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April 4, 2008

Robert L. Martin, Ph.D.
Office of Food Additive Safety (HFS-200)
Center for Food Safety and Applied Nutrition
Food and Drug Administration
5100 Paint Branch Parkway
College Park, MD 20740-3835

Subject: GRAS Notification for Modified Gum Acacia

Dear Dr. Martin:

Pursuant to proposed 21 CFR 170.36 (62 FR 18960; April 17, 1997), TIC Gums, through Exponent as its agent, hereby provides notice of a claim that the food ingredient described in the enclosed notification document is exempt from the premarket approval requirement of the Federal Food, Drug, and Cosmetic Act because it has been determined to be generally recognized as safe (GRAS), based on scientific procedures, for addition to foods as an emulsifier.

Three copies of the notification are provided as required. If you have any questions or require additional information, please do not hesitate to contact me at 202-772-4915, or ntran@exponent.com.

Sincerely,

Nga L. Tran, Dr.PH, MPH
Senior Managing Scientist

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Center for Chemical Regulation and Food Safety

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APR 07 2008

GRAS NOTIFICATION FOR MODIFIED GUM ACACIA

GRAS NOTIFICATION FOR MODIFIED GUM ACACIA

SUBMITTED BY:

TIC Gums, Inc.
4609 Richlynn Drive
Belcamp, MD 21017

SUBMITTED TO:

U.S. Food and Drug Administration
Center for Food Safety and Applied Nutrition
Office of Food Additive Safety
HFS-200
5100 Paint Branch Parkway
College Park, MD 20740-3835

CONTACT FOR TECHNICAL OR OTHER INFORMATION:

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April 4, 2008

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Acronyms and Abbreviations

ADI	Acceptable Daily Intake
CAS	Chemical Abstracts Service
CFR	US Code of Federal Regulations
EDI	Estimated daily intake
EPA	Environmental Protection Agency
FAO/WHO	Food and Agriculture Organization/ World Health Organization
FARE	Foods and Residue Evaluation
FDA	US Food and Drug Administration
FEMA	Flavour and Extract Manufacturers Association
GRAS	Generally Recognized As Safe
HPLC	High Performance Liquid Chromatography
JECFA	Joint FAO/WHO Expert Committee on Food Additives
LD50	Lethal Dose, 50%
NHANES	National Health and Nutrition Examination Survey
NOAEL	No observed adverse effect level
NTP	National Toxicology Program
OECD	Organisation for Economic Cooperation and Development
OPPTS	Office of Pollution Prevention and Toxics
OSA	Octenylsuccinate
OSAn	1-octenylsuccininc anhydride
PDII	Primary dermal irritation index
SDS	Slowly digestible starch
TSCA	Toxic Substances Control Act
USDA	United States Department of Agriculture

I. GRAS EXEMPTION CLAIM

A. Name and Address of Notifier

TIC Gums, through its agent Exponent, hereby notifies the Food and Drug Administration that the use of modified gum acacia described below is exempt from the pre-market approval requirements of the Federal Food, Drug, and Cosmetic Act because TIC Gums has determined that such use is generally recognized as safe (GRAS) through scientific procedures.

April 4, 2008

Nga L. Tran, Dr.PH, MPH
Senior Managing Scientist, Exponent
Agent for TIC Gums

Date

B. Name of GRAS Substance

The name of the substance that is the subject of this Generally Recognized as Safe (GRAS) determination is modified gum acacia (gum arabic, hydrogen octenylbutanedioate, CAS No. 455885-22-0). Modified gum acacia is a cold-water soluble hydrocolloid proposed for use as an emulsifier. It is currently sold as a flavor component by the trade name Ticamulsion®. The modification of gum acacia involves the introduction of lipophilic groups to the polysaccharide in gum acacia by controlled esterification processes analogous to the production of modified food starch-OSA (21CFR172.892(d)).

In 2003, modified gum acacia was granted FEMA GRAS status (GRAS Flavoring Substance Substances 22, FEMA No. 4227) for use in flavorings in a variety of food categories including baked goods, beverages (nonalcoholic and alcoholic), breakfast cereal, cheese, chewing gum, condiments/relishes, confectionery frostings, egg products, fats/oils, fish products, frozen dairy, fruit ices, gelatins/puddings, granulated sugar, gravies, hard candy, imitation dairy, instant coffee/tea, jams/jellies, meat products, milk products, nut products, other grains, poultry, processed fruits, processed vegetables, reconstituted vegetables, seasonings/flavors, snack foods, soft candy, soups, sugar substitutes, and sweet sauces.

C. Intended Use and Consumer Exposure

Modified gum acacia that is the subject of this GRAS determination is intended for use as an emulsifier in pure fruit juices (100%), select fruit flavored drinks, select beverages (carbonated juice, oatmeal and energy drinks and vitamin water), salad dressings, sauces, icing, select breads (whole grain and high fiber breads), and select cereals (high fiber, low sugar and low fat adult cereals). Modified gum acacia would be used at a level of 1,000 ppm in pure fruit juices, 600 ppm in select fruit flavored drinks, 780 ppm in select beverages such as carbonated juice, energy drinks and vitamin water, 10,000 ppm in salad dressings, sauces and icing, 400 ppm in select

breads, and up to 650 ppm select cereals. The food categories, description and use levels are summarized in Table 1, below.

Table 1. Proposed New Uses of Modified Gum Acacia (ppm)

Food Group	Description	Modified Gum Acacia (ppm)
Icings	Icings included the iced portion of all iced cakes and cookies.	10,000
Salad Dressings	All varieties (low cal, regular and mayonnaise)	10,000
Sauces	White sauces, BBQ sauce, butter based and a variety of other sauces	10,000
Pure fruit juice (100%)	Pure fruit juices	1,000
Select fruit flavored drinks	Vitamin fortified fruit flavored and thirst quencher drinks	600
Select beverages	Carbonated juice, oatmeal and energy drinks and vitamin water	780
Select breads (whole grain and high fiber breads)	Breads with whole grain and high in fiber (≥ 5 g per serving)	400
Select cereals (low fat, low sugar and high fiber health foods)	Cereals meeting three conditions: high in fiber (≥5 g per serving); low in fat (≤3 g per serving), and low in sugar (≤20 g per serving), and also excluding all foods that are popular among children such as Fruit Loops™ and Cheerios™)	350 or 650

* Fortification level is 350 ppm for foods with large serving size (55g/svg) and 650 ppm for foods with smaller serving sizes (30g/svg).

Exponent estimated the 2-day average daily intake of modified gum acacia from the current flavoring uses and proposed new uses listed above using the most recent food consumption survey data, the NHANES 2003-2004. About 99.9% of the US population ages 2 and older are consumers of foods in one or more of the currently approved flavoring uses and proposed new uses of modified gum acacia. The estimated daily intake (EDI) from the combined flavoring and proposed new uses at the mean per capita and per user level is 524 mg/day (964 mg/day at the 90th percentile). When intake is divided by bodyweight the mean per capita and per user levels are 9 mg/kg/day (17 mg/kg/day at the 90th percentiles). The actual intake is likely to be lower due to the innate conservatism in the intake assessment, which assumed that a large number of foods under each CFR food category with FEMA approved uses and/or proposed new emulsifier uses are fortified and consumed by consumers.

D. Basis for GRAS Determination

TIC Gums' GRAS determination for the intended uses of modified gum acacia is based on scientific procedures as described under 21 CFR§ 170.30(b).

The estimated daily intake (EDI) of modified gum acacia has been determined to be safe, and has also been determined to be GRAS by demonstrating that safety of this level of intake is based on publicly available and accepted information and is generally recognized by experts qualified by scientific training and experience to evaluate the safety of substances added to food.

The cumulative 90th percentile intake of MGA is estimated to be 17 mg/kg/day. The safety of this level of intake is based the publicly available toxicity data on modified gum acacia combined with an extensive toxicological database for gum acacia and modified food starch. The combination of the publicly available data cover a range of toxicity studies including acute/subchronic toxicity and genotoxicity on modified gum acacia, and acute, subchronic, and chronic toxicity, genotoxicity, reproductive/developmental toxicity, and carcinogenicity data for gum acacia and/or modified food starch. The NOAELs determined in the 90-day dietary study of modified gum acacia for the male and female rats were 3,411 and 4,052 mg/kg/day, respectively, the highest dose tested.

Gum acacia, a precursor material of MGA, has been affirmed as Generally Recognized as Safe (GRAS) in 21 CFR 184.1330 by the US Food and Drug Administration for use as an emulsifier, stabilizer, thickener and formulation aid. Approved food uses include beverages and beverage bases, chewing gum, confections and frostings, dairy product analogs, fats/oils, gelatins, puddings and fillings, hard candy and cough drops, nuts and nut products, quiescently frozen confection products, snack foods, soft candy, and all other food categories. Maximum permitted usage levels in food products range from 1-85%. In addition, gum acacia has been reviewed by the Joint FAO/WHO Expert Committee on Food Additives (JECFA) and an "ADI not specified" applied.

Food starch, modified by an esterification process involving 1-octenyl succinic anhydride is permitted for use as a multipurpose additive for direct addition to human food in 21 CFR 172.892(d). Modified food starch may be safely used in food that has been esterified by treatment with 1-octenyl succinic anhydride not to exceed 3 percent. In addition, modified starches including starch sodium octenyl succinate have been reviewed by the Joint FAO/WHO Expert Committee on Food Additives (JECFA) and an "ADI not specified" applied.

A JECFA ADI in humans of "not specified" means that "on the basis of available data (toxicological, biochemical, and other), the total daily intake of the substance arising from it use or uses at levels necessary to achieve the desired effect and from its acceptable background in food, does not, in the opinion of the Committee, represent a hazard to health. For this reason, and for the reasons stated in individual evaluations, the establishment of an ADI in mg/kg body weight is not deemed necessary."

The Acceptable Daily Intake (ADI) for this GRAS determination of modified gum acacia for use as an emulsifier is based upon the lowest NOAEL determined in the 90-day sub-chronic study in rats. Modified gum acacia was administered in the diet to groups of male and female rats at levels of 0, 10,000, 25,000, or 50,000 ppm. These levels corresponded to mean daily intakes of modified gum acacia of 0, 679, 1715, and 3411 mg/kg/day in male rats and 0, 799, 2,032, and 4,052 mg/kg/day in female rats. No test article-related effects were noted at any level tested. Therefore, NOAELs were 3,411 and 4,052 mg/kg/day, respectively, the highest dose tested. Due to the lack of observed toxicity at any dose level, a conservative estimate of the ADI is calculated

by dividing the NOAEL (for purposes of this assessment, 3,411 mg/kg/day) by an uncertainty factor of 100x. The uncertainty factor represents a 10x factor for differences between rats and a 10x factor for extrapolation of effects in animals to those in humans. Therefore, the ADI is conservatively estimated to be approximately 34 mg/kg/day (or 2,040 mg/day, assuming a 60 kg BW). The cumulative 90th percentile EDI from the intended uses of MGA is 17 mg/kg/day, only ½ of the ADI. The result of this publicly available study, in combination with the other relevant safety data and publicly available information cited in this notice, support the conclusion that the intended uses of MGA not only meet the safety standard of reasonable certainty of no harm, but that the proposed uses of MGA are also generally recognized as safe (GRAS).

In addition, the estimates of modified gum acacia intake are well below those for gum acacia itself. FDA has recently estimated the daily intake of gum acacia to be 3.25 g/day by combining the previously estimated daily intake of 2.5 g/day (FDA, 1983 as cited in the Federal Register, February 17, 2005) with the Kerry, Inc. daily intake estimate of 0.75 g/day for the approved use of gum acacia as a thickener, stabilizer, and emulsifier at a maximum level of 20% in alcoholic beverages (GRAS Notice No. G00058).

