GR

ORIGINAL SUBMISSION

Center for Regulatory Services, Inc.

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November 21, 2008

Office of Premarket Approval (HFS-200)
Center for Food Safety and Applied Nutrition
Food and Drug Administration
5100 Paint Branch Parkway
College Park, MD 20740-3835

Dear Sir or Madam:

SUBJECT: GRAS Notification
Exemption Claim for Polyglycerol Polyricinoleic Acid

On behalf of the notifier, **Stepan Company**, and in accordance with FDA proposed rule of April 17, 1997 (62 FR 18938), relating to the filing of a generally recognized as safe (GRAS) notification, we hereby claim that the use of polyglycerol polyricinoleic acid as a food ingredient is generally recognized as safe and exempt from premarket approval requirements of the Federal Food, Drug, and Cosmetic Act. In conformity with the requirements outlined in the proposed rule, the following information is included with this exemption claim.

GRAS EXEMPTION CLAIM

This claim is an addition to the claims previously notified in GRAS Notification 9 with respect to use of the substance as an emulsifier in chocolate and GRAS Notification No. 179, with respect to the use of polyglycerol polyricinoleic acid as an emulsifier in the production of margarines, low fat margarines, spreads, creamers, and dairy analogues.

The uses that are the subject of this GRAS Notification are for the use of the substance in the formulation of color additives intended for addition to processed foods, with limitation based only on Good Manufacturing Practice.

(1) Identification of the notifier:

Tracy Strilich
Senior Regulatory Chemist
Product Safety and Compliance
Stepan Company
22 West Frontage Road
Northfield, IL 60093
Telephone: 847-501-2416
Faxline: 847-501-2455
E-Mail: tstrilich@stepan.com

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OFFICE OF
FOOD ADDITIVE SAFETY

Regulatory Representative:

William A. Olson, Ph.D.
Center for Regulatory Services, Inc.
5200 Wolf Run Shoals Road
Woodbridge, VA 22192-5755
Telephone: 703-590-7337
Faxline: 703-580-8637
E-Mail: cfrsrv@aol.com

(2) Common or usual name of the substance:

Polyglycerol polyricinoleic acid

(3) Applicable conditions of use:

(a) Foods in which the substance is to be used:

Polyglycerol polyricinoleic acid for this GRAS Notification is intended to be used as an emulsifier in the formulation of color additives intended for use in processed foods.

(b) Purposes for which the substance is used:

Polyglycerol polyricinoleic acid as an emulsifier.

(c) Description of the population expected to consume the substance:

Colors containing polyglycerol polyricinoleic acid is expected to be used by the general public.

(4) Basis for GRAS determination, i.e., through experience based on common use in food (pre-1958) or through scientific procedures:

The basis of the GRAS determination is through scientific procedures.

(5) Availability of Data and Information (references)

The referenced material that is the basis for this GRAS determination are available for the Food and Drug Administration's review and copying at reasonable times at the Product Safety and Compliance Department of Stepan Company, 22 Frontage Road, Northfield, IL 60093, or will be sent to FDA upon request.

William A. Olson, Ph.D.
Regulatory Representative, Stepan Company

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GRAS Exemption Notification

PGPR
Polyglycerol polyricinoleic acid for Use in Food Color Additive Formulation

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Attachments

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PROPOSED

GRAS List Entry

GRN No.	Notifier	Substance	INTENDED USE	GRP #	*BASIS*	*Date* of Filing	*Closure*
	Stepan Company	Polyglycerol polyricinoleic acid	As an emulsifier in the formulation of color additives intended for addition to processed foods, with limitation based only on Good Manufacturing Practice.		Scientific procedures		

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Identity of the Substance

A. Chemical Name:

9-octadecenoic acid, 12-hydroxy-, (9Z, 12R)-, polymer with 1,2,3-propanetriol (9CI)
CAS Registry No. 29894-35-7

B. Common Name:

Polyglycerol polyricinoleic acid

C. Trade Name:

DREWPOL® PGPR

D. Other Names:

Polyglycerol esters of interesterified ricinoleic acid
Polyglycerol polyricinoleate

E. Definition:

Polyglycerol Polyricinoleic Acid occurs as a clear, light brown, viscous liquid. It is prepared by esterification of polyglycerol with condensed castor oil fatty acids. The castor oil fatty acids are mainly composed of 80% to 90% ricinoleic acid. It is soluble in ether, in hydrocarbons, and in halogenated hydrocarbons. It is insoluble in water and in alcohol.

