HERCULES

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August 26, 2004

Division of Dockets Management
Food and Drug Administration
5630 Fishers Lane, Room 1061 (HFA-305)
Rockville, MD 20852

RE: **Docket No. 2003F-0471; FAP No. 3A4749; Glycerol Ester of Gum Rosin**

Dear Dockets Manager:

Hercules Incorporated hereby submits comments in response to Food Additive Petition No. 3A4749 submitted by T&R Chemical. This petitioner proposed to incorporate the glycerol ester of gum rosin under FDA regulation 21 CFR 172.735. Hercules hereby submits arguments against the "equivalency" of glycerol ester of gum rosin and glycerol of wood rosin claimed by the petitioner. You will find enclosed a detailed explanation of the nature of our argument along with supporting data covering issues from raw material differences, to process differences to final product variations. We respectfully request that FDA review these arguments and consider them in reviewing FAP 3A4749. Four copies of the confidential submission and four copies of the public submission are enclosed.

The attachments are research reports from Hercules Incorporates and are considered proprietary information. They are marked accordingly. We request that FDA please limit distribution to authorized FDA personnel only and not distribute these reports without permission of Hercules Incorporated. These attachments have been deleted from the public copies.

Please feel free to contact me if you have any questions regarding this submission.

Sincerely,

G. L. McCallister
Director, Regulatory Affairs
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Attachments

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PUBLIC DOCUMENT

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Dear Dockets Manager:

Hercules Incorporated hereby submits comments in response to Food Additive Petition No. 3A4749 submitted by T&R Chemical. This petitioner proposed to incorporate the glycerol ester of gum rosin under FDA regulation 21 CFR 172.735. In support of that proposal, the petitioner submits, as a primary argument, gum rosin (GR) and wood rosin (WR) are chemically equivalent, implies that the glycerol esters of GR and WR would also be chemically equivalent, and thus argues that the health and safety data supporting the use of glycerol ester of wood rosin (GEWR) would be applicable to the glycerol ester of gum rosin (GEGR).

The petitioner submits detailed chemical analyses comparing GR to WR and comparing GEGR to GEWR in support of this equivalency argument. Indeed, the data appear to show a good similarity between the WR and the GR that was tested. However, Hercules submits that the GR and GEGR data submitted by the petitioner are not representative of all gum rosin sources and are likely representative of only one regional source of GR.

Raw Material Sourcing Differences

WR is derived almost exclusively from 2-3 related species of pine tree – predominantly Long leaf (*Pinus palustris*) and Slash (*Pinus elliotti*) - harvested in the Southeastern US and Central America. (Ref: *Naval Stores: Production, Chemistry and Utilization*, D. F. Zinkel & J. Russell, Pulp Chemicals Assoc., 1989, ICBN 0-96004416-2-5). In contrast, gum rosin is produced in a number of countries throughout the world, from at least ten different species of pine trees from a variety of subgenera. GR production has migrated primarily to developing countries where lower cost labor can offset the labor-intensive harvesting techniques. Major producers include Portugal, China, Indonesia, Brazil, Mexico, Russia, India and Argentina. Various collection/processing methods and chemical stimulants may be used, depending on the region or producer. Not only is GR obtained globally from a wide variety of sources, but its chemical composition varies significantly depending on its geographical harvesting area. Therefore, there is no standard source for GR, and no single GR that is characteristic of the entire grouping. Indeed, in a global study of the Gum Naval Stores industry conducted by the Natural Resources Institute, Kent, England, supported by the FAO, reported that:

> "There are no international standards for rosin, and although the American Society for Testing and Materials (ASTM) describes standard test methods, it stipulates no specifications to which rosin should conform. The appropriate controlling bodies of some producing countries do provide specifications but, inevitably, companies and traders involved in the rosin industry have their own 'in-house' specifications which will vary from company to company, and this makes it difficult to generalize and quote 'typical' analytical data."