Determination of the safety and GRAS status of modified gum acacia for the direct addition to food under its intended conditions of use was made through the deliberation of an Expert Panel consisting of Joseph F. Borzelleca, PhD, Marcia van Gemert, PhD, and Barbara Petersen, PhD, who reviewed a dossier prepared by Exponent as well as other information available to them. These individuals are qualified by scientific training and experience to evaluate the safety of food and food ingredients. They critically reviewed and evaluated the publicly available information and the potential exposure to modified gum acacia resulting from the intended uses, and individually and collectively concluded that no evidence exists in the available information on modified gum acacia that demonstrates, or suggests reasonable ground to suspect, a hazard to the public health when modified gum acacia is used under its intended condition of use described. It is the Expert Panel's opinion that other qualified scientists reviewing the same publicly available data would reach the same conclusion. Therefore, modified gum acacia is GRAS by scientific procedures under the conditions of use described.

Subsequent to the initial GRAS determination, two additional food categories were added: select breads (whole grain and high fiber breads) and select cereals (low fat, low sugar and high fiber health foods). The addition of these two uses did not affect the cumulative EDI at the 90th percentile or the US population.

E. Availability of Information

The data and information that serve as the basis for the GRAS determination, as well as the information that has become available since the GRAS determination, will be sent to the FDA upon request, or are available for the FDA's review and copying at reasonable times from Exponent, 1150 Connecticut Ave, NW, Suite 1100, Washington, DC 20036, telephone 202-772-4915; and email: ntran@exponent.com.

II. Identity of Substance and Production

A. Chemical Name

Modified Gum Acacia (gum arabic, hydrogen octenylbutanedioate) is a cold-water soluble hydrocolloid proposed for use as an emulsifier.

B. Trade or Common Name

It is currently sold as a flavor component by the trade name Ticamulsion®.

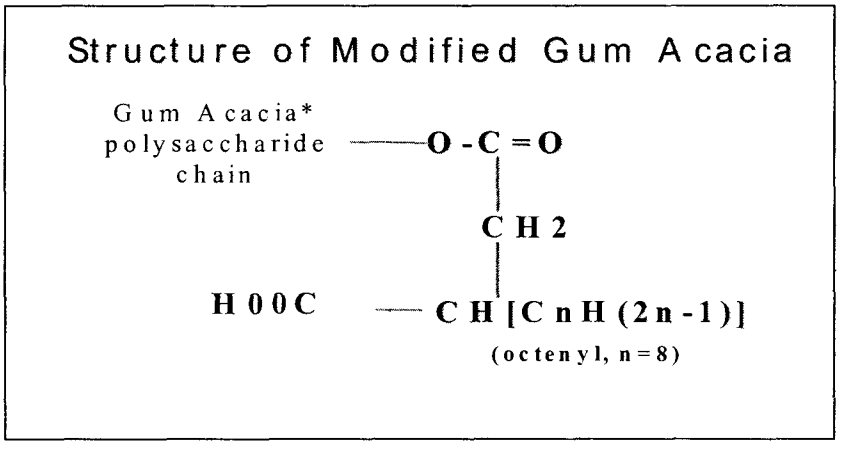
C. CAS Registry Number

The Chemical Abstract Services (CAS) registry number for modified gum acacia is 455885-22-0

D. Molecular and Structural Formula

The modification of gum acacia is described in U.S. patent number 6,455,512 and involves the introduction of lipophilic groups to the polysaccharide in gum acacia by controlled esterification processes (see Figure 1 below).

Figure 1. Modified Gum Acacia Structure

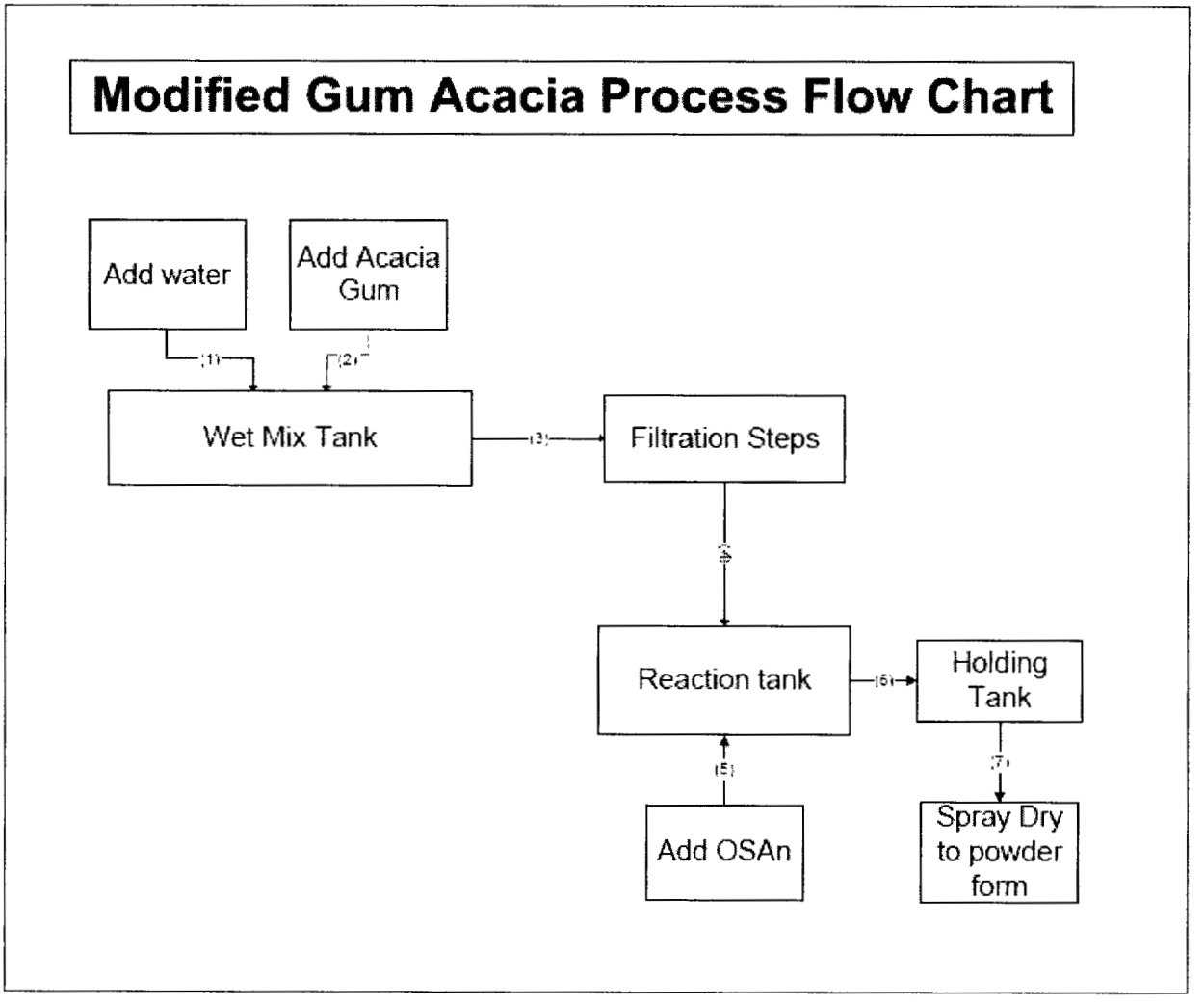


E. Production Process

Modified Gum Acacia is produced from acacia gum (CAS No. 9000-01-5; exudate of Seyal acacia tree, also known as gum arabic) by an esterification reaction involving the addition of 1-octenyl succinic anhydride (OSA; CAS No. 26880-5554-6), a process analogous to the production of modified food starch-OSA (21CFR172.892(d)). Modified gum acacia is produced

as an aqueous solution, which is subsequently spray-dried. The production of modified gum acacia employs food-grade ingredients and is summarized in the process diagram in Figure 2.

Figure 2. Modified Gum Acacia production diagram



F. Product Characteristics

Characteristic properties of modified gum acacia include:

Appearance (qualitative)	Free-flowing spray dried powder
Powder Color (visual)	Off-white to light tan
Melting Point	>300 ° C with decomposition
pH (viscosity solution)	3.5 – 6.5 pH (depends on finished application)
Moisture (infrared and/or loss on drying)	15%

The following is the proposed specifications for modified gum acacia:

SYNONYMS	Gum arabic hydrogenoctenylbutandioate; Gum arabic hydrogen octenylsuccinate; Modified gum arabic
DEFINITION	OSA Modified Gum Acacia (Arabic) is produced by esterifying gum Arabic, *Acacia seyal*, or gum Arabic, *Acacia senegal,* in aqueous solution with not more than 0.3% of 1-octenylsuccininc anhydride (OSA) (CAS No 26880-5554-6) in a process analogous with the production of starch octenyl succinic acid. It is subsequently spray dried to a powder.
CAS number	455885-22-0 (Gum arabic hydrogen octenylbutandioate)
DESCRIPTION	Off –white to light tan, free flowing powder
FUNCTIONAL USES	Emulsifier
CHARACTERISTICS	
IDENTIFICATION	Forms flocculent precipitate in lead sub –acetate solution (TS)
Solubility	1 g in 2 ml water, forms a free flowing solution, acid to litmus; insoluble in ethanol
pH of 5% solution	3.5-6.5
Viscosity of 5% solution	30 cps maximum (5%, 25C)
PURITY	
Degree of esterification	Not more than 0.6%
Loss on drying	15.0% (5 h at 105°)
Total ash	10% (530°C)
Starch or dextrin	(See tests) No bluish or reddish colour produced
Tannin-bearing gums	(See tests) No black coloration or precipitate forms
Residual OSA	(See tests) Not more than 0.3%
Microbiological criteria	*Salmonella.* Absent in 25 g; *E.coli.* Absent in 1 g
Lead	2mg/kg
TESTS	
Starch or dextrin	Boil a 1 in 50 aqueous solution of the sample; add about 0.1 ml iodine TS. No bluish or reddish colour should be produced
Tannin bearing gums	To 10 ml of a 1 in 50 aqueous solution of the sample; add about 0.1 ml ferric chloride TS, No blackish coloration or blackish precipitate should be formed.
Residual OSA	Principle: HPLC method on 2-bromacetophenone-derivatised methanolic extract of a sample. (See JECFA method for OSA starch) (JECFA, 2006)

Certificates of analysis for five representative lots of modified gum acacia can also be found in Appendix A. The data confirm production of a consistent modified gum acacia product.

E. Allergens

Modified gum acacia is derived from acacia gum, a tree exudate, whose major component is carbohydrate based (90g per 100g) with a minor component comprised of a glycoprotein fraction (2g per 100g). Modified gum acacia components do <u>not</u> contain any of the 8 major allergens of milk, egg, fish (e.g., bass, flounder, cod), crustacean shellfish (e.g., crab, lobster, shrimp), tree

nuts (e.g., almonds, pecans, walnuts), wheat, peanuts, and soybeans or an ingredient that contains a protein derived from one of these foods. TIC Gums' certified allergens statement for modified gum acacia is provided in Exhibit II.

III. INTENDED TECHNICAL EFFECT

The intended technical effect of modified gum acacia in food is its emulsifying properties. Modified gum acacia has enhanced emulsifying properties exceeding that of the traditional, emulsifying acacia species (*senegal*). *Acacia senegal* is the emulsifying species that is relatively more expensive than Acacia seyal and is subject to seasonal price fluctuations and availability. The introduction of the lipophilic group to the polysaccharide by controlled esterification procedures (Ward, 2004) enhances its emulsifying properties at lower usage levels, thus saving cost for manufacturer and/or consumer. Extensive work on beverage emulsions, both weighted and unweighted, has been conducted for several years by TIC Gums. The oil-in-water emulsions using modified gum acacia were more stable than those using modified starches, based on particle size distribution and beverage ring tests (Ward and Andon; Technical Bulletin on Ticamulsion, 2005). Investigative studies of modified gum acacia in salad dressing revealed that it yields small oil droplet sizes and a stable oil-in-water emulsions after several months of storage (Nieto, H. 2006).