F. Assay:

Food Chemical Codex, Fifth Edition, page 344, Specifications

G. Description:

Clear light brown viscous liquid

H. Identification Test:

Food Chemical Codex, Fifth Edition, page 344, Identification, Fatty Acids, and Ricinoleic acid.

I. Purity:
Food Chemical Codex, Fifth Edition, page 344, Specifications

Manufacture, Specifications, and Stability

Polyglycerol polyricinoleic acid, PGPR, has been reported in several scientific articles and two previous GRAS Notifications. The first, #0009, was for its use as a rheology modification agent in molten chocolate mass. The second, #0179, was for its use as an emulsifier in the production of margarines, low fat margarines, spreads, creamers and dairy analogs. PGPR is defined as an interesterified polymer of polyricinoleic acid and polyglycerol.

Polyricinoleic acid is a polymer created by the self-condensation of the 12-hydroxy, 9-octadecenoic acid fraction within the fatty acids obtained from castor oil. The condensation reaction is typically carried out by heating castor oil fatty acids to about 200°C, with or without catalyst, and removing water of reaction. Acceptable catalysts are those known in the art and include acids such as phosphoric acid, bases such as sodium hydroxide and lipase enzymes; all of which are currently used to interesterify food grade fats and oils.

PGPR is produced by reaction of polyglycerol and ricinoleic acid. The polyglycerol can be prepared by three routes:

1) By polymerization of glycerin using strong base as a catalyst. This route leads to several different outcomes:
    a) The polymers of interest, namely polyglycerin, but with a broad distribution of homologues and significant levels of free glycerin.
    b) The production of cyclic compounds similar to dioxane, which undergo further polymerization.
    c) Dehydration by-products, namely acrolein, which must be removed by distillation.
2) By polymerization of glycidol, which leads to linear polyglycerin.
3) By polymerization of epichlorohydrin, followed by hydrolysis, which also leads to linear polyglycerin.
    a)The by-product, sodium chloride, is removed by filtration.

Of these three routes used to produce polyglycerol, the polymerization of epichlorohydrin is the preferred method of manufacture. This is the method of choice due to economic advantages as well as enabling the production of PGPR that meets rigid customer specifications.

Polymers of epichlorohydrin (or glycidol) are prepared by methods similar to those of other oxirane monomers. The process used is a catalytic ring opening of the oxirane group to form the polymer through an ether linkage between the monomers. Epichlorohydrin is expected to be completely consumed in this polymerization reaction. The final step in any oxirane polymerization is a steam distillation, or deodorization step.

This deodorization step employs the injection of steam into the reactor at temperatures between 150° C and 200° C with strong vacuum; usually on the order of 25 to 27 inches of mercury. Under these conditions, any residual monomer (epichlorohydrin or glycidol) is typically reduced to levels below 1ppm.

Specifically for the case of epichlorohydrin polymers, the material must then be hydrolyzed to produce polyglycerol. This is accomplished by base catalyzed reaction with water and excess base, either sodium or potassium hydroxide. If any residual monomer escapes the deodorization step in the polymerization process, it will subsequently be hydrolyzed to glycerin in the hydrolysis step. This is followed by drying, 100° C at 25 to 27 inches of mercury, and then filtration of the sodium chloride produced.

The polyglycerol so produced is then used at a level of 9% in the production of Polyglycerol Polyricinoleic Acid, thereby reducing the level of any trace amounts of monomer by a factor of ten. The transesterification step between polyricinoleic acid and the polyglycerol is carried out at 200° C for a period of 12 hours. In the transesterification step, water of reaction is continually released because the terminal carboxylic acid functionality of the polyricinoleic acid is reactive with the polyglycerol. Although unlikely, if any oxirane monomer has survived to this point, the residual water of reaction in this step will cause immediate hydrolysis to glycerol, especially at the temperature levels required for completion of the transesterification step.

