna.palasinaska@argentaglobal.com>

Date: Wednesday, 31 January 2024 at 17:53

To: Justyna Pałasińska <justyna.palasinaska@argentaglobal.com>, DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>

Cc: Ioannis Kartanos <ioannis.kartanos@argentaglobal.com>

Subject: Re: [EXTERNAL] GRN 1122 canola concentrate - update contact person

Dear Steve,

I hope this e-mail finds you well. I was wondering if there are any updates on the finalization of this notification?

Is there any additional information that needs to be provided?

Kind regards,

Justyna Pałasińska

Regulatory Affairs Director – Human Nutrition, Argenta Barcelona



M +34 682 894 653 T +34 936 758 015

www.argentaglobal.com

Image



La información contenida en este mensaje y/o archivo(s) adjunto(s), enviada desde Pen & Tec Consulting SLU cotiza como Argenta, es confidencial/privilegiada y está destinada a ser leída sólo por la(s) persona(s) a la(s) que va dirigida. Le recordamos que sus datos han sido incorporados en el sistema de tratamiento de Pen & Tec Consulting SLU cotiza como Argenta, y que siempre y cuando se cumplan los requisitos exigidos por la normativa, usted podrá ejercer sus derechos de acceso, rectificación, limitación de tratamiento, supresión, portabilidad y oposición/revocación, en los términos que establece la normativa vigente en materia de protección de datos, dirigiendo su petición a la dirección postal Pl. Ausias March 1, 4 planta 08195, Sant Cugat del Vallès (Barcelona) o bien a través de correo electrónico info@pentec-consulting.eu. Si usted lee este mensaje y no es el destinatario señalado, el empleado o el agente responsable de entregar el mensaje al destinatario, o ha recibido esta comunicación por error, le informamos que está totalmente prohibida, y puede ser ilegal, cualquier divulgación, distribución o reproducción de esta comunicación, y le rogamos que nos lo notifique inmediatamente y nos devuelva el mensaje original a la dirección arriba mencionada. Gracias. The information contained in this message and/or attached file(s), sent by Pen & Tec Consulting SLU trading as Argenta, is confidential/privileged and is intended to be read solely by the person(s) to whom it is addressed. We hereby inform you that your data will be incorporated into the processing system owned by Pen & Tec Consulting SLU, and that provided it complies with the requirements included in the law, you may exercise the rights of access, rectification, limitation of processing, deletion, portability and opposition by sending your request to the postal address Pl. Ausias March 1, 4 floor 08195, Sant Cugat del Valles (Barcelona) or to the email address info@pentec-consulting.eu. If you read this message and you are neither the intended recipient, employee or agent in charge of delivering the message to the recipient, or if you have received this message as the result of an error, we hereby inform you that distributing, sharing or reproducing any part of this message is totally forbidden and may be illegal. As a result, we request that you immediately inform us of the error and return this message to the address mentioned above. Thank you.

From: Justyna Pałasińska <justyna@pentec-consulting.eu>

Date: Friday, 22 December 2023 at 13:31

To: DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>

Cc: Ioannis Kartanos <ioannis@pentec-consulting.eu>

Subject: Re: [EXTERNAL] GRN 1122 canola concentrate - update contact person

Dear Stephen,

Many thanks for confirming the change of contact person.

I'm following up on my colleague Ioannis e-mail from 12/12/2023. As he mentioned, we have already provided the answers to the questions to USDA-FSIS. Nevertheless, I have included them in a separate document.

Please let us know in case any additional information is required.

In the meantime, we wish you a Happy Holiday Season & all the best in 2024!

Kind regards,

Ing. Justyna Pałasińska

Regulatory Affairs Director – Human Nutrition | Pen & Tec Consulting
T +34 936 758 015 M +34 682 894 653 F +34 936 758 016 www.pentec-consulting.eu
Pl. Ausias March 1 | 4th floor D01 | 08195 Sant Cugat del Vallès | Barcelona | Spain



La información contenida en este mensaje y/o archivo(s) adjunto(s), enviada desde Pen & Tec Consulting SLU, es confidencial/privilegiada y está destinada a ser leída sólo por la(s) persona(s) a la(s) que va dirigida. Le recordamos que sus datos han sido incorporados en el sistema de tratamiento de Pen & Tec Consulting SLU y que siempre y cuando se cumplan los requisitos exigidos por la normativa, usted podrá ejercer sus derechos de acceso, rectificación, limitación de tratamiento, supresión, portabilidad y oposición/revocación, en los términos que establece la normativa vigente en materia de protección de datos, dirigiendo su petición a la dirección postal Pl. Ausias March 1, 4 planta 08195, Sant Cugat del Vallès (Barcelona) o bien a través de correo electrónico info@pentec-consulting.eu. Si usted lee este mensaje y no es el destinatario señalado, el empleado o el agente responsable de entregar el mensaje al destinatario, o ha recibido esta comunicación por error, le informamos que está totalmente prohibida, y puede ser ilegal, cualquier divulgación, distribución o reproducción de esta comunicación, y le rogamos que nos lo notifique inmediatamente y nos devuelva el mensaje original a la dirección arriba mencionada. Gracias.

The information contained in this message and/or attached file(s), sent by Pen & Tec Consulting SLU, is confidential/privileged and is intended to be read solely by the person(s) to whom it is addressed. We hereby inform you that your data will be incorporated into the processing system owned by Pen & Tec Consulting SLU, and that provided it complies with the requirements included in the law, you may exercise the rights of access, rectification, limitation of processing, deletion, portability and opposition by sending your request to the postal address Pl. Ausias March 1, 4 floor 08195, Sant Cugat del Vallès (Barcelona) or to the email address info@pentec-consulting.eu. If you read this message and you are neither the intended recipient, employee or agent in charge of delivering the message to the recipient, or if you have received this message as the result of an error, we hereby inform you that distributing, sharing or reproducing any part of this message is totally forbidden and may be illegal. As a result, we request that you immediately inform us of the error and return this message to the address mentioned above. Thank you.

From: DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>
Date: Tuesday, 5 December 2023 at 19:05
To: Nikolaas Tilkin-Franssens <niko@pentec-consulting.eu>
Cc: Justyna Pałasińska <justyna@pentec-consulting.eu>
Subject: RE: [EXTERNAL] GRN 1122 canola concentrate - update contact person

Hello Niko and Justyna,

Just confirming the change of contact person for GRN 1122.