IV. INTENDED USES AND CONSUMER EXPOSURE

A. Intended Uses and Use Levels

TIC Gums intended to market modified gum acacia as an emulsifier in pure fruit juices (100%), select fruit flavored drinks, select beverages (carbonated juice, oatmeal and energy drinks and vitamin water), salad dressings, sauces, icing, select breads (whole grain and high fiber breads), and select cereals (high fiber, low sugar and low fat adult cereals).

Modified gum acacia would be used at a level of 1,000 ppm in pure fruit juices, 600 ppm in select fruit flavor drinks, 780 ppm in select beverages (carbonated juice, oatmeal and energy drinks and vitamin water), and 10,000 ppm in salad dressings, sauces and icing, 400 ppm in select breads, up to 650 ppm in select cereals. See proposed use levels in Table 2.

Table 2. Proposed Use Levels of Modified Gum Acacia (ppm)

Food Group	Modified Gum Acacia (ppm)
Select fruit flavored drinks	600
Select beverages (carbonated juice, oatmeal and energy drinks and vitamin water)	780
Pure fruit juice (100%)	1,000
Icing	10,000
Salad Dressings	10,000
Sauces	10,000
Select breads (whole grain and high fiber breads)	400
Select cereals (high fiber, low sugar and low fat adult cereals).	350 or 650

* Fortification level is 350 ppm for foods with large serving size (55g/svg) and 650 ppm for foods with smaller serving sizes (30g/svg).

B. Estimated Daily Intake (EDI) of Modified Gum Acacia

Available Data and Methods

The estimated daily intake (EDI) of modified gum acacia from the current flavoring uses and proposed new uses including pure fruit juices (100%), select fruit flavored drinks, select beverages (carbonated juice, oatmeal and energy drinks and vitamin water), salad dressings, sauces, icing, select breads (whole grain and high fiber breads) and select cereals (high fiber, low sugar and low fat adult cereals) was estimated using consumption data from the most recent National Health and Nutrition Examination Survey (NHANES 2003-2004), use rates provided by TIC Gums, and Exponent's FARE™ software version 8.08. Mean and 90th percentile daily

intakes on both per capita and per user basis (mg/day and mg/kg /day) were estimated for the proposed new use of modified gum acacia for the US population 2 years and older.

Intake from Current Flavoring Uses

Modified gum acacia was granted FEMA GRAS status in 2003 for use in flavorings in a variety of food categories including baked goods, beverages (nonalcoholic and alcoholic), breakfast cereal, cheese, chewing gum, condiments/relishes, confectionery frostings, egg products, fats/oils, fish products, frozen dairy, fruit ices, gelatins/puddings, granulated sugar, gravies, hard candy, imitation dairy, instant coffee/tea, jams/jellies, meat products, milk products, nut products, other grains, poultry, processed fruits, processed vegetables, reconstituted vegetables, seasonings/flavors, snack foods, soft candy, soups, sugar substitutes, and sweet sauces (Smith et al, 2005).

The FEMA's anticipated usual and maximum use levels for modified gum acacia as a flavoring agent ranges from 5,000 ppm to 850,000 ppm and were established based on the FCC use levels for gum acacia, which are permitted in many foods, for various technical effects (e.g., panning coating, sugar crystal management, mouth feel enhancer, oil emulsifier), and at levels well above flavor emulsification uses. In actual application, modified gum acacia is used as part of a flavor emulsion package, as the flavor oil emulsifier, and at levels well below the FEMA listed levels. A typical flavor oil emulsion (or package) is comprised of 10% oils (flavors and weighting agents) and 16% gum acacia, the balance being water and a pH adjuster such as citric acid. Specifically, modified gum acacia is a significantly more efficient emulsifier and will be used at significantly lower use levels (ratios). It is expected that modified gum acacia would replace gum acacia and result in a minimum 50% reduction in concentration compared to gum acacia. Therefore, it would be used at a maximum 8% level within the flavor emulsion package (16% x 50% = 8%).

Actual use rates (or loading rates) of the flavoring emulsion package vary depending on the food. TIC Gums conducted a survey of several of its well-established flavoring house customers,[1] to obtain typical ranges of flavor emulsion loading rates. Using the average flavoring emulsion-loading rate per food category and modified gum acacia present at 8% in the flavor emulsion package, TIC Gums estimated average use levels of modified gum acacia per food category for each surveyed flavoring house. The actual maximum flavoring use level is up to 500 ppm.

Based on the surveyed use rates of the flavoring emulsion, the average daily intake from the current flavoring use of modified gum acacia was estimated to be 270 mg/day for users (268 mg/day per capita). Intakes at the 90th percentile were 506 mg/day on the per capita basis and 508 mg/day for users. When intakes were expressed on a bodyweight basis, the mean per capita intake was 4 mg/kg/day and 5 mg/kg/day, per capita and per user, respectively. The 90th percentile estimate was 9 mg/kg/day for both the per capita and per user.

[1] Mission Flavors and Virginia Dare: both are well-established flavor houses supporting a wide and diverse group food application ranges.

Intake from New Uses

TIC Gums intends to market modified gum acacia as an emulsifier in pure fruit juices (100%), select fruit flavored drinks, select beverages, salad dressings, sauces, icing, select breads, and select cereals. Pure fruit juices are all 100% fruit juices. Select fruit flavored drinks are vitamin fortified fruit flavored and thirst quencher drinks. Select beverages are carbonated juice, oatmeal and energy drinks and vitamin water. Salad dressings include all varieties including low cal, regular and mayonnaise. Sauces include white sauces, BBQ sauce, butter based and a variety of other sauces. Icings include the iced portion of all iced cakes and cookies. Select breads are breads with whole grain and high in fiber ($\geq$ 5 g per serving).[2] Select cereals are foods meeting three conditions: high in fiber ($\geq$5 g per serving); low in fat ($\leq$3 g per serving), and low in sugar ($\leq$20 g per serving), and also excluding all foods that are popular among children such as Fruit Loops™ and Cheerios™.

The per capita and per user intake estimates of modified gum acacia for the US population from the uses in select beverages (carbonated juice, oatmeal and energy drinks and vitamin water) and pure fruit juices have the highest intakes, with mean per user estimates at 311 mg/day (5.3 mg/kg/day) and 228 mg/day (5.5 mg/kg/day), respectively. The 90th percentile per user estimate for the uses in pure fruit juice is 455 mg/day (12 mg/kg/day); the 90th percentile is not estimated for the uses in select beverages due to inadequate sample size. The select breads and cereals categories have the lowest EDI, with mean per user at 10 mg/day (0.2 mg/kg/day) and 15 mg/day (0.1 mg/kg/day), respectively. The per user 90th percentile estimate for uses in select breads are unreliable due to sample size. For cereals, the per user 90th percentile estimate is 30mg/day (0.5 mg/kg/day). Data summaries in mg/day and in mg/kg/day are provided in Table 3.

Cumulative Estimated Daily Intake of Modified Gum Acacia

The estimated daily intake of modified gum acacia from the combined current flavoring and proposed new uses for the US population 2 years and older at the mean per capita and per user level is 524 mg/day (964 mg/day at the 90th percentile. When intake is divided by bodyweight, the mean per capita and per user levels for the US population are 9 mg/kg/day (17 mg/kg/day at the 90th percentiles for both per capita and per user), see Table 4.

[2] Serving sizes are based on FDA reference amounts customarily consumed (RACC as defined in 21 CFR 101.12. Nutrient content of foods were derived based on the USDA What We Eat In America Search Tool (USDA, 2008)

Table 3. US Population Average Daily Intake of Modified Gum Acacia from Proposed New Uses – NHANES 2003-2004

Food Group	mg/day				mg/kg/day			
	Per Capita		Per User		Per Capita		Per User	
	Mean	90th Percentile	Mean	90th Percentile	Mean	90th Percentile	Mean	90th Percentile
Sauces	9	25	48	104	0.1	0.4	0.7	1.6
Icing	11	40	68	131	0.2	0.6	1.3	2.4
Select fruit flavored drinks	17	0**	201	441	0.3	0**	3.7	7.7
Salad dressings	92	301	191	442	1.3	4.3	2.8	6.4
Pure fruit juice (100%)	84	274	228	455	2.0	5.6	5.5	12
Select beverages (carbonated juice, oatmeal and energy drinks and vitamin water)	1.8	NA	311	NA	0	NA	5.3	NA
Select breads (whole grain and high fiber breads)	0.3	NA	10	NA	0	NA	0.2	NA
Select cereals (low sugar, low fat and high fiber adult cereals)	1	0*	15	30	0	0*	0.2	0.5

NA: Inadequate sample size for 90th percentile estimation
* Weighted percent of users is 6.23%
**Weighted percent of users is 8.49%

Table 4. Cumulative Average Daily Intake of Modified Gum Acacia from Current Flavoring and Intended New Uses- NHANES 2003-04; US Population 2+

	Per Capita		Per User	
	Mean	90th Percentile	Mean	90th Percentile
mg/day	524	964	524	964
mg/kg/day	9	17	9	17

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EX

V. REVIEW OF SAFETY DATA

This section contains a review of the safety of modified gum acacia as well as gum acacia and modified food starch. A comprehensive search of the scientific literature from 1955 to June 2007 for safety and toxicity information on modified gum acacia, gum acacia, and modified food starch was conducted by Exponent. Databases searched included PubMed, Medline, Toxline, Highwire, the Chemical Carcinogenesis Research Information System, the Hazardous Substances Data Bank, the Developmental and Reproductive Toxicology database, the European Union Inventory of Existing Commercial Chemical substances, the U.S. Environmental Protection Agency, the International Association for Research on Cancer, the Domestic Substances List of Canada, the National Toxicology Program, the National Cancer Institute, the World Health Organization, the Joint FAO/WHO Expert Committee on Food Additives, the Food and Agricultural Organization, and the U.S. Food and Drug Administration and focused on the keywords "gum acacia," "gum arabic," "acacia," "modified food starch," "starch octenylsuccinate," starch octenyl succinate," "octenylsuccinate," and octenyl succinate." The data include acute, subchronic, and chronic toxicity, genotoxicity, reproductive/developmental toxicity, and carcinogenicity studies in animals, and human tolerance studies. This extensive toxicologic database provides a sufficient basis for an assessment of the safety of modified acacia gum for the proposed use as an emulsifier.

A. Modified Gum Acacia

1. Absorption, Distribution, Metabolism, and Excretion

Production of modified gum acacia involves the introduction of lipophilic groups to the polysaccharide in gum acacia by controlled esterification processes identical/analogous to the production of modified food starch-OSA (21CFR172.892(d)). It is known that modified food starch is poorly digested in the small intestine and incompletely fermented in the large intestine. Gum acacia has also been shown to be digested/metabolized by GI bacteria during passage through the colon (Ross et al, 1983). Gum acacia is composed of high-molecular weight polysaccharides, that upon hydrolysis yield arabinose, galactose, rhamnose, and glucuronic acid (Anderson et al, 1982 as cited in Anderson et al, 1983).

Starch sources (also polysaccharides) have been chemically modified with the goal of making modified food starch products with high contents of slowly digestible starch (SDS) and resistant starch (RS) (Han and BeMiller, 2007). Han and BeMiller (2007) have demonstrated that esterification of various starches with OSA results in a modified food starch product with the highest concentration of SDS and significant levels of RS. A modified food starch product with these digestibility characteristics would provide the nutritional benefits of starch (glucose supply), but not the high glycemic index or postprandial hypereglycemic and hyperinsulinemic increases associated with rapidly digestible starch. The OSA-modification of gum acacia (a polysaccharide source like starch) is expected to result in similar digestion/fermentation of modified gum acacia by colonic microflora of the large intestine (i.e., de-esterification in the stomach to gum acacia).

2. Animal Studies

Acute Studies

Two acute oral studies in rats and a primary dermal irritation study in rabbits have been conducted. The two oral studies employed either Ticamulsion A-1 (3% OSAN) or modified gum acacia OS-10 (10% OSAN) as the test article. The primary dermal irritation study employed modified gum acacia OS-10.

