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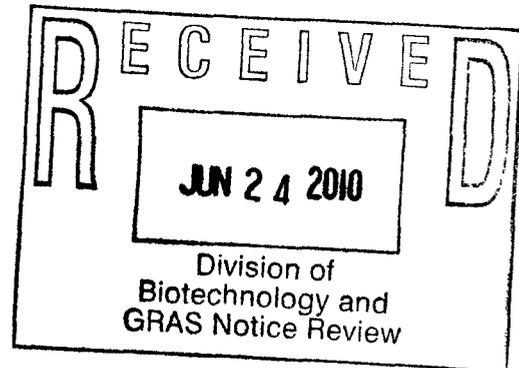
ORIGINAL SUBMISSION

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VitaGac, LLC
Law Offices of Shula Barash
9454 Wilshire Blvd, suite 500
Beverly Hills, CA 90212

June 14, 2010

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



Division of Biotechnology and GRAS Notice Review

Dear Dr. Martin:

VitaGac, LLC submits a GRAS notification for agency evaluation. VitaGac, LLC submits three copies of the GRAS notification for Freeze-Dried Gac Fruit Powder. Please let us know if you have any questions or need clarification about the enclosed materials.

Yours very truly,

(b) (6)

Miriam Lewenzstain, Managing Member
VitaGac, LLC
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in care of Law Offices of S. Barash
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Beverly Hills, CA 90212

Enclosures: GRAS Notification for Freeze-Dried Gac Fruit Powder

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GRAS notification for Freeze-Dried Gac Fruit Powder

Prepared by:

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Evaluation by:

Charles M. Heldebrant, Ph.D.

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APPENDIX A Credentials of Expert Panel

1. GRAS EXEMPTION CLAIM

A. Claim of Exemption From the Requirement for Premarket Approval Pursuant to Proposed 21 CFR 170.36(c)(1)

Freeze-Dried Gac Fruit Powder, which meets the specifications for Freeze-Dried Gac Fruit Powder, as described below, has been determined to be Generally Recognized As Safe (GRAS), in accordance with Section 201(s) of the *Federal Food, Drug, and Cosmetic Act*. This determination was made by an expert qualified by scientific training and experience; the GRAS evaluation is based on scientific procedures as described in the following sections; and the evaluation accurately reflects the conditions of the intended use of freeze-dried Gac fruit powder in foods.

Signed:

(b) (6)

Date:

15 June 2010

Charles M. Heldebrant, Ph.D.
VitaGac, LLC
In care of Law Offices of S. Barash
Suite 500
9454 Wilshire Blvd, Suite 500
Beverly Hills, CA 90212

B. Names & Addresses of Notifiers

VitaGac, LLC
in care of Law Offices of S. Barash
Suite 500
9454 Wilshire Blvd, Suite 500
Beverly Hills, CA 90212

VitaGac, LLC is the notifier and accepts the responsibility for the GRAS determination that has been made for the freeze dried Gac fruit powder; consequently, the freeze dried Gac fruit powder meeting the conditions described herein are exempt from pre-market approval requirements for food ingredients.

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C. Common Name & Identity of the Notified Substance

Freeze dried Gac fruit powder.

D. Conditions of Intended Use in Food

VitaGac concludes that the freeze-dried Gac fruit powder is generally recognized as safe when used as follows.

Conditions of Use, Levels, Purpose and Population

Foods in which the substance is to be used	Levels of use in such foods Gac powder/kg food	Purposes for which the substance is used	Population expected to consume the substance
Juice Mixture or Beverage	Not more than 20 mg/kg	Source of lycopene and β -carotene	All ages and sexes, no restriction for pregnancy or nursing
Nutritional bars	Not more than 10 mg/kg	Source of lycopene and β -carotene	All ages and sexes, no restriction for pregnancy or nursing
Dietary Supplement	Not more than 20 mg/dose	Source of lycopene and β -carotene	All ages and sexes, no restriction for pregnancy or nursing
Functional Food	Not more than 20 mg/dose	Source of lycopene and β -carotene	All ages and sexes, no restriction for pregnancy or nursing

E. Basis for the GRAS Determination

Freeze-dried Gac fruit powder has been determined to be GRAS on the basis of scientific procedures as discussed in the detailed description provided below, Pursuant to 21 CFR § 170.30.