In addition to this Natural Resources Institute report, the Joint FAO/WHO Expert Committee on Food Additives (JECFA) also recognizes the difference among the various rosin sources in their definition of the glycerol ester of wood rosin:

> A complex mixture of tri- and diglycerol esters of resin acids from wood rosin obtained by the solvent extraction of aged pine stumps followed by a liquid-liquid solvent refining process. Excluded from these specifications are substances derived from gum rosin, and exudate of living pine trees, and substances derived from tall oil rosin, a by-product of kraft (paper) pulp processing. The final product is composed of approximately 90% resin acids and 10% neutrals (non-acidic compounds). The resin acid fraction is a complex mixture of isomeric diterpenoid monocarboxylic acids having the typical empirical formula of $C_{20}H_{30}O_2$, of which the main component is abietic acid. The substance is purified by steam stripping or by countercurrent steam distillation.
>
> *Prepared at the 46th JECFA (1996), published in FNP 52 Add 4 (1996) superseding specifications prepared at the 37th JECFA (1988), published in FNP 38 (1988) and in FNP 5 (1992) Ester Gum, INS No. 445*

Raw Material Processing Differences

As FDA is undoubtedly aware, rosin, the raw material for production of the glycerol ester of rosin, can come from several different processes as well. Wood rosin (WR) is the term applied to rosin derived from aged pine stumps that have been shredded into chips and solvent extracted, followed by liquid-liquid solvent refining of the crude rosin extract. Gum rosin (GR) is derived from the exudate obtained by tapping live trees and collecting the crude oleoresin (also called crude gum or gum dip). Tall oil rosin (TOR) is recovered as a by-product from the paper pulp manufacturing process. While the tree is the origin in all three cases, there are significant differences in the actual rosin generated from those different processes. Hercules Incorporated has a long history of manufacturing rosin-based products and is one of the few US manufacturers who have used all three sources of rosin in manufacturing our rosin-based products. Based on our experience, we recognize that the three rosins themselves are individually unique, and products made thereof are distinguishable, and frequently have discernible performance differences in end use applications.

GR is generally manufactured via a single stage 'flash' distillation process whereby the terpene (turpentine) fraction is volatilized leaving the rosin as a bottoms product. The rosin therefore may contain any metals, less volatile impurities, and chemical stimulants (often used to increase the flow of exudates from the tree) that were present in the crude oleoresin.

WR is manufactured via a multistage purification and refining process involving solvent extraction of the pine wood chips followed by solvent-solvent refining of the crude rosin extract. This unique process removes volatile terpene fractions as well as less volatile impurities such as metals and chromophoric, polar, and oxidized species. As a result of these multiple purification steps, some of the natural variation of rosin is removed leaving a more consistent, standardized raw material for subsequent esterification. The refining process also includes countercurrent steam stripping as the final step prior to esterification.

WR is manufactured to a single, unique set of specifications within the United States, by a well-defined processing method that has been used for over a half century. Wood rosin is synonymous not only with the source (pine stumps), but with the process.

Compositional Differences and Variation in Gum Rosin

Attachment 1 is a research report generated by Hercules in 1989 entitled *'Rosin Profiles – GC Characterization'*. This report not only demonstrated differences among WR, GR and TOR, but also demonstrated significant differences within GR depending upon the geographic source. GRs from Brazil, Mexico, Indonesia, China, Indonesia and Portugal were analyzed. Table II (p.16) of this report shows significant variation in the total rosin acid content from a low of 77% in Mexican gum rosin to a high of almost 97% in Chinese gum rosin. The table below (reconstructed from table II, p.16 of attachment 1) summarizes the resin acid content across the various sources of gum rosin and the calculated average, standard deviation (SD) and relative standard deviation (RSD) for the most significant rosin acids.

Reference: Hercules DDR report 11-017-01, September 25, 1989 (p.16) by B. Moyers								
Resin Acid (%)	CGR	BGR	MGR	IGR	PGR	mean	SD	RSD
Pimaric	8.3	4.0	5.4	0.2	8.6	5.3	3.4	65%
Sandaracopimaric	2.3	2.0	1.3	7.8	1.9	3.1	2.7	87%
Palustric	13.1	12.3	23.4	18.5	21.5	17.8	4.9	28%
Isopimaric	1.5	15.9	12.4	16.0	4.5	10.1	6.7	67%
Abietic	48.4	36.1	12.8	28.9	26.3	30.5	13.1	43%
Dehydroabietic	4.5	3.1	5.4	3.6	5.9	4.5	1.2	26%
Neoabietic	12.4	12.8	10.3	6.0	18.1	11.9	4.4	37%
Dihydroabietic	0.8	0.4	0.6	0.0	0.0	0.4		
Mercusic	0.0	0.0	0.0	6.5	0.0	0.0		

CGR = Chinese gum rosin, BGR = Brazilian gum rosin, MGR=Mexican gum rosin
IGR=Indonesian gum rosin, PGR = Portuguese gum rosin

Similar data can also be found in Zinkel and Russell, including a table summarizing the resin acid analyses of thirteen different commercial gum rosins (Ref: *Naval Stores: Production, Chemistry and Utilization*, D. F. Zinkel & J. Russell, Pulp Chemicals Assoc., 1989, pp. 276-277).