Lastly, it is important to note that the PGPR will be used at a level less than 5% in the food color additive. The level of any remaining monomer would then be decreased by an additional factor. Therefore, the end result is that residual monomers from oxirane polymerization in the PGPR final product, as well as the final food color additive product, are negligible, far below detectable limits.

A full description of PGPR is given in the Fifth Edition of the Food Chemical Codex (FCC), published by the Institute of Medicine. Specifications and all analytical chemistry associated with this food additive are included in this reference text. The FCC monograph, "Polyglycerol polyricinoleic acid" is incorporated by reference with this submission.

Stability tests of physical and chemical parameters were performed between 1986 to 1988 over a 32-month period. This was reported in GRN #0009. The substance was held at a constant temperature of 15°C in a 200 kg drum. No significant change was observed. The stability of Polyglycerol polyricinoleic acid is shown to be excellent.

ATTACHMENT No. 3

Use Information

The proposed use of polyglycerol polyricinoleic acid of this GRAS Notification is for use of the substance in emulsifying color additives intended for use in foods for which color additives are commonly added.

Emulsification of the color additives is accomplished by addition as low as 0.1% of PGPR in the color additive with a maximum of 5% by weight of the formulation being used. The concentration is based upon the amount needed for emulsification of the specific color additive.

Color additives in foods are self-limiting as the quantity for use is based upon the visual effect desired. It is estimated that the emulsification by PGPR would only be appropriate for 10% of the food color market and of this one-half (5%) would be in oil-based applications and 5% would be in water-based applications.

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Safety Evaluation

This GRAS notification is for the use of polyglycerol as is outlined in Attachment 3. This notification is limited to use of the substance as an emulsifier in color additive formulations for use in foods in which color is commonly added.

Polyglycerol polyricinoleic acid has been reviewed by the Joint Expert Committee on Food Additives with information and conclusion presented in the 17th Report of the Joint FAO/WHO Expert Committee on Food Additives, World Health Organization, Technical Report Series 1974, No. 539, and the FAO Nutrition Meeting, Series 1974, No. 53. Also, previous GRAS Notifications have been made for this substance, including GRAS Notification No. 0009, Quest International for the use of polyglycerol polyricinoleic acid as an emulsifier in chocolate. Stepan Company also submitted a GRAS Notification No. 179 for polyglycerol polyricinoleic acid as an emulsifier in the production of margarines, low fat margarines, spreads, creamers, and dairy analogues. Both of the GRAS Notifications have been reviewed by FDA with no question from the agency.

Also, the polyglycerol polyricinoleic acid is described in Food Chemical Codex, 5th Edition, which includes both the method of preparation and specifications for the polyglycerol polyricinoleic acid.

The product as prepared by Stepan Company is consistent with the manufacture and specification established by Food Chemical Codex.

The bibliography of safety data and biological study summaries are provided in Attachment 5 of this notification.

The Joint Experts Committee on Food and Color Additives which met in Geneva, June/July 1973, reviewed 15 publications which included laboratory animal toxicological studies, human clinical studies, and metabolic fate studies. The long term studies in rats and mice did not show carcinogenic potential, and it was established that in long term dietary feeding studies in rats there was no toxicological effect at 15,000 ppm, 1.5%, which was equivalent to 750 mg/kg/body weight, leading to the conclusion that the acceptable daily intake for man with 100 fold margin would be 7.5 mg/kg/body weight.

Since 1973 there have been many additional studies conducted including multi-generation reproduction studies and assessment of the carcinogenic potential in rats and mice, and human studies which are cited in Attachment No. 5. Also, summaries of the data have been submitted as part of the previous GRAS Notifications.

ESTIMATED DAILY INTAKE

In the previous GRAS Notification, GRN 0009, there has been report of the EDI being for the 90th percentile consumers of chocolate at 4.7 mg/kg/day with an average EDI of 2.4 mg/kg/day.

With the additional uses as discussed in GRAS Notification No. 179, this resulted in the average EDI of 2.7 mg/kg, thus giving a cumulative EDI of 5.1 mg/kg/body weight. Even if one used only the 90th percentile of consumers of each of the types of foods containing polyglycerol polyricinoleic acid, this would not exceed the acceptable daily intake.

With respect to the intakes expected with the use of polyglycerol polyricinoleic acid in formulation aid in color additives, the functional effect of an emulsifier would be achieved at the addition of 0.03%.