As for timeline, FDA reviews are complete but USDA-FSIS is requesting a few pieces of information regarding the uses of canola concentrate under USDA jurisdiction, namely:

Please provide SDS for the at use concentrations of the substance and include a description of how the use of this technology will not adversely affect the safety of FSIS inspectors. Workplace safety and health hazards include inhalation, direct skin contact (skin, eyes, mouth), and fire/explosion caused by exposure to the product, its working solution or dry mixture and potential by-products formed and/or off-gassed during the application process. The employee safety information should demonstrate how the New Technology will not “jeopardize the safety of Federal inspection personnel” as specified in the [FSIS Compliance Guideline Procedures for New Technology Notifications and Protocols, April 2015](#).

Although I'm not anticipating any issues here, FSIS workplace and employee safety must be specifically addressed. Please refer to Appendix A on page 17,

Workplace Safety and Health Criteria, for clarification on what to provide in the response. For additional clarity with respect to employee safety, the following are examples of information that are typically needed by FSIS' employee safety and health group;

1. Potential workplace exposures that could result from inhalation and direct contact during use of the substance/technology. This information is required in addition to a Safety Data Sheet (SDS) to determine accurate hazard potential and recommended exposure control measures for IPP work areas in accordance with Occupational Safety and Health Administration (OSHA) regulations: 29 CFR 1910.1200, Hazard Communication, 29 CFR 1910.132, Personal Protective Equipment, and 29 CFR 1910.1000, Air Contaminants. The information should be included as a specific section in each of the protocols.
2. If the SDS workplace hazards/precautions do not apply to the type of exposure that would be expected for the FSIS IPP, please have the submitter provide specific information (per the April 2015 FSIS Compliance Guideline Procedures) for the actual type of exposures expected.
3. If no IPP workplace exposures are expected and no control measures are required, please have the submitter state this and provide the reasons why (e.g., such as the substance “as used” [for all concentrations] is not hazardous by inhalation or direct contact and/or IPP would not be exposed to the substance based on the system design, operation and/or control measures that will be in place).
4. Please also indicate how will FSIS IPP be informed of the above information so that it is clear that the information contained in the SDS for the concentrate does not apply to their actual workplace exposure.
5. Are there any potential hazards from chemical mixing or low pH as a result of discharges of the various solutions to floor drains? Are dedicated drain lines or any other enclosures required?
6. With respect to potential airborne exposures to FSIS IPP in the use/application areas, does the submitter have air sampling results taken during the use of the various concentrations of the technology in the listed mixture?

Suitability data:

The intended use of this product in FSIS meat and poultry products is apparently as a binder/extender. The suitability support provided in Appendix 6 does sufficiently support no significant difference in yield and other organoleptic qualities when used as a partial replacement for another binder in a processed meat and poultry product, such as sausage.

However, **additional suitability support is needed:**

- No suitability data was provided for **whole muscle meat and poultry products at the maximum proposed use level**. We would need to see similar data as provided in Appendix 6 for:
 - Whole muscle red meat control containing no other binders, extenders, or moisture retention agents, as compared to a whole muscle red meat product containing 15% isolated canola product.
 - Whole muscle poultry control containing no other binders, extenders, or moisture retention agents as compared to a whole muscle poultry product containing 15% isolated canola product.

You responses can be emailed directly to me and I will distribute to the necessary staff inside FDA and USDA.

Thanks,

Steve

Stephen DiFranco, PhD

Regulatory Review Scientist/Chemist

Center for Food Safety and Applied Nutrition
Office of Food Additive Safety
Division of Food Ingredients
U.S. Food and Drug Administration
Tel: 240-402-2710
stephen.difranco@fda.hhs.gov



From: Nikolaas Tilkin-Franssens <niko@pentec-consulting.eu>
Sent: Monday, December 4, 2023 4:36 AM
To: DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>
Cc: Justyna Pałasińska <justyna@pentec-consulting.eu>
Subject: [EXTERNAL] GRN 1122 canola concentrate - update contact person

CAUTION: This email originated from outside of the organization. Do not click links or open attachments unless you recognize the sender and know the content is safe.

Hi Mr. DiFranco,

Hope this email finds you well.

Due to a change in position, I will no longer be the contact person for the GRAS Notice 1122 (Canola Protein Concentrate). Could you please update your records to ascertain that Justyna Pałasińska, in copy to this email, is informed of any relevant updates?

Could you kindly confirm receipt of this email for our records?

And if possible, let us know if there is any estimate on the timeline re. finalization of the review of this GRAS Notice.

Many thanks for your great and flexible support on this application.

Kind regards,

Niko

Nikolaas Tilkin-Franssens

Regulatory Affairs Manager | Pen & Tec Consulting

T +34 936 758 015 M +34 649 840 417 F +34 936 758 016 www.pentec-consulting.eu

Pl. Ausias March 1 | 4th floor D01 | 08195 Sant Cugat del Vallès | Barcelona | Spain



La información contenida en este mensaje y/o archivo(s) adjunto(s), enviada desde Pen & Tec Consulting SLU, es confidencial/privilegiada y está destinada a ser leída sólo por la(s) persona(s) a la(s) que va dirigida. Le recordamos que sus datos han sido incorporados en el sistema de tratamiento de Pen & Tec Consulting SLU y que siempre y cuando se cumplan los requisitos exigidos por la normativa, usted podrá ejercer sus derechos de acceso, rectificación, limitación de tratamiento, supresión, portabilidad y oposición/revocación, en los términos que establece la normativa vigente en materia de protección de datos, dirigiendo su petición a la dirección postal Pl. Ausias March 1, 4 planta 08195, Sant Cugat del Vallès (Barcelona) o bien a través de correo electrónico info@pentec-consulting.eu. Si usted lee este mensaje y no es el destinatario señalado, el empleado o el agente responsable de entregar el mensaje al destinatario, o ha recibido esta comunicación por error, le informamos que está totalmente prohibida, y puede ser ilegal, cualquier divulgación, distribución o reproducción de esta comunicación, y le rogamos que nos lo notifique inmediatamente y nos devuelva el mensaje original a la dirección arriba mencionada. Gracias.