Ticamulsion A-1 was employed in a single dose acute oral study in male and female Sprague-Dawley albino rats. Ten animals (five male/five female) were administered a dose of 2000 mg Ticamulsion A-1/kg via gavage. The study was conducted to comply with good laboratory practices (EPA/TSCA and FDA). Animals were observed for 14-days post-exposure for mortality, signs of overt toxicity, behavioral changes and bodyweight. Evaluation of the skin and fur, eyes, mucous membranes, respiratory, circulatory, autonomic and central nervous system, and somatomotor activity was also conducted. Particular attention was directed to observation of tremors, convulsions, salivation, diarrhea and coma. At necropsy on day 14, tissues and organs of the thoracic and abdominal cavities were examined. All animals survived, gained weight and appeared healthy. No overt signs of toxicity were observed and no gross abnormalities were noted at necropsy. Therefore, the single dose acute oral LD_{50} value for modified gum acacia (Ticamulsion A-1) is > 2,000 mg/kg (PSL, 2002).

A similar second study was conducted with modified gum acacia OS-10 in female Sprague-Dawley albino rats only. Five female rats were administered a dose of 2,000 mg OS-10/kg via gavage. The study was conducted to comply with good laboratory practices (EPA/TSCA and FDA). Animals were observed for 14-days post-exposure for mortality, signs of overt toxicity, behavioral changes and bodyweight. Evaluation of the skin and fur, eyes, mucous membranes, respiratory, circulatory, autonomic and central nervous system, and somatomotor activity was also conducted. Particular attention was directed to observation of tremors, convulsions, salivation, diarrhea and coma. At necropsy on day 14, tissues and organs of the thoracic and abdominal cavities were examined. All animals survived, gained weight and appeared healthy. No overt signs of toxicity were observed and no gross abnormalities were noted at necropsy. Therefore, the single dose acute oral LD_{50} value for modified gum acacia (OS-10) is > 2,000 mg/kg (PSL, 2003a).

A primary skin irritation study was conducted in New Zealand White rabbits. Five-tenths of a gram of modified gum acacia OS-10 was applied to the intact and abraded skin of six rabbits (3 male/3female) and covered with occlusive wrapping. After a period of 4 hours the compound was removed from the skin. The study was conducted to comply with good laboratory practices (EPA/TSCA and FDA). The dose application sites were examined for erythema and edema at 1, 24, 48, and 72 hours and at 7, 10 and 14 days after patch removal. Dermal irritation was evaluated using the method of Draize et al (1944). Animals were also observed for mortality, overt signs of toxicity, behavioral changes and bodyweight gain. Evaluation of the skin and fur, eyes, mucous membranes, respiratory, circulatory, autonomic and central nervous system, and somatomotor activity was also conducted. Particular attention was directed to observation of tremors, convulsions, salivation, diarrhea and coma. The primary dermal irritation index (PDII) was calculated to be 1.6 for abraded sites and 1.4 for intact sites. Modified gum acacia OS-10

was slightly irritating through day 10, although the scores decreased over time, and was considered non-irritating by day 14. Using the EPA OPPTS classification system, modified gum acacia OS-10 was considered slightly irritating to the skin for both abraded and intact sites. It was not considered to be a primary irritant according to Consumer Product Safety Commission Guidelines. Other than slight irritation, no other overt signs of toxicity were noted (PSL, 2003b).

Subchronic Studies

A 14-day dietary palatability and general toxicity study was conducted along with a subsequent 90-day dietary study in rats (OECD Section 4, Part 408 and FDA Redbook, 2000). The 14-day pilot study data was used to select dietary levels for the subsequent 90-day dietary study in rats.

In the palatability study, modified gum acacia was administered in the diet for 14 days to forty Hsd:Sprague Dawley® SD® rats (five male and five females/group) at levels of 0, 15,000, 30,000, or 50,000 ppm. These levels corresponded to mean daily intakes of modified gum acacia of 0, 1,237, 2,534, and 4,198 mg/kg/day in male rats and 0, 1,325, 2,674, and 4,481 mg/kg/day in female rats. Animals were observed daily for viability, overt signs of toxicity, and behavioral changes and weekly for a battery of clinical observations. Body weights and food consumption were recorded. Gross necropsies were performed on all animals. No mortality was observed during the course of the study. No treatment-related changes were noted in clinical observations, food consumption/efficiency, body weight/body weight gain, or at gross necropsy. A NOAEL of 50,000 ppm was identified for both male and female rats and levels of 0, 10,000, 25,000, and 50,000 ppm were selected for the 90-day dietary study (Eurofins/PSL, 2006; Schmitt et al, 2008).

In the subsequent subchronic toxicity study conducted in compliance with OECD and FDA Redbook regulations, modified gum acacia was administered in the diet for 90 days to eighty Hsd:Sprague Dawley® SD® rats (ten male and ten females/treatment group) at levels of 0, 10,000, 25,000, or 50,000 ppm. Signs of toxicity were recorded daily and body weights weekly. Ophthalmological examinations were conducted prior to treatment and again prior to termination. A functional observational battery and motor activity evaluation were conducted prior to test termination. Food consumption was measured weekly and food efficiency calculated. Hematology, clinical chemistry, and urinalysis examinations were conducted on samples collected prior to test termination. All animals were sacrificed and necropsied at the end of the study. Histological examination of tissues and organs from the control and high dose groups were conducted.

No mortality or clinical signs of toxicity were observed during the course of the study. Modified gum acacia consumption had no significant effect on body weight parameters or food consumption. The administered concentrations corresponded to mean daily intakes of modified gum acacia of 0, 679, 1,715, and 3,411 mg/kg/day in male rats and 0, 799, 2,032, and 4,052 mg/kg/day in female rats. There were no adverse changes in hematology, coagulation, urinalysis, or clinical chemistry parameters in male or female rats at any dose level. No significant macroscopic and organ weight changes were noted upon necropsy. No pathological evidence of toxicity was evident at levels up to 50,000 ppm in the diet. The NOAEL in this study is 50,000 ppm, the highest level tested (Eurofins/PSL, 2007; Schmitt el al 2008).

Genotoxicity Studies

The Bacterial Reverse Mutation assay (Ames test) was employed for detection of point mutations in the form of substitutions, additions or deletions of DNA base pairs in amino acid requiring strains of *Salmonella typhimurium* and *Escherichia coli*. Modified gum acacia was evaluated in the Ames assay employing *Salmonella* strains TA97a, TA98, TA100, and TA1535 and *E. coli* strain WP2 *uvr*A (328) both in the presence and absence of an exogenous metabolic activation system (Aroclor induced rat liver S9). Deionized ultra filtered water was employed as the test article solvent, diluent, and negative control. The mean number of revertants observed in the negative control was within the acceptable range for each strain used in the study. Mean positive controls demonstrated greater than a two-fold increase in revertant colonies per plate over the means of their respective negative controls. Test article concentrations of 5, 10, 50, 100, 500, 1,000, 2,500, and 5,000 µg per plate were tested in the plate incorporation assay and 100, 500, 1,000, 2,500, and 5,000 µg per plate were assessed in the confirmatory preincubation assay. No test concentration resulted in a mean number of revertants two times greater than the mean of the concurrent controls. Therefore, under the conditions of the study, modified gum acacia was negative for the induction of mutagenicity in the bacterial reverse mutation assay and was not considered genotoxic (Next Century Incorporated, 2006).

B. Gum Acacia

1. Animal Studies

Acute Studies

Acute studies by Morgareidge (1972) report oral LD50 values of 16, 18, 16, and 8 g/kg/day for mice, rats, hamsters, and rabbits, respectively (as cited in JECFA, 1982a)

Short-Term Studies

Groups of three male rats were administered diets containing 0, 1, 4, and 8% of gum arabic for 28 days (Anderson et al, 1984 as cited in JECFA, 1990). Macroscopic examination of all organs at necropsy was followed by collection of materials for electron microscopy and microsomal P-450 assays. These were the stated objectives of the study. No detectable abnormalities were found in any of the organelles in the heart and liver specimens from any of the test animals and no inclusions or other pathological changes were observed. Gum arabic did not induce cytochrome P-450 or microsomal protein.

Subchronic/Chronic Studies

Male and female Wistar rats were fed gum arabic at dietary concentrations of 0, 1, 2, 4, 8, and 20% for 13 weeks (Anderson et al, 1982). Signs of toxicity were recorded daily and body weights weekly. Food and water consumption were measured weekly. Hematology, clinical chemistry, and urinalysis examinations were conducted on samples collected prior to test termination. All animals were sacrificed and necropsied at the end of the study. No adverse effects were noted at dose levels below that which caused a dietary/nutritional imbalance. At the 20% level, female rats demonstrated a small reduction in kidney weight, cecal enlargement, and changes in serum urea and CO2. At the 20% level, male rats demonstrated decreases in food and

water consumption, body weight, liver and kidney weights, as well as cecal enlargement. However, no histopathological changes were evident in any of the high-dose animals. The authors concluded that the NOAELs were 8% (5,200 mg/kg/day) and 20% (13,800 mg/kg/day) for male and female rats, respectively.

A new type of heat-treated gum acacia (SUPER GUM™) was administered in the diet for 90 days to eighty F34/DuCrj rats (ten male and ten females/treatment group) at levels of 0, 12,500, 25,000, or 50,000 ppm (Doi et al, 2006). Signs of toxicity were recorded daily and body weights weekly. Ophthalmological examinations were conducted prior to and during treatment. Food and water consumption were measured weekly. Hematology, clinical chemistry, and urinalysis examinations were conducted on samples collected prior to test termination. All animals were sacrificed and necropsied at the end of the study. Histological examination of tissues and organs from the control and high dose groups were conducted. No mortality or clinical signs of toxicity were observed during the course of the study. Gum acacia consumption had no significant effect on body weight parameters or food/water consumption. The administered levels corresponded to mean daily intakes of gum acacia of 0, 770, 1,505, and 3,117 mg/kg/day in male rats and 0, 839, 1,666, and 3,296 mg/kg/day in female rats. There were no adverse changes in hematology, coagulation, urinalysis, or clinical chemistry parameters in male or female rats at any dose level. No significant macroscopic and organ weight changes were noted upon necropsy. No pathological evidence of toxicity was produced at levels up to 50,000 ppm in the diet. An increased incidence of relative cecum (filled) weights in both sexes of the 5% group and females of the low- and mid-dose groups were considered to be a physiological adaptation and no corresponding histopathological alterations were noted in the cecum. The NOAEL was 50,000 ppm (3,117 mg/kg/day in males; 3,296 mg/kg/day in females).

The National Toxicology Program (NTP) conducted carcinogenicity studies of gum arabic in both rats and mice (Melnick et al, 1983). Groups of fifty male and fifty female F344 rats and B6C3F1 mice were fed diets containing 0, 25,000 (2.5%) or 50,000 ppm (5.0%) gum arabic for 103 weeks. No significant differences were observed in survival between any of the dosed groups of rats or mice and their control groups. Decreased body weight gain (>5%) was observed in female rats fed diets containing gum arabic. No histopathological effects were noted and therefore, under the conditions of the assays, gum arabic was considered non-carcinogenic to rats or mice.

Reproductive/Developmental Studies

The teratogenic potential of gum arabic was studied following administration of gum arabic in the diet at 0, 1, 2, 4, 7.5, or 15% to male and female Osborne-Mendel rats for 13 weeks before mating, during mating and throughout gestation (Collins et al, 1987). During gestation, female rats consumed 683 mg/kg/day (1%) up to 10,647 mg/kg/day (15%). Animals were euthanized on gestation day 20. No dose-related changes in maternal findings, numbers of fetuses, fetal viability, or external, visceral, or skeletal variations were noted. No developmental effects were observed and it was concluded that gum arabic is not a developmental toxicant.

Groups of Wistar rats, CD-1 mice, and outbred golden hamsters were dosed by gavage on days 6-15 (rats and mice) and days 6-10 (hamsters) of gestation with 0, 16, 75, 350, or 1,600 mg/kg/day of gum arabic in corn oil (Morgareidge 1972, as cited in JECFA, 1982a). No

compound-related effects were noted other than slightly depressed fetal body weight at birth in rats and mice. No developmental effects were observed.