The petition submitter offers an analogous table in Table 5 (p.19) of the petition as a representation of the various resin acids on gum rosin. Hercules submits that these gum rosin sources were most likely all from one geographic location and as such do not fully represent the global sample population and the inherent natural variability. Figures 4 through 10 (pages 9 through 15 of attachment 1) offer visual evidence of the variations in gum rosin composition by location. The term "gum rosin" is applied equally to Indonesian gum rosin, which contains a unique dicarboxylic rosin acid (mercusic acid) not present in WR and therefore possesses a high acid number in the range of 185-195, to Chinese gum rosin, with a total abietic-type acids content of about 70% and an acid number of 165-175, and to Mexican gum rosin, with a total abietic-type acids content of about 50% and an acid number of 150-165.

These differences within the gum rosin global sourcing pool can lead to significant performance differences in downstream processing and end use applications. For example, producers of the soap of disproportionated rosin may experience different processing difficulties with different GRs, e.g., crystallization due to the high rosin acid content of Chinese GR, or lack of reactivity due to the low rosin acid content of Mexican GR.

By contrast, WR shows much less variability as noted in the table below that summarizes analyses of samples from 1981 to 2000.

	Sample Designation									
Resin Acid (%)	39-1	39-2	19-1	52-1	Wood	Pale Rosin	95-1	Mean	SD	RSD
Pimaric	4	4	6	5	6	6	6	5.3	1.0	18%
Palustric	8	8	11	10	10	12	9	9.7	1.5	15%
Isopimaric	12	12	12	11	15	13	11	12.3	1.4	11%
Abietic	37	37	40	39	40	37	41	38.7	1.7	4%
Dehydroabietic	6	6	9	9	7	6	6	7.0	1.4	20%
Neoabietic	7	7	10	9	10	8	7	8.3	1.4	17%
Reference	2	2	4	4	1	3	5			
1 = Attachment 1: Hercules DDA report 11-017-01, September 25, 1989, B.M. Moyers, p. 16										
2 = Attachment 2: Hercules DDR report 11-105-77, October 1, 1982, E. C. Linsay, p. 4										
3 = Attachment 3: Hercules memo from J. M. McGuire to R.B. Merck, November 25, 1998, p. 4										
4 = Attachment 4: Hercules DDR report 11-084-01, January 20, 1982, E.C. Linsay, p. 12										
5 = Attachment 5: Hercules memo from J.M. McGuire to R.B. Merck, August 11, 2000, p. 2										

39-1 = wood rosin sample from Brunswick, GA facility, March 1981
39-2 = wood rosin sample from Brunswick, GA facility, September 1981
19-1 = wood rosin sample from Hattiesburg, MS facility, 1981

52-1 = wood rosin sample from Hattiesburg, MS facility, 1981

Wood = wood rosin sample from Brunswick, GA facility, 1989
Pale Rosin = wood rosin sample from Brunswick, GA facility, 1998
95-1 = wood rosin sample from Brunswick, GA facility, 2000

Esterification Differences

Following the solvent-solvent purification step, WR is esterified with Kosher-grade glycerine to generate the GEWR. The rosin and glycerine are added in a fixed ratio to yield a product consisting predominantly of the triglycerol ester of rosin. Since the resin acid content and mix is relatively standard, the process conditions and reaction stoichoimetry are relatively fixed. Hercules has included for reference, molecular weight analyses of five different samples of Ester Gum 8BG taken from production over the past 10 months (see attachments 6 and 7). These data show the uniformity and reliability of the esterification process for wood rosin.

Variations in the rosin acid content of GR lead to potential variation during the esterification process which can equate to variation in the final GEGR. As shown above, GR harvested from different geographical locations can have significantly different rosin acid isomer distributions and physical properties. In addition to the variation in individual resin acids, the variation in *total* rosin acid content is also significant. The total rosin acid content will obviously determine the maximum amount of rosin triglycerides that would result from the esterification process and thus the regulated physical properties of softening point and acid number. Esterification of different gum rosins with glycerine will

therefore yield glycerol esters with different rosin ester distribution and properties. Consequently, the "glycerol ester of gum rosin" cannot be a unique or well-defined entity as is the GEWR. Furthermore, to produce a consistent GEGR the esterification process must be manipulated, altered or changed to compensate for the natural variation in rosin acid isomer content. In order to meet the softening point and acid number specifications in the final rosin ester as defined under 21 CFR 172.735, the esterification process will require manipulation for each source of GR.