The information contained in this message and/or attached file(s), sent by Pen & Tec Consulting SLU, is confidential/privileged and is intended to be read solely by the person(s) to whom it is

addressed. We hereby inform you that your data will be incorporated into the processing system owned by Pen & Tec Consulting SLU, and that provided it complies with the requirements included in the law, you may exercise the rights of access, rectification, limitation of processing, deletion, portability and opposition by sending your request to the postal address Pl. Ausias March 1, 4 floor 08195, Sant Cugat del Valles (Barcelona) or to the email address info@pentec-consulting.eu. If you read this message and you are neither the intended recipient, employee or agent in charge of delivering the message to the recipient, or if you have received this message as the result of an error, we hereby inform you that distributing, sharing or reproducing any part of this message is totally forbidden and may be illegal. As a result, we request that you immediately inform us of the error and return this message to the address mentioned above. Thank you.

From: DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>
Date: Monday, 17 July 2023 at 17:01
To: Nikolaas Tilkin-Franssens <niko@pentec-consulting.eu>
Subject: RE: [EXTERNAL] Re: GRN 1122 canola concentrate items for clarification - Reply
Hello Niko,

No problem—I'll distribute this to the team for review.

Best,

Steve

Stephen DiFranco, PhD

Regulatory Review Scientist/Chemist

Center for Food Safety and Applied Nutrition
Office of Food Additive Safety
Division of Food Ingredients
U.S. Food and Drug Administration
Tel: 240-402-2710
stephen.difranco@fda.hhs.gov



From: Nikolaas Tilkin-Franssens <niko@pentec-consulting.eu>
Sent: Monday, July 17, 2023 10:35 AM
To: DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>
Subject: [EXTERNAL] Re: GRN 1122 canola concentrate items for clarification - Reply

CAUTION: This email originated from outside of the organization. Do not click links or open attachments unless you recognize the sender and know the content is safe.

Hi Stephen,

Apologies for this inconvenience.

We noticed that the reply to question 9 refers to Canola protein isolate (as per GRN 1103). I have updated the answer for it to be mentioning Canola protein concentrate (GRN 1122).

We hope this can be taken into consideration.

Kind regards,

Nikolaas Tilkin-Franssens

Regulatory Affairs Manager | Pen & Tec Consulting

T [+34 936 758 015](tel:+34936758015) **M** [+34 649 840 417](tel:+34649840417) **F** [+34 936 758 016](tel:+34936758016) www.pentec-consulting.eu

Pl. Ausias March 1 | 4th floor D01 | 08195 Sant Cugat del Vallès | Barcelona | Spain



La información contenida en este mensaje y/o archivo(s) adjunto(s), enviada desde Pen & Tec Consulting SLU, es confidencial/privilegiada y está destinada a ser leída sólo por la(s) persona(s) a la(s) que va dirigida. Le recordamos que sus datos han sido incorporados en el sistema de tratamiento de Pen & Tec Consulting SLU y que siempre y cuando se cumplan los requisitos exigidos por la normativa, usted podrá ejercer sus derechos de acceso, rectificación, limitación de tratamiento, supresión, portabilidad y oposición/revocación, en los términos que establece la normativa vigente en materia de protección de datos, dirigiendo su petición a la dirección postal Pl. Ausias March 1, 4 planta 08195, Sant Cugat del Vallès (Barcelona) o bien a través de correo electrónico info@pentec-consulting.eu. Si usted lee este mensaje y no es el destinatario señalado, el empleado o el agente responsable de entregar el mensaje al destinatario, o ha recibido esta comunicación por error, le informamos que está totalmente prohibida, y puede ser ilegal, cualquier divulgación, distribución o reproducción de esta comunicación, y le rogamos que nos lo notifique inmediatamente y nos devuelva el mensaje original a la dirección arriba mencionada. Gracias.

The information contained in this message and/or attached file(s), sent by Pen & Tec Consulting SLU, is confidential/privileged and is intended to be read solely by the person(s) to whom it is addressed. We hereby inform you that your data will be incorporated into the processing system owned by Pen & Tec Consulting SLU, and that provided it complies with the requirements included in the law, you may exercise the rights of access, rectification, limitation of processing, deletion, portability and opposition by sending your request to the postal address Pl. Ausias March 1, 4 floor 08195, Sant Cugat del Valles (Barcelona) or to the email address info@pentec-consulting.eu. If you read this message and you are neither the intended recipient, employee or agent in charge of delivering the message to the recipient, or if you have received this message as the result of an error, we hereby inform you that distributing, sharing or reproducing any part of this message is totally forbidden and may be illegal. As a result, we request that you immediately inform us of the error and return this message to the address mentioned above. Thank you.

From: Nikolaas Tilkin-Franssens <niko@pentec-consulting.eu>
Date: Tuesday, 11 July 2023 at 17:03
To: DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>
Cc: Justyna Pałasińska <justyna@pentec-consulting.eu>
Subject: Re: GRN 1122 canola concentrate items for clarification - Reply

Dear Stephen,

Thank you for reaching out with the questions for clarification.
We have worked closely with Napiferyn to close the doubts.

Kindly find attached a Word file including the Questions&Answers, a report on the requested literature review, a SDS sheet as requested by the USDA-FSIS, and a report on the suitability assessment.

We remain available for any further questions or updates.

Thanks for taking the application in further consideration,
best regards,

Nikolaas Tilkin-Franssens

Regulatory Affairs Manager | Pen & Tec Consulting

T +34 936 758 015 **M** +34 649 840 417 **F** +34 936 758 016 www.pentec-consulting.eu

Pl. Ausias March 1 | 4th floor D01 | 08195 Sant Cugat del Vallès | Barcelona | Spain



La información contenida en este mensaje y/o archivo(s) adjunto(s), enviada desde Pen & Tec Consulting SLU, es confidencial/privilegiada y está destinada a ser leída sólo por la(s) persona(s) a la(s) que va dirigida. Le recordamos que sus datos han sido incorporados en el sistema de tratamiento de Pen & Tec Consulting SLU y que siempre y cuando se cumplan los requisitos exigidos por la normativa, usted podrá ejercer sus derechos de acceso, rectificación, limitación de tratamiento, supresión, portabilidad y oposición/revocación, en los términos que establece la normativa vigente en materia de protección de datos, dirigiendo su petición a la dirección postal Pl. Ausias March 1, 4 planta 08195, Sant Cugat del Vallès (Barcelona) o bien a través de correo electrónico info@pentec-consulting.eu. Si usted lee este mensaje y no es el destinatario señalado, el empleado o el agente responsable de entregar el mensaje al destinatario, o ha recibido esta comunicación por error, le informamos que está totalmente prohibida, y puede ser ilegal, cualquier divulgación, distribución o reproducción de esta comunicación, y le rogamos que nos lo notifique inmediatamente y nos devuelva el mensaje original a la dirección arriba mencionada. Gracias.