Groups of pregnant Dutch-belted rabbits were dosed by gavage on days 6-18 of gestation with 0, 8, 37, 173, or 800 mg/kg/day of gum arabic in corn oil (Morgareidge 1972, as cited in JECFA, 1982a). Maternal toxicity was noted in the majority of animals in the 173 and 800 mg/kg/day treatment groups and consisted of bloody diarrhea, urinary incontinence, anorexia, and death. Surviving animals remained normal, delivered at term, and produced normal offspring in all respects. No developmental effects were observed and it was concluded that gum arabic was not a teratogen.

Genotoxicity Studies

Numerous studies of the genotoxic potential of gum arabic have been conducted. Most are unpublished but cited by JECFA in its review of gum arabic safety (1982). Gum arabic was not mutagenic in *Saccharomyces cerevisiae* or *Salmonella typhimurium* strains G46 and TA1530 in the host-mediated assay or *in vitro* (Newell and Maxwell 1972, as cited in JECFA, 1982a).

Similarly, gum arabic was not mutagenic in *Saccharomyces cerevisiae* strain D4 or *Salmonella typhimurium* strains TA1535, TA1537, and TA1538, with and without activation. Both suspension and plate tests were used (Brusick 1975, as cited in JECFA 1982). In addition, gum arabic was not mutagenic in the sex-linked dominant lethal test employing Drosophila (Valencia and Abramson, as cited in JECFA 1982a).

An increased incidence in chromosomal breaks was observed in cultures of bone marrow metaphase chromosomes taken from rats dosed in vivo with 50 mg or 2.5 g/kg of gum arabic and in vitro in human WI-38 embryonic lung cells (Newell and Maxwell 1972, as cited in JECFA 1982a).

Sheu et al. (1986) tested gum arabic for mutagenicity in rodent germ cells employing the dominant lethal study (rats and mice) and the heritable translocation study (mice only). Male rats and mice were fed gum arabic in the diet at 3% and 2% levels, respectively for either 10 (rats) or 8 (mice) weeks. A statistically significant dominant lethal effect was noted in male rats but not male mice. No adverse effects were observed in the mouse heritable translocation study. The authors concluded that the biological significance of the dominant lethal response in male rats was not known.

The available information demonstrates the non-genotoxicity of gum arabic.

2. Human Tolerance Studies

Ross et al. (1983) administered 25g gum arabic once a day for 3 weeks to human subjects. The effect of dietary gum arabic on glucose absorption, cecal and colonic function, and hematologic and clinical chemistry parameters was studied. Decreases in serum cholesterol were observed but dietary gum arabic had no effect on glucose tolerance, stool weight, or fecal bile acids and neutral sterols. Gum arabic was not recovered in stool samples, suggestive of metabolism of gum arabic bacteria in the colon.

C. Modified Food Starch

1. Animal Studies

Short-Term Studies

JECFA (1982b) evaluated a caloric utilization study and two short-term studies in rats. No adverse effects were seen in the caloric utilization study in which the 2.74 g of a basal diet was supplemented with either 1.5 or 3 grams of starch sodium octenyl succinate for 4 weeks. Body weight gain was similar to a sucrose control group. The caloric value of starch sodium octenyl succinate was determined to be similar to that of cornstarch.

In one of the short-term studies, weanling albino rats fed a 35% starch diet containing 1% or 10% aluminum starch octenyl succinate in the diet grew slightly slower than control rats fed cornstarch and was associated with decreased food consumption. The second short-term study was a two-generation study in rats (Buttolph and Newberne, 1980). Charles River rats were maintained on diets containing 6, 12, or 30% starch sodium octenyl succinate or 30% cornstarch (control) and bred twice. High-dose and control animals were euthanized at 30 or 90 days post-weaning. Body weights and food intake were measured. Clinical pathology measurements were conducted. Necropsies were performed and organ weights recorded. A complete histological evaluation was performed on principal organs and tissues. The only significant effect noted during the course of the study was at the highest concentration tested (30% of the diet) and consisted of corticomedullary mineralization of the kidney in both sexes and in animals receiving either the modified or unmodified starch in the diet. This effect was considered by the authors to be a result of a marginal deficiency of dietary magnesium due to carbohydrate comprising a major proportion of the diet.

One additional review paper was identified which had not been evaluated by JECFA. In 2002, the Cosmetic Ingredient Review Expert panel published a paper on the safety assessment of aluminum starch octenylsuccinate (Nair and Yamarik, 2002). They found that aluminum starch octenylsuccinate and its related sodium salt had no adverse systemic, reproductive or developmental effects. Dermal injections produced no abnormal skin or systemic reactions in guinea pigs. No ocular toxicity or acute inhalation toxicity was seen. Clinical tests indicated little irritation potential and no sensitization. Based on available data, the expert panel concluded that aluminum starch octenylsuccinate was safe as used in cosmetic formulations.

D. Summary

The available toxicity data on modified gum acacia combined with the extensive toxicologic database and food uses for gum acacia and modified food starch, both precursor materials for the modified gum acacia, provide a sufficient basis for an assessment of the safety of modified gum acacia for the proposed use in fruit juices (100%), select fruit flavored drinks, select beverages (carbonated juice, oatmeal and energy drinks and vitamin water), salad dressings, sauces, icing, select breads (whole grain and high fiber breads), and select cereals (high fiber, low sugar and low fat adult cereals). The summarized studies include acute/subchronic toxicity and genotoxicity on modified gum acacia and acute, subchronic, and chronic toxicity, genotoxicity,

reproductive/developmental toxicity, and carcinogenicity data for gum acacia and/or modified food starch.

Modified gum acacia is not mutagenic. The acute oral LD_{50} in rats for modified gum acacia has been demonstrated to be greater than 2000 mg/kg of body weight. In a 90-day subchronic dietary study, administration of modified gum acacia at levels of 0, 1.0, 2.5, and 5.0% in the diet for 13 weeks did not produce any significant toxicologic manifestations. Microscopic evaluation of select organs and tissues revealed no unusual lesions or patterns of distribution that would suggest an effect of exposure to modified gum acacia in the diet. The no observed adverse effect level (NOAEL) was determined to be 3,411 mg/kg/day for males, and 4,052 mg/kg/day for females. Modified gum acacia is non-irritating to slightly irritating as demonstrated by the results of a primary dermal irritation study in rabbits. The results obtained from these studies support the safety of modified gum acacia for its proposed food use as an emulsifier.

VI. SAFETY ASSESSMENT AND GRAS DETERMINATION

A. Introduction

The regulatory framework for determining whether a substance can be considered generally recognized as safe (GRAS) in accordance with section 201(s) (21 U.S.C. § 321(s)) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. § 301 et. Seq.) ("the Act"), is set forth at 21 CFR 170.30, which states:

> General recognition of safety may be based only on the view of experts qualified by scientific training and experience to evaluate the safety of substances directly or indirectly added to food. The basis of such views may be either (1) scientific procedures or (2) in the case of a substance used in food prior to January 1, 1958, through experience based on common use in food. General recognition of safety requires common knowledge about the substance throughout the scientific community knowledgeable about the safety of substances directly or indirectly added to food.
>
> General recognition of safety based upon scientific procedures shall require the same quantity and quality of scientific evidence as is required to obtain approval of a food additive regulation for the ingredient. General recognition of safety through scientific procedures shall ordinarily be based upon published studies which may be corroborated by unpublished studies and other data and information.

These criteria are applied below in an analysis of whether the use of modified gum acacia as an emulsifier in pure fruit juices (100%), select fruit flavored drinks, select beverages (carbonated juice, oatmeal and energy drinks and vitamin water), salad dressings, sauces, icing, select breads (whole grain and high fiber breads), and select cereals (high fiber, low sugar and low fat adult cereals) is GRAS based upon scientific procedures.

B. FEMA, FDA, and JECFA Reviews

In 2003, modified gum acacia was granted FEMA GRAS status for use in flavorings in a variety of food categories including baked goods, beverages (nonalcoholic and alcoholic), breakfast cereal, cheese, chewing gum, condiments/relishes, confectionery frostings, egg products, fats/oils, fish products, frozen dairy, fruit ices, gelatins/puddings, granulated sugar, gravies, hard candy, imitation dairy, instant coffee/tea, jams/jellies, meat products, milk products, nut products, other grains, poultry, processed fruits, processed vegetables, reconstituted vegetables, seasonings/flavors, snack foods, soft candy, soups, sugar substitutes, and sweet sauces (Smith et al, 2005).

Gum acacia is approved as a direct food additive in 21 CFR 184.1330 and is Generally Recognized as Safe (GRAS) by the US Food and Drug Administration for use as an emulsifier, stabilizer, thickener and formulation aid. Approved food uses include beverages and beverage bases, chewing gum, confections and frostings, dairy product analogs, fats/oils, gelatins,

puddings and fillings, hard candy and cough drops, nuts and nut products, quiescently frozen confection products, snack foods, soft candy, and all other food categories. Maximum permitted usage levels in food products range from 1-85%. In addition, gum acacia has been reviewed by the Joint FAO/WHO Expert Committee on Food Additives (JECFA) and an "ADI not specified" applied (JECFA 1982a, 1993).

Food starch, modified by an esterification process involving 1-octenyl succinic anhydride is approved as a multipurpose additive for direct addition to human food for consumption in 21 CFR 172.892(d). Modified food starch may be safely used in food that has been esterified by treatment with 1-octenyl succinic anhydride not to exceed 3 percent. In addition, modified starches including starch sodium octenyl succinate has been reviewed by the Joint FAO/WHO Expert Committee on Food Additives (JECFA) and an "ADI not specified" applied (JECFA 1982b).

A JECFA ADI in man of "not specified" means that "on the basis of available data (toxicological, biochemical, and other), the total daily intake of the substance arising from it use or uses at levels necessary to achieve the desired effect and from its acceptable background in food, does not, in the opinion of the Committee, represent a hazard to health. For this reason, and for the reasons stated in individual evaluations, the establishment of an ADI in mg/kg body weight is not deemed necessary."

C. Safety Assessment of Modified Gum Acacia for Its Intended Uses

Exponent estimated the cumulative daily intake of modified gum acacia from the existing uses and proposed new uses in pure fruit juices (100%), select fruit flavored drinks, select beverages (carbonated juice, oatmeal and energy drinks and vitamin water), salad dressings, sauces, icing, select breads (whole grain and high fiber breads), and select cereals (high fiber, low sugar and low fat adult cereals). The estimated modified gum acacia intake from the combined intake of existing and approved flavoring uses and proposed new uses for the US population 2 years and older at the mean per capita and per user level is 524 mg/day (964 mg/day at the 90th percentile). When intake is divided by bodyweight, the mean per capita and per user levels for the US population are 9 mg/kg/day (17 mg/kg/day at the 90th percentiles for both per capita and per user).

The Acceptable Daily Intake (ADI) for this safety assessment is based upon the lowest NOAEL determined in the 90-day subchronic study in rats. Modified gum acacia was administered in the diet to eighty Hsd:Sprague Dawley® SD® rats (ten male and ten females/treatment group) at levels of 0, 10,000, 25,000, or 50,000 ppm. These levels corresponded to mean daily intakes of modified gum acacia of 0, 679, 1715, and 3411 mg/kg/day in male rats and 0, 799, 2,032, and 4,052 mg/kg/day in female rats. No test article-related effects were noted at any level tested. Therefore, NOAELs were 3,411 and 4,052 mg/kg/day, respectively. Due to the lack of observed toxicity at any level, a conservative estimate of the ADI is calculated by dividing the NOAEL (for purposes of this assessment, 3,411 mg/kg/day) by an uncertainty factor of 100x. The uncertainty factor represents a 10x factor for differences between rats and a 10x factor for

extrapolation of effects in animals to those in humans. Therefore, the ADI is estimated to be approximately 34 mg/kg/day.

Since the estimated cumulative 90th percentile EDI for modified gum acacia is ½ of the ADI, it may be concluded that modified gum acacia is safe for its intended uses.