The NAS/NRC Food Color Publication, 1971, reports that the amount of certified colors used in food is self-limiting and reports the major categories of foods with average ppm in each type of food. If one assumed that the food colors would be added to all processed foods (approximately 1 kg of food/person/day), this would calculate to be an estimated daily intake of 0.25 mg/kg/body weight.

Therefore, this additional use of polyglycerol polyricinoleic acid as an emulsifier in food color additives would result in an EDI much lower than for the other uses of this substance in foods in the United States and would result in a cumulative EDI of 5.35 mg/kg/body weight, and if one assumed the 90th percentile of intake, the cumulative EDI will remain consistent with the established EDI (7.5 mg/kg/body weight).

CONCLUSION

Stepan Company, after critical review and analysis of the available information on polyglycerol polyricinoleic acid has concluded that the body of data supports the use of polyglycerol polyricinoleic acid in the additional use as an emulsifier for use in color additives intended to be added to food.

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Bibliography

Safety Data / Biological Studies Summaries

Food Colors, Food Protection; National Research Council, National Academy of Sciences, 1971

Seventeenth Report of the Joint FAO/WHO Expert Committee on Food Additives; World Health Organization Technical Report Series, 1974, No. 539 (246-253); FAO Nutrition Meetings Report Series, 1974, No. 53

Assessment of the carcinogenic potential of Polyglycerol polyricinoleic acid (PGPR) in rats and mice; Smith, Wilson & Hepburn; Food and Chemical Toxicology 36(9-10) 1998

Human studies on Polyglycerol polyricinoleic acid; Wilson & Smith; Food and Chemical Toxicology 36(9-10) 1998

A three-generation reproduction study on Polyglycerol polyricinoleic acid (PGPR) in Wistar rats; Wilson & Smith; Food and Chemical Toxicology 36(9-10) 1998

The fate of ingested glycerin esters of condensed castor oil fatty acids [Polyglycerol polyricinoleic acid (PGPR)] in the rat; Howes, Wilson & James; Food and Chemical Toxicology 36(9-10) 1998

Overview of the preparation, use and biological studies on Polyglycerol polyricinoleic acid (PGPR); Wilson, Van Schie & Howes; Food and Chemical Toxicology 36(9-10) 1998

A three-generation reproduction study on Polyglycerol polyricinoleic acid (PGPR) in Wistar rats. Reply to comments; Howes & Wilson; Food and Chemical Toxicology 37 (2-3) 1999

GRAS Notification, Quest International, Report 9; The safety of polyglycerol-polyricinoleic acid emulsifier for use in chocolate, Received FDA, October 22, 1998, Closure, March 2, 1999

Food Chemical Codex; Fifth Edition, 2004, pp. 343-344.

GRAS Notification, Stepan Company, Report 179; Polyglycerol-polyricinoleic acid for use in margarines, low fat margarines, spreads, creamers and dairy analogs, Received FDA, July 19, 2005, Closure, January 20, 2006

GRN PGPR 11-21-08

SUBMISSION END

AM

Mcmahon, Carrie

From: CFRSRV@aol.com
Sent: Friday, March 27, 2009 12:16 PM
To: Mcmahon, Carrie
Cc: TStrilich@stepan.com
Subject: Re: GRN 270 - PGPR intended use
Attachments: GRN 270 PGPR 01-06-09.doc

Dear Dr. McMahon

Subject: GRN 270 - PGPR intended use

This follows your request for clarification of my letter of January 6, 2009. The last paragraph was incorrect, and it has been corrected with the attached letter as corrected 3/25/09.

As to the FSIS categories, the use expected would be for Sausage/Hotdogs.

Let me know if there is any further questions or need for clarification.

Sincerely:

William A. Olson, Ph.D.
Center for Regulatory Services, Inc.
5200 Wolf Run Shoals Road
Woodbridge, VA 22192
Telephone: 703 590 7337
Faxline: 703 580 8637

In a message dated 3/25/2009 1:13:24 PM Eastern Daylight Time, Carrie.McMahon@fda.hhs.gov writes:

> Dr. Olson -
>
> Regarding: GRN 270 (PGPR for use as an emulsifier in the formulation of color additives)
>
> Per our telephone conversation this afternoon, I will look for your revised letter of "intended use" for PGPR. As this would include the use of color additives formulated with PGPR in processed meat products, we have sent a copy to USDA. They have asked for more detail in the specific categories of products included in such use. I have attached a "categories of products" list for meat and poultry products under their responsibility. Please respond to me by indicating which of these categories is included in the intended uses by the notifier (Stepan Company).