The information contained in this message and/or attached file(s), sent by Pen & Tec Consulting SLU, is confidential/privileged and is intended to be read solely by the person(s) to whom it is addressed. We hereby inform you that your data will be incorporated into the processing system owned by Pen & Tec Consulting SLU, and that provided it complies with the requirements included in the law, you may exercise the rights of access, rectification, limitation of processing, deletion, portability and opposition by sending your request to the postal address Pl. Ausias March 1, 4 floor 08195, Sant Cugat del Valles (Barcelona) or to the email address info@pentec-consulting.eu. If you read this message and you are neither the intended recipient, employee or agent in charge of delivering the message to the recipient, or if you have received this message as the result of an error, we hereby inform you that distributing, sharing or reproducing any part of this message is totally forbidden and may be illegal. As a result, we request that you immediately inform us of the error and return this message to the address mentioned above. Thank you.

From: DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>
Date: Wednesday, 28 June 2023 at 17:41
To: Nicoleta Pasecinic <nicoleta@pentec-consulting.eu>
Cc: Nikolaas Tilkin-Franssens <niko@pentec-consulting.eu>
Subject: [EXTERNAL]: GRN 1122 canola concentrate items for clarification

CAUTION: This email originated from outside of the organization. Do not click links or open attachments unless you recognize the sender and know the content is safe.

Hello Ms. Pasecinic,

After evaluating NapiFeryn's GRAS Notice No. GRN 1122 on canola concentrate we noted a few issues that should be addressed.
Please respond to the following points for clarification:

1. On p. 9, NapiFeryn states that the major storage proteins in canola seed are cruciferins and napins, and that canola concentrate consists of 30-45% protein and 40-70% dietary fiber. Please provide the typical cruciferin content and napin content in canola concentrate.
2. Please confirm that all raw materials and processing aids used in the manufacturing process are used in accordance with the U.S. regulations, are GRAS for their respective uses or are the subject of an effective food contact notification. For the record, we note that the food additive regulations cited in Table 4 (p. 15) for ascorbic acid (21 CFR 182.8013), ethanol (21 CFR 184.1293), and ethyl acetate (21 CFR 173.228) do not appear to be applicable to your intended uses of these substances.
3. In Table 6 (p. 18-19), NapiFeryn provides the results from the batch analyses for heavy metals. We would like to bring to your attention a relevant FDA's "[Closer to Zero](#)" initiative that focuses on reducing the levels of heavy metals in foods and recommend that you lower the specification limits for heavy metal to better reflect the batch analyses results and to be as low as possible.
4. In Table 10 (p. 22), NapiFeryn provides batch analyses data for residual solvents and processing aids. In addition, in Table 21 (p. 50), you provided the results from the batch analyses for erucic acid in your canola concentrate ranging from 0.37% to < 0.1%.
Please include limits for residual ethanol, ethyl acetate, and sulphur dioxide as well as a limit for erucic acid in the specifications for canola concentrate and specify the analytical methods used to test for these parameters.
In addition, please provide an updated Tables 5 and 6 (p. 16-19) to include the additional specification parameters mentioned above, corresponding analytical methods, and batch analyses.

5. Please state that all analytical methods used to test batches were validated and are fit for their respective purpose.
6. Please state that canola concentrate is not intended for use in infant formula or in foods where standards of identity preclude its use.
7. In Table 15 (p.), NapiFeryn provides the results of the batch analyses for total plate count in the raw material (rapeseed press cake). Please address the significant variation in the results (from <10 to 28,000 CFU/g) and discuss whether this will impact safety of the final ingredient.
8. On p. 19, NapiFeryn states that the levels of mycotoxins in canola concentrate are below the limit of quantitation (LOQ) and provide the results from the analyses of five batches to support your statement. Please clarify whether you expect mycotoxins to be present in canola concentrate manufactured in accordance with good manufacturing practices.
9. In Part 1.4 (p. 6) and Part 3.1 (p. 33), NapiFeryn states that the intended use of canola concentrate is as a source of protein and/or fiber, thickener, or texturizer. However, we note that on p. 33 you also state the intended use of canola concentrate is as a flavoring agent or binder in various comminuted or whole muscle meat and poultry products. In addition, in Appendix 3 (p. 5) you state that canola concentrate may also be used “to create a flavored salt” or as “a flavor enhancer like monosodium glutamate”. Please confirm these additional uses of canola concentrate are within the scope of GRN 001122.
10. On p. 10, the notifier describes the protein composition of canola concentrate, being primarily cruciferins, napin, oleosin, and squalene monooxygenase. However, the pivotal safety data provided appear to only be relevant to the cruciferin and napin fractions of the canola concentrate. Please provide a brief narrative to confirm the safety of oleosin and squalene monooxygenase exposure from the intended uses.
11. On p. 31-32 of the notice, the notifier clearly establishes that canola concentrate is intended to be substitutive to protein and fiber consumption and will not contribute to additional exposure to protein or fiber in general. Please elaborate on this conclusion, and clarify if the intended uses of canola concentrate are additive or substitutive to other canola protein products currently on the market (i.e., GRNs 327, 386, and 683)?
12. On p. 37, the notifier concludes exposure to canola concentrate from the intended uses is safe since the EDI reported is “still much lower (approximately 7- to 22-fold lower) than the no-observed-adverse-effect level (NOAEL) values established” for cruciferin- and napin-rich protein isolates in male rats following a 13-week oral exposure regimen (Mejia *et al.*, 2009a & 2009b). We note that an uncertainty factor, or margin of safety (MOS), of 100 (10 for interindividual variability × 10 for interspecies variability) is normally used when assessing safety of a food ingredient by comparing estimated human exposure levels to the NOAEL from animal toxicology data. Therefore, it is not clear why MOS that is ~5-10-fold lower can be concluded as safe without proper justification. Additionally, we note that potential thyrotoxic effects were observed at the highest doses in these two rat studies, as well as for rapeseed products in general tested in other species, as cited in Table 20 of the GRAS notice. This effect was mostly attributed to the presence of glucosinolate; however, we note that since the level of glucosinolate was low or absent in both the test articles from Mejia *et al.* and the article of commerce, the rationale used by the study authors to conclude that the observed NOAEL was not in fact the LOAEL may be questionable. Regardless, it appears that the provided safety narrative lacks sufficient basis to conclude MOS of 7-22 is adequate to reach the conclusion of “reasonable certainty of no harm.” Based on generally available data and information, please provide additional narrative to explain your rationale for your GRAS conclusion.
13. We note that when discussing the absorption, distribution, metabolism, and excretion of canola concentrate (p. 49), the notifier reports unpublished data from an EU Novel Foods application for “defatted rapeseed powder” to support their conclusion. Similarly, genotoxicity conclusions are made using unpublished data from an EFSA Panel conclusion on defatted rapeseed powder. Given other data and information have been used in prior GRAS notices for canola ingredients (e.g., GRN 327), please confirm that the EFSA Panel and EU Novel Foods conclusions are only considered as corroborative, not pivotal, to the safety determination of canola concentrate at its intended use level?
14. On p. 40, the notifier discusses the allergenicity potential of canola concentrate being determined via a “bioinformatics approach” and concludes that canola concentrate “may elicit possible allergenic effects.” Additionally, on p. 59 the notifier reiterates that the bioinformatics analysis indicated “possible allergenic effects” of canola concentrate, but no further discussion is provided. While data from an allergen online database search is provided as part of Appendix 4, no discussion of these data are included in the current GRAS notice. Please briefly detail the “possible allergenic effects” of canola concentrate similar to previous notices (e.g., GRN 683), and discuss why they would not be expected to pose a safety concern from the intended use.
15. We note that a recent study on rapeseed protein isolate was published (Xiong *et al.*, 2022).
 1. Please discuss if this study presents additional safety concerns for the article of commerce or contradicts the current GRAS conclusion.
 2. Please also perform an updated literature review from 2021 to present and discuss if any additional studies relevant to the safety of canola concentrate were identified that would contradict the current GRAS conclusion.