The estimates of modified gum acacia intake are well below those for gum acacia itself. FDA has recently estimated the current daily intake of gum acacia to be 3.25 g/day by combining the previously estimated daily intake of 2.5 g/day (FDA, 1983 as cited in the Federal Register, February 17, 2005, Volume 70, No. 32; http://www.cfsan.fda.gov/~lrd/fr050217.html) with the Kerry, Inc. daily intake estimate of 0.75 g/day for the use of gum acacia as a thickener, stabilizer, and emulsifier at a maximum level of 20% in alcoholic beverages (GRAS Notice No. G00058).

E. General Recognition of the Safety of Modified Gum Acacia

The intended use of modified gum acacia has been determined to be safe through scientific procedures as set forth in 21 CFR§170.30(b). Because this safety evaluation was based on generally available information, it satisfies the first component of the common knowledge element of a GRAS determination. Determination of the safety and GRAS status of modified gum acacia for addition to foods under its intended conditions of use has been made through the deliberations of an Expert Panel comprising of Joseph Borzelleca, Ph.D., Marcia van Gemert, Ph.D., and Barbara Petersen, Ph.D. These individuals are qualified by scientific training and experience to evaluate the safety of substances intended to be added to food. They have critically reviewed and evaluated the publicly available information summarized in this document and have individually and collectively concluded that modified gum acacia, produced consistent with Good Manufacturing Practice and meeting the specifications described herein, is safe under its intended conditions of use. The Panel further unanimously concludes that these uses of modified gum acacia would be GRAS based on scientific procedures when the pivotal studies are published and that other experts qualified to assess the safety of foods and food ingredients would concur with these conclusions. The Panel's GRAS opinion is included as Exhibit I to this document.

The pivotal studies referred to by the Expert Panel are the toxicity data for modified gum acacia described in section (V)(A) of this document. These studies have been published by Schmitt et al in Food and Chemical Toxicology since November 2007 (E-Pub). Also subsequent to the Expert Panel review, uses for two food categories were added: select breads (whole grain and high fiber breads) and select cereals (low fat, low sugar and high fiber health foods). The addition of these select uses did not change the cumulative EDI at the 90th percentile or the US population.

Exponent is not aware of information that would be inconsistent with a finding that the proposed use of modified gum acacia as an emulsifier in pure fruit juices (100%), select fruit flavored drinks, select beverages (carbonated juice, oatmeal and energy drinks and vitamin water), salad dressings, sauces, icing, select breads (whole grain and high fiber breads), and select cereals (high fiber, low sugar and low fat adult cereals) meeting appropriate specifications and used

according to Good Manufacturing Practice, is GRAS. A recent search of the scientific literature revealed no potential adverse health concerns.

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Appendix A

APPENDIX A.
CERTIFICATES OF ANALYSIS

000041

EX

QA RELEASE REPORT

Average of validated and waived samples

10017 TMUL A-2010

Level 2		Specification		Result	Approved	
Bacteriological					-------	
APCR10	Aerobic Plate Count (AOAC 988 18)	0	5000	0 00	YES	
YMB10	Combined Yeast and Mold (BAM)	0	400	0 00	YES	
SAL25	Salmonella - 25g	Negative /25g		Negative /25g	YES	
COLIR10	Total Coliforms (AOAC 989 11)	0	10	0 00	YES	
Mesh					-------	
MESH80PA	USS#80 Mesh On	30	85	70 00	YES	
Physical and Chemical					-------	
FLAVOR	Flavor (Qualitative)	Bland		Bland	YES	
MOISTIR	Moisture (Infrared)	0	13	6 13	YES	
ODOR	Odor (Qualitative)	Characteristic		Characteristic	YES	
PHVISC	pH (viscosity solution)	3 3	6	5 63	YES	
COLOR	Powder Color (Visual)	Cream-Light Tan		Cream-Light Tan	YES	
SEDIMENT	Sediment (25 micron)	0	2.5	1 17	YES	
TEXTURE	Texture (Qualitative)	Free Flowing Powder		Free Flowing Powder	YES	
Level 1		**Specification**		**Result**	**Approved**	
Mesh					-------	
MESH020A	USS#20 Mesh On	0	10	0 00	YES	
MESH40PA	USS#40 Mesh On	0	30	2 00	YES	
Physical and Chemical					-------	
BULKDENG	Bulk Density	0.2	0 4	0.39	YES	
HUNTWI	Color Value (Hunter)	-5	15	-1.20	YES	
TMULEM900	Peak Micron Size - Emulsion Stability	0	1 04	0 25	YES	
TMULEMUL	TMULEMUL	0	1 04			MISSING DATA
VM5L	Viscosity (5 0%,LV@30rpm)	0	15	11 25	YES	
BULKDENG	Volume			230 00		
BULKDENG	Weight			90 75		
Standard					------	
ASHFCC	Crucible			16 85		
ASHFCC	Crucible Ash			17 14		
DEGEST	Degree of Esterification	0	0 2	0 18	YES	
OSAFREE	OSA (Residual)	0	0.3	0 07	YES	
ASHFCC	Sample Weight			3 54		
ASHFCC	Total Ash Content (FCC)	0	5	8 14	NO	

10017			pm	Open Event	
Correct Mesh?	Yes	Cleaned Magnet?	Yes	Open Dispo.	
Foreign Material?	No	Above Limit?	No		

Conforming Units:	NonConforming Units:	Nonconformance#

Approved by:	Approved Date:4/13/2007

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EX

QA RELEASE REPORT

Average of validated and waived samples

11376 TMUL A-2010

Level 2		Specification		Result	Approved
Bacteriological					-------
APCR10	Aerobic Plate Count (AOAC 988 18)	0	5000	0 00	YES
YMB10	Combined Yeast and Mold (BAM)	0	400	0.00	YES
SAL25	Salmonella - 25g	Negative /25g		Negative /25g	YES
COLIR10	Total Coliforms (AOAC 989.11)	0	10	0 00	YES
Mesh					-------
MESH80PA	USS#80 Mesh On	30	85	59 10	YES
Physical and Chemical					-------
FLAVOR	Flavor (Qualitative)	Bland		Bland	YES
MOISTIRP	Moisture (Infrared)	0	13	8.08	YES
ODOR	Odor (Qualitative)	Characteristic		Characteristic	YES
PH5	pH (5 0%)	3.3	6.0	5 46	YES
COLOR	Powder Color (Visual)	Cream-Light Tan		Cream-Light Tan	YES
SEDIMENT	Sediment (25 micron)	0	2.5	1 00	YES
TEXTURE	Texture (Qualitative)	Free Flowing Powder		Free Flowing Powder	YES

Level 1		Specification		Result	Approved	
Mesh					-------	
MESH020A	USS#20 Mesh On	0	10			MISSING DATA
MESH40PA	USS#40 Mesh On	0	30	17 10	YES	
Physical and Chemical					-------	
BULKDENG	Bulk Density	0 2	0.4			MISSING DATA
HUNTWI	Color Value (Hunter)	-5	15	9.45	YES	
TMULEM900	Peak Micron Size - Emulsion Stability	0	1.04	0.26	YES	
TMULEMUL	TMULEMUL	0	1.04			MISSING DATA
VM5L	Viscosity (5 0%,LV@30rpm)	0	15	5 78	YES	
BULKDENG	Volume					MISSING DATA
BULKDENG	Weight					MISSING DATA
Standard					-------	
ASHFCC	Crucible			19 87		
ASHFCC	Crucible Ash			20 10		
DEGEST	Degree of Esterification	0	0 2	0 17	YES	
OSAFREE	OSA (Residual)	0	0.3	0.16	YES	
ASHFCC	Sample Weight			3 34		
ASHFCC	Total Ash Content (FCC)	0	10	6.77	YES	

11376			BK	Open Event	
Correct Mesh?	Yes	Cleaned Magnet?	Yes	Open Dispo:	
Foreign Material?	No	Above Limit?	No		

Conforming Units:	NonConforming Units:	Nonconformance#

Approved by:	Approved Date:4/13/2007

QA RELEASE REPORT

Average of validated and waived samples

10754 TMUL A-2010

Level 2		Specification		Result	Approved	
Bacteriological					-------	
APCR10	Aerobic Plate Count (AOAC 988 18)	0	5000	0 00	YES	
YMB10	Combined Yeast and Mold (BAM)	0	400	4.25	YES	
SAL25	Salmonella - 25g	Negative /25g		Negative /25g	YES	
COLIR10	Total Coliforms (AOAC 989 11)	0	10	0.00	YES	
Mesh					-------	
MESH80PA	USS#80 Mesh On	30	85	55 70	YES	
Physical and Chemical					-------	
FLAVOR	Flavor (Qualitative)	Bland		Bland	YES	
MOISTIRP	Moisture (Infrared)	0	13	6 01	YES	
ODOR	Odor (Qualitative)	Characteristic		Characteristic	YES	
PHVISC	pH (viscosity solution)	3.3	6	5.27	YES	
COLOR	Powder Color (Visual)	Cream-Light Tan		Cream-Light Tan	YES	
SEDIMENT	Sediment (25 micron)	0	2.5	1 17	YES	
TEXTURE	Texture (Qualitative)	Free Flowing Powder		Free Flowing Powder	YES	

Level 1		Specification		Result	Approved	
Mesh					-------	
MESH020A	USS#20 Mesh On	0	10	0.23	YES	
MESH40PA	USS#40 Mesh On	0	30	2.30	YES	
Physical and Chemical					-------	
BULKDENG	Bulk Density	0 2	0.4	0.43	NO	
HUNTWI	Color Value (Hunter)	-5	15	1 93	YES	
TMULEM900	Peak Micron Size - Emulsion Stability	0	1 04	0 27	YES	
TMULEMUL	TMULEMUL	0	1 04			MISSING DATA
VM5L	Viscosity (5 0%,LV@30rpm)	0	15	11 50	YES	
BULKDENG	Volume			231.00		
BULKDENG	Weight			98.68		
Standard					-------	
ASHFCC	Crucible			17 43		
ASHFCC	Crucible Ash			17 71		
DEGEST	Degree of Esterification	0	0 2	0.18	YES	
OSAFREE	OSA (Residual)	0	0.3	0.10	YES	
ASHFCC	Sample Weight			3.62		
ASHFCC	Total Ash Content (FCC)	0	5	7.73	NO	

Correct Mesh? Cleaned Magnet? Open Event:
Foreign Material? Above Limit? Open Dispo

Conforming Units:	NonConforming Units:	Nonconformance#

Approved by:	Approved Date:4/13/2007

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EX

QA RELEASE REPORT

Average of validated and waived samples

10523 TMUL A-2010

Level 2		Specification		Result	Approved	
Bacteriological					-------	
APCR10	Aerobic Plate Count (AOAC 988.18)	0	5000	0 00	YES	
YMB10	Combined Yeast and Mold (BAM)	0	400	25.00	YES	
SAL25	Salmonella - 25g	Negative /25g		Negative /25g	YES	
COLIR10	Total Coliforms (AOAC 989 11)	0	10	0.00	YES	
Mesh					-------	
MESH80PA	USS#80 Mesh On	30	85	67 80	YES	
Physical and Chemical					-------	
FLAVOR	Flavor (Qualitative)	Bland		Bland	YES	
MOISTIRP	Moisture (Infrared)	0	13	6.83	YES	
ODOR	Odor (Qualitative)	Characteristic		Characteristic	YES	
PHVISC	pH (viscosity solution)	3.3	6	5.79	YES	
COLOR	Powder Color (Visual)	Cream-Light Tan		Cream-Light Tan	YES	
SEDIMENT	Sediment (25 micron)	0	2 5	1 83	YES	
TEXTURE	Texture (Qualitative)	Free Flowing Powder		Free Flowing Powder	YES	