This process alteration could include addition of a larger excess of glycerine to keep the softening point lower, by altering the reaction to yield less tri-ester and more of the lower molecular weight mono- and di-esters. Higher amounts of mono- and di-ester may render the ester more bioavailable by virtue of their lower molecular weight. Hercules is not aware of data demonstrating bioavailability, or lack thereof, for rosin esters higher in mono- and di-esters.

Comparison of Wood Rosin and Gum Rosin via Saponification and GC Analysis

The petitioner apparently analyzed samples of glycerol esters of gum and wood rosin by the traditional method of saponification and gas chromatography to estimate the RAs in the original rosin. However, it is well known that such techniques can induce isomerization of the rosin acids, thereby changing the composition compared to the starting rosin. While this may be valid for determining the *total* RA content of the rosin raw material, it may not be valid for determining the original RA isomer concentrations because the saponification process can impact the isomer distribution. In other words, rosin that has been esterified then saponified will not necessarily have the same RA mix as the original unreacted rosin. It is not a technically sound argument to compare WR esters to GR esters based on saponification and GC analysis of the rosin ester products without further substantiation of the analytical methodology.

Conclusion:

Based on our data combined with years of research and production experience, Hercules respectfully submits that gum rosin and wood rosin are *not* chemically equivalent. The source and processing of the raw materials are different, comparing different gum rosins to one another, or comparing GR to WR. The total rosin acid and isomer mixtures in gum rosin are considerably more variable (mainly due to geographic source), and the esterification processes may be altered to compensate for the source material.

The term "gum rosin" encompasses a wide variety of individual rosins, with unique analytical fingerprints and performance properties. There is no single GR that is representative or characteristic of the entire group. The collection methods, chemical composition and processing methodology for GR vary from one geographic location to another. Different gum rosins do not always produce equivalent products when derivatized, e.g., esterified, and their derivatives do not always perform equivalently when compared side-by-side in end use applications. Consequently, the "glycerol ester of gum rosin" cannot be a unique or well-defined substance.

Although chemical equivalency may be argued by comparing WR to a carefully selected, narrow slice of the GR population, this argument ignores the known variations in GR origin, processing, and quality. An equally convincing argument against equivalency could be made by comparing two distinctly different GRs to each other, or by comparing a distinctively different GR to WR.

Given that gum rosin is highly variable in origin and composition, and that the glycerol ester of gum rosin necessarily incorporates this variability, it is not reasonable to make a blanket claim of chemical equivalency with wood rosin. As such, one should *not* assume that the safety and toxicological data currently applicable for wood rosin or its glycerol ester are also applicable to gum rosin or its glycerol ester.

Apart from these substantive comments on the contents of FAP No. 3A4749, we object to the petitioner's reliance on a significant body of safety data generated by Hercules. FDA's regulations governing food additive petitions state that "any reference to unpublished information furnished [previously to FDA] by a person other than the applicant will not be considered unless use of such information is authorized in a written statement signed by the person who submitted it [previously to FDA]." 21 CFR 171.1(b). FAP No. 3A4749 seems to disregard this requirement.

The principal approach of FAP No. 3A4749 is to argue that the glycerol ester of gum rosin is chemically similar to the glycerol ester of wood rosin. The petitioner then concludes that because the wood rosin product is safe in this particular application, the gum rosin product must also be safe. Even if this approach were properly supported, it is premised on the safety of the glycerol ester of wood rosin, as reflected in its clearance for this use under section 172.735. Petitioner has not obtained permission from Hercules and has not cited permission obtained from any other source to rely on unpublished data submitted to FDA in support of the existing food additive clearance. Thus, it would not be appropriate for FDA to refer to any previous toxicological evaluations conducted within the agency or FDA memoranda on the safety of the glycerol ester of wood rosin or gum rosin that were based on unpublished data submitted previously to the Agency. To the extent that FAP No. 3A4749 depends on the safety of the glycerol ester of wood rosin, the petitioner must demonstrate its safety without relying on data submitted to FDA by Hercules or conclusions based upon Hercules' data.

Respectfully submitted,

G. L. McCallister
Director, Regulatory Affairs
Hercules Incorporated

GLM:clj
Attachments

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