References cited:

Xiong Z, Fu Y, Yao J, Zhang N, He R, Ju X, Wang Z. Removal of anti-nutritional factors of rapeseed protein isolate (RPI) and toxicity assessment of RPI. *Food Funct.* 2022 Jan 24;13(2):664-674. doi: 10.1039/d1fo03217h. PMID: 34933325.

Additionally, we received the following questions from USDA FSIS regarding their review of the uses of GRN 1122 concerning products within their purview. Please respond to the following and we will pass your responses along to them.

Please provide Safety Data Sheet (SDS) for the at use concentrations of the substance and include a description of how the use of this technology will not adversely affect the safety of FSIS inspectors. Workplace safety and health hazards include inhalation, direct skin contact (skin, eyes, mouth), and fire/explosion caused by exposure to the product, its working solution or dry mixture and potential by-products formed and/or off-gassed during the application process. The employee safety information should demonstrate how the New Technology will not “jeopardize the safety of Federal inspection personnel” as specified in the [FSIS Compliance Guideline Procedures for New Technology Notifications and Protocols, April 2015](#). FSIS workplace and employee safety must be specifically addressed. Please refer to Appendix A on p. 17, Workplace Safety and Health Criteria, for clarification on what to provide in the response. For additional clarity with respect to employee safety, the following are examples of information that are typically needed by FSIS’ employee safety and health group;

1. Potential workplace exposures that could result from inhalation and direct contact during use of the substance/technology. This information is required in addition to a SDS to determine accurate hazard potential and recommended exposure control measures for IPP work areas in accordance with Occupational Safety and Health Administration (OSHA) regulations: 29 CFR 1910.1200, Hazard Communication, 29 CFR 1910.132, Personal Protective Equipment, and 29 CFR 1910.1000, Air Contaminants. The information should be included as a specific section in each of the protocols.
2. If the SDS workplace hazards/precautions do not apply to the type of exposure that would be expected for the FSIS IPP, please have the submitter provide specific information (per the April 2015 FSIS Compliance Guideline Procedures) for the actual type of exposures expected.
3. If no IPP workplace exposures are expected and no control measures are required, please have the submitter state this and provide the reasons why (e.g., such as the substance “as used” [for all concentrations] is not hazardous by inhalation or direct contact and/or IPP would not be exposed to the substance based on the system design, operation and/or control measures that will be in place).
4. Please also indicate how will FSIS IPP be informed of the above information so that it is clear that the information contained in the SDS for the concentrate does not apply to their actual workplace exposure.
5. Are there any potential hazards from chemical mixing or low pH as a result of discharges of the various solutions to floor drains? Are dedicated drain lines or any other enclosures required?
6. With respect to potential airborne exposures to FSIS IPP in the use/application areas, does the submitter have air sampling results taken during the use of the various concentrations of the technology in the listed mixture?
7. The intended use of this product in FSIS meat and poultry products is apparently as a binder/extender. The suitability support provided in Appendix 6 does sufficiently support no significant difference in yield and other organoleptic qualities when used as a partial replacement for another binder in a processed meat and poultry product, such as sausage.

However, **additional suitability support is needed:**

1. No suitability data was provided for **whole muscle meat and poultry products at the maximum proposed use level**. We would need to see similar data as provided in Appendix 6 for:
Whole muscle red meat control containing no other binders, extenders, or moisture retention agents, as compared to a whole muscle red meat product containing 15% isolated canola product.
Whole muscle poultry control containing no other binders, extenders, or moisture retention agents as compared to a whole muscle poultry product containing 15% isolated canola product.

Responses may be sent in an email or in a separate document. We respectfully request a response within 10 business days. If you are unable to complete the response within that time frame, please contact me to discuss further options.

If you have any additional questions or concerns, please don’t hesitate to contact me at stephen.difranco@fda.hhs.gov or by phone at 240.402.2710.