Level 1		Specification		Result	Approved	
Mesh					-------	
MESH020A	USS#20 Mesh On	0	10	0 08	YES	
MESH40PA	USS#40 Mesh On	0	30	2 10	YES	
Physical and Chemical					-------	
BULKDENG	Bulk Density	0.2	0 4			MISSING DATA
HUNTWI	Color Value (Hunter)	-5	15	-11 18	NO	
TMULEM900	Peak Micron Size - Emulsion Stability	0	1 04			MISSING DATA
TMULEMUL	TMULEMUL	0	1.04			MISSING DATA
VM5L	Viscosity (5 0%.LV@30rpm)	0	15	26 80	NO	
BULKDENG	Volume					MISSING DATA
BULKDENG	Weight					MISSING DATA
Standard					-------	
ASHFCC	Crucible			18 07		
ASHFCC	Crucible Ash			18 38		
DEGEST	Degree of Esterification	0	0 2			MISSING DATA
OSAFREE	OSA (Residual)	0	0 3			MISSING DATA
ASHFCC	Sample Weight			3 34		
ASHFCC	Total Ash Content (FCC)	0	5	9.38	NO	

10523			csf	Open Event	
Correct Mesh?	Yes	Cleaned Magnet?	Yes	Open Dispo:	
Foreign Material?	No	Above Limit?	No		

Conforming Units:	NonConforming Units:	Nonconformance#

Approved by:	Approved Date:4/13/2007

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EX

QA RELEASE REPORT

Average of validated and waived samples

10575 TMUL A-2010

Level 2		Specification		Result	Approved	
Bacteriological					-------	
APCR10	Aerobic Plate Count (AOAC 988 18)	0	5000	1 67	YES	
YMB10	Combined Yeast and Mold (BAM)	0	400	6 67	YES	
SAL25	Salmonella - 25g	Negative /25g		Negative /25g	YES	
COLIR10	Total Coliforms (AOAC 989 11)	0	10	0 00	YES	
Mesh					-------	
MESH80PA	USS#80 Mesh On	30	85	52 80	YES	
Physical and Chemical					-------	
FLAVOR	Flavor (Qualitative)	Bland		Bland	YES	
MOISTIRP	Moisture (Infrared)	0	13	7.64	YES	
ODOR	Odor (Qualitative)	Characteristic		Characteristic	YES	
PHVISC	pH (viscosity solution)	3 3	6	5 48	YES	
COLOR	Powder Color (Visual)	Cream-Light Tan		Cream-Light Tan	YES	
SEDIMENT	Sediment (25 micron)	0	2 5	1.33	YES	
TEXTURE	Texture (Qualitative)	Free Flowing Powder		Free Flowing Powder	YES	
Level 1		**Specification**		**Result**	**Approved**	
Mesh					-------	
MESH020A	USS#20 Mesh On	0	10			MISSING DATA
MESH40PA	USS#40 Mesh On	0	30	3.00	YES	
Physical and Chemical					------	
BULKDENG	Bulk Density	0 2	0 4	0 44	NO	
HUNTWI	Color Value (Hunter)	-5	15	-1 88	YES	
TMULEM900	Peak Micron Size - Emulsion Stability	0	1 04	0 24	YES	
TMULEMUL	TMULEMUL	0	1 04			MISSING DATA
VM5L	Viscosity (5 0%,LV@30rpm)	0	15	8 33	YES	
BULKDENG	Volume			230 00		
BULKDENG	Weight			100 17		
Standard					-------	
ASHFCC	Crucible			17.98		
ASHFCC	Crucible Ash			18 25		
DEGEST	Degree of Esterification	0	0 2	0 18	YES	
OSAFREE	OSA (Residual)	0	0 3	0 11	YES	
ASHFCC	Sample Weight			3.37		
ASHFCC	Total Ash Content (FCC)	0	5	8.01	NO	

10575			DAC	Open Event:	
Correct Mesh?	Yes	Cleaned Magnet?	Yes	Open Dispo	
Foreign Material?	No	Above Limit?	No		

Conforming Units:	NonConforming Units:	Nonconformance#

Approved by:	Approved Date:4/13/2007

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EX

STRASBURGER
&SIEGEL,INC.
Food Testing Laboratories

7249 National Drive
Hanover, MD 21076
www.sas-labs.com
Tel: 800-875-6532
410-712-7373
Fax 410-712-7378

CERTIFICATE OF ANALYSIS

JOB NO.:
INV. NO.:
P.O. NO.:

RECEIVED DATE: 02/21/2007
REPORT DATE: 03/05/2007
DISCARD DATE: 03/19/2007

TIC GUMS, INC.

4609 RICHLYNN DRIVE
BELCAMP, MD 21017
U.S.A.

ATTENTION: DR. NABIL NAOULI

==========

SAMPLE TYPE: GUM
CONTAINER TYPE & SIZE: WHIRL-PACK BAG APPROX. 50 G

SAMPLE DESCRIPTION:

MODIFIED GUM ACACIA 10575

RESULTS (as received, unless otherwise stated):

Iron as Fe, mg/100g	2.43
Heavy Metals as Pb, %	NDLT(0.001) *

* None Detected, Less Than

REFERENCE:

Official Methods of Analysis of AOAC International (2005), 18th Ed., AOAC International, Gaithersburg, MD

Food Chemical Codex (2004), 5th Ed., Food and Nutrition Board, and Institute of Medicine of the National Academies. The National Academies Press, Washington, DC

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Prepared for TIC Gums
By Exponent, Inc
WD00869 001 P0T0 0408 0001

EX

STRASBURGER
&SIEGEL,INC.
Food Testing Laboratories

7249 National Drive
Hanover, MD 21076
www.sas-labs.com
Tel: 800-875-6532
410-712-7373
Fax. 410-712-7378

CERTIFICATE OF ANALYSIS

JOB NO.:
INV. NO.:
P.O. NO.:

RECEIVED DATE: 03/28/2007
REPORT DATE: 04/09/2007
DISCARD DATE: 04/23/2007

TIC GUMS, INC.

4609 RICHLYNN DRIVE
BELCAMP, MD 21017
U.S.A.

ATTENTION: MR. TIM ADAMS

SAMPLE TYPE: GUM
CONTAINER TYPE & SIZE: WHIRL-PAK BAGS

SAMPLE DESCRIPTION:

TMUL A-2010
1. 10575
2. 10754
3. 11376
4. 10523
5. 10017

RESULTS (as received, unless otherwise stated):

	As Is	FCC Limits	Limits of Detection
Sample No.	1,2,3,4,5		
Identification	Passes Test	White Precipitate	
Arsenic as As, mg/Kg	ND*	<3	1
Lead as Pb, mg/Kg	ND	<5	1
Starch or Dextrin, %	Passes Test	No Blue or Red Color	
Tannin-Bearing Gums	Passes Test	No Black Precipitate	

* None Detected

Note: JECFA Limits: Heavy Metals as Pb (<40 mg/Kg), Solublity & Reaction (Flows readily and acid to litmus).

REFERENCE:

Official Monographs for USP 30 and NF 25 (2007), U.S Pharmacopieal Convention, Rockville, MD

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EX

Exhibit I

EXHIBIT I.
EXPERT PANEL'S OPINION

000050

EX

OPINION OF AN EXPERT PANEL ON THE GENERALLY RECOGNIZED AS SAFE STATUS (GRAS) OF MODIFIED GUM ACACIA FOR USE AS AN EMULSIFIER

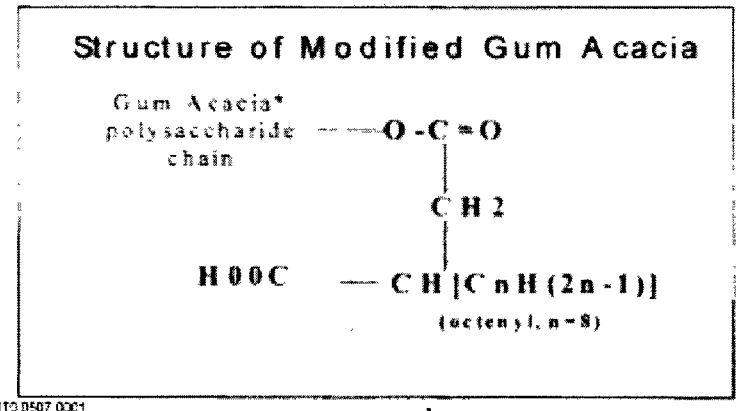
Introduction

The undersigned, an independent panel of experts, qualified by their scientific training and relevant experience to evaluate the safety of food and food ingredients, was requested by TIC Gums, Inc. to determine the safety and Generally Recognized as Safe (GRAS) status of modified gum acacia for use as an emulsifier in pure fruit juices (100%), select fruit flavored drinks, select beverages (carbonated juice, oatmeal, energy drinks and vitamin water), salad dressings, sauces and icing. A comprehensive search of the scientific literature from the mid-1950s to the present for safety and toxicity information on modified gum acacia, gum acacia, and modified food starch was conducted by Exponent and focused on the keywords "gum acacia," "gum arabic," "acacia," "modified food starch," "starch octenylsuccinate," "starch octenyl succinate," "octenylsuccinate," and "octenyl succinate." The data include acute, subchronic, and chronic toxicity, genotoxicity, reproductive/developmental toxicity, and carcinogenicity studies in animals, and human tolerance studies. The Expert Panel members critically evaluated a safety assessment document (GRAS Dossier) prepared by Exponent and other information deemed appropriate and necessary and unanimously agreed to the decision described herein.

Data and information that are the basis for this GRAS determination are available for review and reproduction at Exponent.

Description

The subject matter of this review is modified gum acacia. Modified Gum Acacia (gum arabic, hydrogen octenylbutanedioate, CAS No. 455885-22-0) is a cold-water soluble hydrocolloid proposed for use as an emulsifier. It is currently sold as a flavor component by the trade name Ticamulsion®. The modification of gum acacia is described in U.S. patent number 6,455,512 and involves the introduction of lipophilic groups to the polysaccharide in gum acacia by controlled esterification processes (see below).



WD00869 C01 J0T0 0507 0001

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By Exponent, Inc
WD00869.001 P0T0 0408 0001

EX

Typical assays of modified gum acacia include the following: Appearance (qualitative), free-flowing spray dried powder; Powder color (visual), cream-light tan; Melting point, >300 ° C with decomposition; pH (viscosity solution), 3.3 - 6.0 pH; Moisture (infrared drying), 0-13%; USS#80 Mesh on, 30-85%; Sediment (25 micron), 0-2.5 SU.

Modified gum acacia is further distinguished by physical, chemical, and functional properties, and by its specifications, all of which are described in the referenced safety assessment (GRAS Dossier).

Manufacturing Process

Modified Gum Acacia is produced from acacia gum (CAS No. 9000-01-5; exudate of Seyal acacia tree, also known as gum arabic) by an esterification reaction involving the addition of 1-octenyl succinic anhydride (OSA; CAS No. 26880-5554-6), a process analogous to the production of modified food starch-OSA (21CFR172.892(d)). Modified gum acacia is produced as an aqueous solution, which is subsequently spray-dried. The production of modified gum acacia employs food-grade ingredients.

Additional information concerning the synthesis of modified gum acacia may be found in the referenced safety assessment.

Functionality

Modified gum acacia that is the subject of this GRAS self-affirmation is proposed for use as an emulsifier in pure fruit juices (100%), select fruit flavored drinks, select beverages (carbonated juice, oatmeal, energy drinks and vitamin water), salad dressing, sauces, and icing. Modified gum acacia would be used at a level of 1000 ppm in pure fruit juices, 600 ppm in select fruit flavored drinks, 780 ppm in select beverages such as carbonated juice drinks, oatmeal beverages, energy drinks, and vitamin water, and 10,000 ppm in salad dressings, sauces, and icing.

In 2003, modified gum acacia was granted FEMA GRAS status for use in flavorings in a variety of food categories including baked goods, beverages (nonalcoholic and alcoholic), breakfast cereal, cheese, chewing gum, condiments/relishes, confectionery frostings, egg products, fats/oils, fish products, frozen dairy, fruit ices, gelatins/puddings, granulated sugar, gravies, hard candy, imitation dairy, instant coffee/tea, jams/jellies, meat products, milk products, nut products, other grains, poultry, processed fruits (juices), processed vegetables, reconstituted vegetables, seasonings/flavors, snack foods, soft candy, soups, sugar substitutes, and sweet sauces.