Center for Regulatory Services, Inc.

5200 Wolf Run Shoals Road * Woodbridge, VA 22192-5755
Telephone 703 590 7337 * Fax 703 580 8637
cfrsrv@aol.com

January 6, 2009
Corrected 3/25/09

Dr. Carrie McMahon
Division of Biotechnology & GRAS Review
Center for Food Safety and Applied Nutrition
Food and Drug Administration
5100 Paint Branch Parkway
College Park, MD 20740-3835

Dear Dr. McMahon:

SUBJECT: GRAS Notification 000270
Polyglycerol Polyricinoleic Acid

This follows a request as made via telephone with respect to the refinement of the foods that may be colored with formulations that include the GRN substance as an emulsifier.

In discussing with the notifier, the substance would be limited to use in processed foods for which colors are permitted, and would not include beverages and infant formula. Enclosed is a revised proposed GRAS list entry in which this is included in the intended use description.

Therefore, the notifier is willing to specify the use excluding beverages and infant formula.

Since the notifier does characterize the food types as being processed, that would include use in foods such as processed fruits and vegetables, milk, eggs, and meat. Also, it would include any processed foods that are subject to standards of identity by USDA or FDA in which colors are permitted.

Sincerely,

William A. Olson, Ph.D.
Consultant

WAO:gbt
GRN 270 PGPR 01-06-09

Enclosure:
Revised Proposed GRAS List Entry

ec: T. Strilich

AM

Mcmahon, Carrie

From: CFRSRV@aol.com
Sent: Wednesday, May 13, 2009 11:26 AM
To: Mcmahon, Carrie
Cc: TStrilich@stepan.com
Subject: Re: GRN 270, GRAS notification, PGPR

Dear Dr. McMahon:

Thank you for your e-mail of yesterday regarding the request for clarification of the conditions for determination of refractive index.

Stepan Company was aware of the error in the FCC Monograph and in 2006 contacted the USP and they agreed to make the change in the next edition.

The refractive index measured at a temperature of 65 degrees has been included in the specifications for the previous polyglycerol polyricinoleic acid GRNs, and also is specified in the EU Monograph.

The polyglycerol polyricinoleic acid (PGPR) which is produced by Stepan Company is consistent with the acceptance criteria in the specification for refractive index, as in the monograph of the sixth edition of Food Chemical Codex, including the temperature as specified at 65 degrees.

Please let me know if there are any other questions.

William A. Olson, Ph.D.
Center for Regulatory Services, Inc.
5200 Wolf Run Shoals Road
Woodbridge, VA 22192
Telephone: 703 590 7337
Faxline: 703 580 8637

In a message dated 5/12/2009 3:41:46 PM Eastern Daylight Time, Carrie.McMahon@fda.hhs.gov writes:

> Dr. Olson -
>
> Regarding GRN 270 - Polyglycerol polyricinoleic acid (PGPR) for use in the formulation of color additives
>
> I have a request for a minor point of clarification. In your specifications, you reference the monograph for PGPR in the fifth edition of the Food Chemicals Codex (2004). FDA notes that fifth edition contained an oversight in the specification of the temperature at which the refractive index is determined (i.e., the temperature wasn't specified in the monograph itself, and so defaulted to the temperature of 25 degrees as specified in Appendix II: Physical Tests and Determination). This oversight was corrected in the sixth edition of the Food Chemicals Codex (2008) where the temperature is specified at 65 degrees. I have highlighted the refractive index specification in the

attached monograph for your convenience.

Please confirm that your food-grade PGPR meets the specifications per the monograph in the 6th edition (the most current) of the Food Chemicals Codex.

Regards,

Carrie

Carrie H. McMahon, Ph.D.
Consumer Safety Officer
U.S. Food and Drug Administration
Center for Food Safety and Applied Nutrition
Division of Biotechnology and GRAS Notice Review

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