Best,
Steve

Stephen DiFranco, PhD

Regulatory Review Scientist/Chemist

Center for Food Safety and Applied Nutrition

Office of Food Additive Safety

Division of Food Ingredients

U.S. Food and Drug Administration

Tel: 240-402-2710

stephen.difranco@fda.hhs.gov



CAUTION: This email, including any attachments, is confidential. If you are not the intended recipient, please notify the sender and delete the email and any attachments from your system. In addition, you must not use, distribute or reproduce this email or any

attachments. Opinions and other information in this email and any attachments which do not relate to the official business of Argenta are neither given by nor endorsed by Argenta. While Argenta uses anti-virus software, Argenta accepts no liability for any viruses in this email or any attachment, or for any effects this email or any attachment may have on your network or computer system.

CAUTION: This email, including any attachments, is confidential. If you are not the intended recipient, please notify the sender and delete the email and any attachments from your system. In addition, you must not use, distribute or reproduce this email or any attachments. Opinions and other information in this email and any attachments which do not relate to the official business of Argenta are neither given by nor endorsed by Argenta. While Argenta uses anti-virus software, Argenta accepts no liability for any viruses in this email or any attachment, or for any effects this email or any attachment may have on your network or computer system.

Este correo electrónico y los archivos adjuntos, enviados por Pen & Tec Consulting SLU, que opera bajo el nombre comercial de Argenta® (Argenta), son confidenciales y pueden estar protegidos por ley. Si usted no es el destinatario, cualquier divulgación, reproducción, copia, distribución u otro tipo de difusión o uso de esta comunicación está estrictamente prohibido. Si ha recibido esta transmisión por error, notifíquelo al remitente y elimine inmediatamente el correo electrónico y cualquier archivo adjunto de su sistema. Argenta no emite ni respalda las opiniones y demás información contenida en este correo electrónico y en sus anexos que no estén relacionadas con las actividades oficiales de Argenta. Aunque Argenta utiliza software antivirus, Argenta no acepta ninguna responsabilidad por cualquier virus en este correo electrónico o cualquier archivo adjunto, o por cualquier efecto que este correo electrónico o cualquier archivo adjunto pueda tener en su red o sistema informático. Argenta registra y almacena los correos electrónicos enviados a nosotros o a nuestros afiliados de acuerdo con nuestras políticas y procedimientos internos. Consulte www.pentec-consulting.eu para obtener información sobre Argenta y/o nuestra política de privacidad.

This email and any attached file(s), sent by Pen & Tec Consulting SLU trading as Argenta® (Argenta), are confidential and may be legally privileged. If you are not the intended recipient, any disclosure, reproduction, copying, distribution, or other dissemination or use of this communication is strictly prohibited. If you have received this transmission in error, please notify the sender and delete the email and any attachments from your system immediately. Opinions and other information in this email and any attachments which do not relate to the official business of Argenta are neither given by nor endorsed by Argenta. While Argenta uses anti-virus software, Argenta accepts no liability for any viruses in this email or any attachment, or for any effects this email or any attachment may have on your network or computer system. Argenta records and stores emails sent to us or our affiliates in keeping with our internal policies and procedures. Please see www.pentec-consulting.eu for information regarding Argenta and/or our privacy policy.

Este correo electrónico y los archivos adjuntos, enviados por Pen & Tec Consulting SLU, que opera bajo el nombre comercial de Argenta® (Argenta), son confidenciales y pueden estar protegidos por ley. Si usted no es el destinatario, cualquier divulgación, reproducción, copia, distribución u otro tipo de difusión o uso de esta comunicación está estrictamente prohibido. Si ha recibido esta transmisión por error, notifíquelo al remitente y elimine inmediatamente el correo electrónico y cualquier archivo adjunto de su sistema. Argenta no emite ni respalda las opiniones y demás información contenida en este correo electrónico y en sus anexos que no estén relacionadas con las actividades oficiales de Argenta. Aunque Argenta utiliza software antivirus, Argenta no acepta ninguna responsabilidad por cualquier virus en este correo electrónico o cualquier archivo adjunto, o por cualquier efecto que este correo electrónico o cualquier archivo adjunto pueda tener en su red o sistema informático. Argenta registra y almacena los correos electrónicos enviados a nosotros o a nuestros afiliados de acuerdo con nuestras políticas y procedimientos internos. Consulte www.pentec-consulting.eu para obtener información sobre Argenta y/o nuestra política de privacidad.

This email and any attached file(s), sent by Pen & Tec Consulting SLU trading as Argenta® (Argenta), are confidential and may be legally privileged. If you are not the intended recipient, any disclosure, reproduction, copying, distribution, or other dissemination or use of this communication is strictly prohibited. If you have received this transmission in error, please notify the sender and delete the email and any attachments from your system immediately. Opinions and other information in this email and any attachments which do not relate to the official business of Argenta are neither given by nor endorsed by Argenta. While Argenta uses anti-virus software, Argenta accepts no liability for any viruses in this email or any attachment, or for any effects this email or any attachment may have on your network or computer system. Argenta records and stores emails sent to us or our affiliates in keeping with our internal policies and procedures. Please see www.pentec-consulting.eu for information regarding Argenta and/or our privacy policy.

Este correo electrónico y los archivos adjuntos, enviados por Pen & Tec Consulting SLU, que opera bajo el nombre comercial de Argenta® (Argenta), son confidenciales y pueden estar protegidos por ley. Si usted no es el destinatario, cualquier divulgación, reproducción, copia, distribución u otro tipo de difusión o uso de esta comunicación está estrictamente prohibido. Si ha recibido esta transmisión por error, notifíquelo al remitente y elimine inmediatamente el correo electrónico y cualquier archivo adjunto de su sistema. Argenta no emite ni respalda las opiniones y demás información contenida en este correo electrónico y en sus anexos que no estén relacionadas con las actividades oficiales de Argenta. Aunque Argenta utiliza software antivirus, Argenta no acepta ninguna responsabilidad por cualquier virus en este correo electrónico o cualquier archivo adjunto, o por cualquier efecto que este correo electrónico o cualquier archivo adjunto pueda tener en su red o sistema informático. Argenta registra y almacena los correos electrónicos enviados a nosotros o a nuestros afiliados de acuerdo con nuestras políticas y procedimientos internos. Consulte www.pentec-consulting.eu para obtener información sobre Argenta y/o nuestra política de privacidad.