Gum acacia is approved as a direct food additive in 21 CFR 184.1330 and is Generally Recognized as Safe (GRAS) by the US Food and Drug Administration for use as an emulsifier, stabilizer, thickener and formulation aid. Approved food uses include beverages and beverage bases, chewing gum, confections and frostings, dairy product analogs, fats/oils, gelatins, puddings and fillings, hard candy and cough drops, nuts and nut products, quiescently frozen confection products, snack foods, soft candy, and all other food categories. Maximum permitted

usage levels in food products range from 1-85%. In addition, gum acacia has been reviewed by the Joint FAO/WHO Expert Committee on Food Additives (JECFA) and an "ADI not specified" applied.

Food starch, modified by an esterification process involving 1-octenyl succinic anhydride is approved as a multipurpose additive for direct addition to human food for consumption in 21 CFR 172.892(d). Modified food starch that has been esterified by treatment with 1-octenyl succinic anhydride (not to exceed 3 percent) may be safely used in food. In addition, modified starches including starch sodium octenyl succinate have been reviewed by the Joint FAO/WHO Expert Committee on Food Additives (JECFA) and an "ADI not specified" applied.

A JECFA ADI in man of "not specified" means that "on the basis of available data (toxicological, biochemical, and other), the total daily intake of the substance arising from it use or uses at levels necessary to achieve the desired effect and from its acceptable background in food, does not, in the opinion of the Committee, represent a hazard to health. For this reason, and for the reasons stated in individual evaluations, the establishment of an ADI in mg/kg body weight is not deemed necessary."

Exposure

The modified gum acacia that is the subject of this GRAS self-affirmation is proposed for use as an emulsifier in pure fruit juices (100%), select fruit flavored drinks, select beverages (carbonated juice, oatmeal beverages, energy drinks, and vitamin water), salad dressings, sauces, and icing. Modified gum acacia would be used at a level of 1000 ppm in pure fruit juices, 600 ppm in select fruit flavored drinks, 780 ppm in select beverages such as carbonated juices, energy drinks, and vitamin water, and 10,000 ppm in salad dressing, sauces, and icing.

The cumulative daily intake of modified gum acacia from the current flavoring uses and proposed new uses in pure fruit juices (100%), select fruit flavored drinks, select beverages (carbonated juice, oatmeal, energy drinks and vitamin water), salad dressings, sauces, and icing has been estimated. For the US population, the estimated daily intake (EDI) from combined uses at the mean per capita is 510.8 mg/day (662.1 mg/day at the 90th percentile), and the per-user is 515.3 mg/day (951.4 mg/day at the 90th percentile). When intake is divided by bodyweight the mean per capita and per user levels for the US population are 8.9 mg/kg/day and 9.0 mg/kg/day (17.9 and 18.0 mg/kg/day at the 90th percentiles per capita and per user, respectively). The sub-population of males 13-19 has the highest EDI on a mg/day basis (per user mean at 687.9 mg/day and 90th percentile estimate at 1320.1 mg/day), while the children 2-12 sub-group has the highest intake on the body weight basis (per user mean and 90th percentile at 17.4 mg/kg/day and 33.9 mg/kg/day, respectively). The actual intake is likely to be lower due to the innate conservatism in the intake assessment, which assumed that a large number of foods under each CFR food category with FEMA approved uses and/or proposed new emulsifier uses are fortified and consumed by consumers.

The above estimates of modified gum acacia intake are well below those for gum acacia itself. FDA has recently estimated the daily intake of gum acacia to be 3.25 g/day (54.2 mg/kg/day) by combining the previously estimated daily intake of 2.5 g/day (FDA, 1983 as cited in the Federal

Register, February 17, 2005) with the Kerry, Inc. daily intake estimate of 0.75 g/day for the approved use of gum acacia as a thickener, stabilizer, and emulsifier at a maximum level of 20% in alcoholic beverages (GRAS Notice No. G00058).

Safety Data

The available published toxicity data on modified gum acacia combined with an extensive published toxicologic database for gum acacia and modified food starch provides a sufficient basis for an assessment of the safety of modified gum acacia for the proposed use in pure fruit juices (100%), select fruit flavored drinks, select beverages (carbonated juice, oatmeal, energy drinks and vitamin water), salad dressings, sauces, and icing. The data cover a range of toxicity studies including acute/subchronic toxicity and genotoxicity on modified gum acacia, and acute, subchronic, and chronic toxicity, genotoxicity, reproductive/developmental toxicity, and carcinogenicity data for gum acacia and/or modified food starch.

Modified gum acacia is not mutagenic. The acute oral LD_{50} in rats for modified gum acacia has been demonstrated to be greater than 2000 mg/kg of body weight. In a 90-day subchronic dietary study in rats, administration of modified gum acacia at levels of 0, 1.0, 2.5, and 5.0% in the diet for 13 weeks did not produce any significant toxicologic manifestations. Microscopic evaluation of select organs and tissues revealed no unusual lesions that would suggest an effect of exposure to modified gum acacia in the diet. The no observed adverse effect level (NOAEL) was determined to be 5% in the diet, the highest level fed, which is equivalent to 3411 mg/kg/day for males, and 4052 mg/kg/day for females. The results obtained from these studies support the safety of modified gum acacia for its proposed food use as an emulsifier.

It is known that modified food starch is poorly digested in the small intestine and incompletely fermented in the large intestine. Gum acacia has also been shown to be digested/metabolized by GI bacteria during passage through the colon. The OSA-modification of gum acacia (a polysaccharide source like starch) is expected to result in similar digestion/fermentation of modified gum acacia by colonic microflora of the large intestine.

Summary

An Acceptable Daily Intake (ADI) for this safety assessment is based upon the lowest NOAEL determined in the 90-day subchronic study in rats. NOAELs were 3411 and 4052 mg/kg/day for male and female rats, respectively. Due to the lack of observed toxicity at any dose level, a conservative estimate of the ADI is calculated by dividing the NOAEL (for purposes of this assessment, 3411 mg/kg/day) by an uncertainty factor of 100x. The uncertainty factor represents a 10x factor for differences between rats and a 10x factor for extrapolation of effects in animals to those in humans. Therefore, the ADI is conservatively estimated to be approximately 34 mg/kg/day and is equivalent to 2.04 grams/day for a 60 kg individual.

Exposure to modified gum acacia from its current use in flavors combined with its proposed use as an emulsifier in pure fruit juices (100%), select fruit flavored drinks, select beverages (carbonated juice, oatmeal, energy drinks and vitamin water), salad dressings, sauces, and icing

is below the ADI. Actual exposure is likely to be lower than estimates due to the innate conservatism in the intake assessment, which assumes that a large number of foods under each CFR food category with FEMA approved uses and/or proposed new emulsifier uses are fortified and consumed by consumers. Based on these data, we conclude that the conservatively estimated exposures associated with the proposed use of modified gum acacia as an emulsifier in pure fruit juices (100%), select fruit flavored drinks, select beverages (carbonated juice, oatmeal beverages, energy drinks, and vitamin water), salad dressing, sauces, and icing do not pose any harm to consumers and can be considered safe.

Conclusion

We, the members of the Expert Panel have independently and collectively critically evaluated the available published information on modified gum acacia, gum acacia, and modified food starch and unanimously conclude that modified gum acacia, produced consistent with Good Manufacturing Practice and meeting the specifications described herein, is safe for use as an emulsifier in pure fruit juices (100%), select fruit flavored drinks, select beverages (carbonated juice, oatmeal beverages, energy drinks, and vitamin water), salad dressings, sauces, and icing at levels described herein.

The Expert Panel further unanimously concludes that these uses of modified gum acacia would be GRAS based on scientific procedures when the pivotal studies are published. It is our opinion that other experts qualified to assess the safety of food and food ingredients would concur with these conclusions.

Signatures

Joseph F. Borzelleca, Ph.D.
Virginia Commonwealth University
Medical College of Virginia

30 August 2007
Date

Marcia van Gemert, Ph.D.
Senior Managing Scientist
Exponent

9/4/07
Date

Barbara Petersen, Ph.D.
Principal Scientist
Exponent

August 17, 2007
Date

Exhibit II

EXHIBIT II
ALLERGENS STATEMENT

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Ex

EXHIBIT II

MODIFIED GUM ACACIA (TICAMULSION)™ ALLERGENS STATEMENT

Allergens Statement

This document certifies that MODIFIED GUM ACACIA (TICAMULSION)™ manufactured by TIC Gums, Inc. does not contain nor has been exposed to potential contamination from any of the following listed known allergens:

Artificial Colors
Egg or egg products
Milk or milk products
Peanuts or peanut products
Seed or seed products (cotton, poppy, sesame, sunflower)
Seafood or seafood products (including crustaceans or mollusks)
Soybeans or soybean products
Tree nuts (almonds, brazils, cashews, chestnuts, hazelnuts, pine nuts, pistachios, pecans, Macadamias, walnuts)
Wheat or wheat products
Sulfites

Authorized Signature

April 4, 2008
Date

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EX

SUBMISSION END

AM

Ricker, Karin

From: Nga Tran [ntran@exponent.com]
Sent: Wednesday, June 11, 2008 4:27 PM
To: Ricker, Karin
Subject: RE: clarification re. GRN 247- modified gum acacia

Dear Dr. Ricker,

We do not expect the 2% glycoprotein fraction of the modified gum acacia to be of any greater concern for allergenicity than the protein fraction of unmodified or regular gum acacia, as the modification process does not alter the protein present in unmodified gum acacia. Furthermore, we do not believe the modified gum acacia will present allergenicity concerns as FDA itself conducted searches of the scientific literature on acacia in 1983, 1987, 1988, and 1992, with a special emphasis on potential hypersensitivity and allergic reaction and concluded that while there was evidence that acacia is associated with dermal/bronchial hypersensitivity in workers handling acacia dust in the workplace (e.g., printing industry), the evidence for the allergic potential of acacia was extremely weak. (http://www.cfsan.fda.gov/~lrd/fr050217.html). We would concur with this assessment. The few reported cases of allergic responses following ingestion of food containing acacia gum are old (i.e., Gelfand, 1949*) and involved ingestion of foods containing multiple gum products. Based on its review of the safety data in 2005, FDA concluded that the additional use of acacia in alcoholic beverages was safe. Finally, the estimates of modified gum acacia intake (mean 524 mg/day; 90th percentile 964 mg/day) are well below those for gum acacia itself. FDA has recently estimated the daily intake of gum acacia to be 3.25 g/day by combining the previously estimated daily intake of 2.5 g/day (FDA, 1983 as cited in the Federal Register, February 17, 2005) with the Kerry, Inc. daily intake estimate of 0.75 g/day for the approved use of gum acacia as a thickener, stabilizer, and emulsifier at a maximum level of 20% in alcoholic beverages (GRAS Notice No. G00058). Therefore, given that the protein fraction in modified gum acacia has not been altered in comparison to regular gum acacia, daily exposure to the glycoprotein fraction from the modified gum acacia product is well below that from gum acacia itself.

* Gelfand, H.H. 1949. The vegetable gums by ingestion in the etiology of allergic disorders. J. Allergy 20: 311-321.

Please let me know if the above clarifying response in an email format is acceptable. Otherwise, I can prepare and send our response in a memo format.

Best regards,

Nga L. Tran, Dr.PH, MPH, CIH
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Email: ntran@exponent.com

From: Ricker, Karin [mailto:karin.ricker@fda.hhs.gov]
Sent: Tuesday, June 10, 2008 2:08 PM
To: Nga Tran
Subject: clarification re. GRN 247- modified gum acacia

Dear Dr. Tran:

One of our reviewers has a minor clarification question regarding your submission of GRN 247, modified gum acacia. The question is:

Does the company expect the 2% glycoprotein fraction of their product to be allergenic?
Thanks so much if you can address this question and get back to us. Feel free to call me if you have any other questions.

Regards,
Karin Ricker

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