This email and any attached file(s), sent by Pen & Tec Consulting SLU trading as Argenta® (Argenta), are confidential and may be legally privileged. If you are not the intended recipient, any disclosure, reproduction, copying, distribution, or other dissemination or use of this communication is strictly prohibited. If you have received this transmission in error, please notify the sender and delete the email and any attachments from your system immediately. Opinions and other information in this email and any attachments which do not relate to the official business of Argenta are neither given by nor endorsed by Argenta. While Argenta uses anti-virus software, Argenta accepts no liability for any viruses in this email or any attachment, or for any effects this email or any attachment may have on your network or computer system. Argenta records and stores emails sent to us or our affiliates in keeping with our internal policies and procedures. Please see www.pentec-consulting.eu for information regarding Argenta and/or our privacy policy.

Este correo electrónico y los archivos adjuntos, enviados por Pen & Tec Consulting SLU, que opera bajo el nombre comercial de Argenta® (Argenta), son confidenciales y pueden estar protegidos por ley. Si usted no es el destinatario, cualquier divulgación, reproducción, copia, distribución u otro tipo de difusión o uso de esta comunicación está estrictamente prohibido. Si ha recibido esta transmisión por error, notifíquelo al remitente y elimine inmediatamente el correo electrónico y cualquier archivo adjunto de su sistema. Argenta no emite ni respalda las opiniones y demás información contenida en este correo electrónico y en sus anexos que no estén relacionadas con las actividades oficiales de Argenta. Aunque Argenta utiliza software antivirus, Argenta no acepta ninguna responsabilidad por cualquier virus en este correo electrónico o cualquier archivo adjunto, o por cualquier efecto que este correo electrónico o cualquier archivo adjunto pueda tener en su red o sistema informático. Argenta registra y almacena los correos electrónicos enviados a nosotros o a nuestros afiliados de acuerdo con nuestras políticas y procedimientos internos. Consulte www.pentec-consulting.eu para obtener información sobre Argenta y/o nuestra política de privacidad.

This email and any attached file(s), sent by Pen & Tec Consulting SLU trading as Argenta® (Argenta), are confidential and may be legally privileged. If you are not the intended recipient, any disclosure, reproduction, copying, distribution, or other dissemination or use of this communication is strictly prohibited. If you have received this transmission in error, please notify the sender and delete the email and any attachments from your system immediately. Opinions and other information in this email and any attachments which do not relate to the official business of Argenta are neither given by nor endorsed by Argenta. While Argenta uses anti-virus software, Argenta accepts no liability for any viruses in this email or any attachment, or for any effects this email or any attachment may have on your network or computer system. Argenta records and stores emails sent to us or our affiliates in keeping with our internal policies and procedures. Please see www.pentec-consulting.eu for information regarding Argenta and/or our privacy policy.

Este correo electrónico y los archivos adjuntos, enviados por Pen & Tec Consulting SLU, que opera bajo el nombre comercial de Argenta® (Argenta), son confidenciales y pueden estar protegidos por ley. Si usted no es el destinatario, cualquier divulgación, reproducción, copia, distribución u otro tipo de difusión o uso de esta comunicación está estrictamente prohibido. Si ha recibido esta transmisión por error, notifíquelo al remitente y elimine inmediatamente el correo electrónico y cualquier archivo adjunto de su sistema. Argenta no emite ni respalda las opiniones y demás información contenida en este correo electrónico y en sus anexos que no estén relacionadas con las actividades oficiales de Argenta. Aunque Argenta utiliza software antivirus, Argenta no acepta ninguna responsabilidad por cualquier virus en este correo electrónico o cualquier archivo adjunto, o por cualquier efecto que este correo electrónico o cualquier archivo adjunto pueda tener en su red o sistema informático. Argenta registra y almacena los correos electrónicos enviados a nosotros o a nuestros afiliados de acuerdo con nuestras políticas y procedimientos internos. Consulte www.pentec-consulting.eu para obtener información sobre Argenta y/o nuestra política de privacidad.

This email and any attached file(s), sent by Pen & Tec Consulting SLU trading as Argenta® (Argenta), are confidential and may be legally privileged. If you are not the intended recipient, any disclosure, reproduction, copying, distribution, or other dissemination or use of this communication is strictly prohibited. If you have received this transmission in error, please notify the sender and delete the email and any attachments from your system immediately. Opinions and other information in this email and any attachments which do not relate to the official business of Argenta are neither given by nor endorsed by Argenta. While Argenta uses anti-virus software, Argenta accepts no liability for any viruses in this email or any attachment, or for any effects this email or any attachment may have on your network or computer system. Argenta records and stores emails sent to us or our affiliates in keeping with our internal policies and procedures. Please see www.pentec-consulting.eu for information regarding Argenta and/or our privacy policy.

Este correo electrónico y los archivos adjuntos, enviados por Pen & Tec Consulting SLU, que opera bajo el nombre comercial de Argenta® (Argenta), son confidenciales y pueden estar protegidos por ley. Si usted no es el destinatario, cualquier divulgación, reproducción, copia, distribución u otro tipo de difusión o uso de esta comunicación está estrictamente prohibido. Si ha recibido esta transmisión por error, notifíquelo al remitente y elimine inmediatamente el correo electrónico y cualquier archivo adjunto de su sistema. Argenta no emite ni respalda las opiniones y demás información contenida en este correo electrónico y en sus anexos que no estén relacionadas con las actividades oficiales de Argenta. Aunque Argenta utiliza software antivirus, Argenta no acepta ninguna responsabilidad por cualquier virus en este correo electrónico o cualquier archivo adjunto, o por cualquier efecto que este correo electrónico o cualquier archivo adjunto pueda tener en su red o sistema informático. Argenta registra y almacena los correos electrónicos enviados a nosotros o a nuestros afiliados de acuerdo con nuestras políticas y procedimientos internos. Consulte www.pentec-consulting.eu para obtener información sobre Argenta y/o nuestra política de privacidad.

This email and any attached file(s), sent by Pen & Tec Consulting SLU trading as Argenta® (Argenta), are confidential and may be legally privileged. If you are not the intended recipient, any disclosure, reproduction, copying, distribution, or other dissemination or use of this communication is strictly prohibited. If you have received this transmission in error, please notify the sender and delete the email and any attachments from your system immediately. Opinions and other information in this email and any attachments which do not relate to the official business of Argenta are neither given by nor endorsed by Argenta. While Argenta uses anti-virus software, Argenta accepts no liability for any viruses in this email or any attachment, or for any effects this email or any attachment may have on your network or computer system. Argenta records and stores emails sent to us or our affiliates in keeping with our internal policies and procedures. Please see www.pentec-consulting.eu for information regarding Argenta and/or our privacy policy.

Este correo electrónico y los archivos adjuntos, enviados por Pen & Tec Consulting SLU, que opera bajo el nombre comercial de Argenta® (Argenta), son confidenciales y pueden estar protegidos por ley. Si usted no es el destinatario, cualquier divulgación, reproducción, copia, distribución u otro tipo de difusión o uso de esta comunicación está estrictamente prohibido. Si ha recibido esta transmisión por error, notifíquelo al remitente y elimine inmediatamente el correo electrónico y cualquier archivo adjunto de su sistema. Argenta no emite ni respalda las opiniones y demás información contenida en este correo electrónico y en sus anexos que no estén relacionadas con las actividades oficiales de Argenta. Aunque Argenta utiliza software antivirus, Argenta no acepta ninguna responsabilidad por cualquier virus en este correo electrónico o cualquier archivo adjunto, o por cualquier efecto que este correo electrónico o cualquier archivo adjunto pueda tener en su red o sistema informático. Argenta registra y almacena los correos electrónicos enviados a nosotros o a nuestros afiliados de acuerdo con nuestras políticas y procedimientos internos. Consulte www.pentec-consulting.eu para obtener información sobre Argenta y/o nuestra política de privacidad.

This email and any attached file(s), sent by Pen & Tec Consulting SLU trading as Argenta® (Argenta), are confidential and may be legally privileged. If you are not the intended recipient, any disclosure, reproduction, copying, distribution, or other dissemination or use of this communication is strictly prohibited. If you have received this transmission in error, please notify the sender and delete the email and any attachments from your system immediately. Opinions and other information in this email and any attachments which do not relate to the official business of Argenta are neither given by nor endorsed by Argenta. While Argenta uses anti-virus software, Argenta accepts no liability for any viruses in this email or any attachment, or for any effects this email or any attachment may have on your network or computer system. Argenta records and stores emails sent to us or our affiliates in keeping with our internal policies and procedures. Please see www.pentec-consulting.eu for information regarding Argenta and/or our privacy policy.

Este correo electrónico y los archivos adjuntos, enviados por Pen & Tec Consulting SLU, que opera bajo el nombre comercial de Argenta® (Argenta), son confidenciales y pueden estar protegidos por ley. Si usted no es el destinatario, cualquier divulgación, reproducción, copia, distribución u otro tipo de difusión o uso de esta comunicación está estrictamente prohibido. Si ha recibido esta transmisión por error, notifíquelo al remitente y elimine inmediatamente el correo electrónico y cualquier archivo adjunto de su sistema. Argenta no emite ni respalda las opiniones y demás información contenida en este correo electrónico y en sus anexos que no estén relacionadas con las actividades oficiales de Argenta. Aunque Argenta utiliza software antivirus, Argenta no acepta ninguna responsabilidad por cualquier virus en este correo electrónico o cualquier archivo adjunto, o por cualquier efecto que este correo electrónico o cualquier archivo adjunto pueda tener en su red o sistema informático. Argenta registra y almacena los correos electrónicos enviados a nosotros o a nuestros afiliados de acuerdo con nuestras políticas y procedimientos internos. Consulte www.pentec-consulting.eu para obtener información sobre Argenta y/o nuestra política de privacidad.

This email and any attached file(s), sent by Pen & Tec Consulting SLU trading as Argenta® (Argenta), are confidential and may be legally privileged. If you are not the intended recipient, any disclosure, reproduction, copying, distribution, or other dissemination or use of this communication is strictly prohibited. If you have received this transmission in error, please notify the sender and delete the email and any attachments from your system immediately. Opinions and other information in this email and any attachments which do not relate to the official business of Argenta are neither given by nor endorsed by Argenta. While Argenta uses anti-virus software, Argenta accepts no liability for any viruses in this email or any attachment, or for any effects this email or any attachment may have on your network or computer system. Argenta records and stores emails sent to us or our affiliates in keeping with our internal policies and procedures. Please see www.pentec-consulting.eu for information regarding Argenta and/or our privacy policy.

Este correo electrónico y los archivos adjuntos, enviados por Pen & Tec Consulting SLU, que opera bajo el nombre comercial de Argenta® (Argenta), son confidenciales y pueden estar protegidos por ley. Si usted no es el destinatario, cualquier divulgación, reproducción, copia, distribución u otro tipo de difusión o uso de esta comunicación está estrictamente prohibido. Si ha recibido esta transmisión por error, notifíquelo al remitente y elimine inmediatamente el correo electrónico y cualquier archivo adjunto de su sistema. Argenta no emite ni respalda las opiniones y demás información contenida en este correo electrónico y en sus anexos que no estén relacionadas con las actividades oficiales de Argenta. Aunque Argenta utiliza software antivirus, Argenta no acepta ninguna responsabilidad por cualquier virus en este correo electrónico o cualquier archivo adjunto, o por cualquier efecto que este correo electrónico o cualquier archivo adjunto pueda tener en su red o sistema informático. Argenta registra y almacena los correos electrónicos enviados a nosotros o a nuestros afiliados de acuerdo con nuestras políticas y procedimientos internos. Consulte www.pentec-consulting.eu para obtener información sobre Argenta y/o nuestra política de privacidad.

This email and any attached file(s), sent by Pen & Tec Consulting SLU trading as Argenta® (Argenta), are confidential and may be legally privileged. If you are not the intended recipient, any disclosure, reproduction, copying, distribution, or other dissemination or use of this communication is strictly prohibited. If you have received this transmission in error, please notify the sender and delete the email and any attachments from your system immediately. Opinions and other information in this email and any attachments which do not relate to the official business of Argenta are neither given by nor endorsed by Argenta. While Argenta uses anti-virus software, Argenta accepts no liability for any viruses in this email or any attachment, or for any effects this email or any attachment may have on your network or computer system. Argenta records and stores emails sent to us or our affiliates in keeping with our internal policies and procedures. Please see www.pentec-consulting.eu for information regarding Argenta and/or our privacy policy.