F. Availability of Information

The data and information that serve as the basis for this GRAS Notification will be sent to the Food and Drug Administration (FDA) upon request or will be available for review and copying at reasonable times at the offices of VitaGac, LLC, in care of Law Offices of S. Barash, Suite 500, 9454 Wilshire Blvd, Suite 500, Beverly Hills, CA 90212.

II. INTRODUCTION

A. Objective

VitGac, LLC has undertaken a safety evaluation of freeze-dried Gac fruit powder as a food additive.

B. Foreword

VitaGac, LLC have evaluated the Gac fruit and its major components. The safety assessment for freeze-dried Gac fruit powder is based upon the extensive safety evaluations and dietary intake recommendations for the major components of freeze-dried Gac fruit powder.

C. History of Gac Fruit Intake and Summary of Regulatory History

Use of the substance, including the date when use began.

Vita-Gac is not aware of a specified use of the freeze-dried Gac fruit powder.

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Gac fruit is listed as a component of the product Azul Marine Phytoplankton. The available information from the manufacturer website [<http://www.differentplankton.com/azul-ingredients.html>] does not list the amount or the form of Gac fruit used in this formulation.

Gac fruit has been in common use as a food prior to January 1, 1958 in Vietnam and other Southeast Asian countries and remains in such use today. The freeze-dried Gac fruit pulp is a minimally processed concentrate of the fresh Gac fruit pulp and should be generally recognized as safe when used at safe levels of the bioactive components, lycopene and beta-carotene.

In Vietnam, the Gac vine is often seen growing on lattices at the entrances of rural homes. The Vietnamese use the seed membranes and the pulp of the fruit in the preparation of xoi gac (red rice). Traditionally, xoi gac is served at weddings, the New Year (Tet), and for other important celebrations. During these occasions, it is essential to mask the white color of rice, since white is considered the color of death. To make xoi gac, the pulp of Gac fruit is mixed with rice.

VitaGac, LLC is unaware of a regulatory history for freeze-dried Gac fruit powder. There is an extensive regulatory history for lycopene and β -carotene, the major components of the freeze-dried Gac fruit powder.

D. FDA Regulatory Framework

Freeze-dried Gac fruit powder used as a dietary supplement in accordance with FDA regulation of foods must undergo premarket approval by FDA as food additives or, alternatively, must be determined to be generally recognized as safe (GRAS).

III. MANUFACTURE OF FREEZE-DRIED GAC FRUIT POWDER

A. Common or Usual Name

Common or usual name.

Freeze-Dried Gac Fruit Powder

Chemical name.

The freeze-dried biomass of deseeded Gac (*Momordica cochinchinensis*, Spreng) fruit tissue including the oily aril.

Chemical Abstract Service (CAS) registry number.

None

Empirical formula.

None

Structural formula.

None

B. Chemistry of Freeze-Dried Gac Fruit Powder

The Gac Fruit and the freeze-dried Gac fruit powder contain high levels of lycopene and β -carotene.

C. Specifications for Food Grade Freeze-Dried Gac Fruit Powder

Specifications for food grade material.

The specifications for the freeze-dried Gac fruit powder are as follows.

A. Overall Composition

Component	Specification	Method
Total Fat	5 - 7%	AOAC 996.06
Total Protein	<1%	AOAC 984.13
Total Carbohydrate	84 - 89%	By Difference
Moisture	3 - 6%	AOAC 984.25
Ash	3 - 5%	AOAC 923.03

B. Detailed Fat Composition

Component	Specification	Method
Trans-Fat	<0.1%	AOAC 996.06
Cholesterol	<0.1 mg/100g	AOAC 970.51

C. Minerals and Metals

Component	Specification	Method
Sodium	<10 mg/100g	AOAC 984.27
Calcium	<120 mg/100g	AOAC 984.27
Iron	<10 mg/100g	AOAC 984.27
Arsenic	<1 mg/kg	AOAC 993.14M
Lead	<1 mg/kg	AOAC 993.14M

D. Vitamins and Related Substances

Component	Specification	Method
Vitamin A as retinol	<10 mg/100g	Ultraviolet Spectroscopy
Vitamin C	80 - 100 mg/100g	Ultraviolet Spectroscopy
β-carotene	0.9 -1.8 g/100g	Ultraviolet Spectroscopy
Lycopene	3 - 5 g/100g	Ultraviolet Spectroscopy

E. Microbiological Component	Specification	Method
Total Aerobic Plate Count	<10 CFU/g	USP
Coliforms	<10 CFU/g	AOAC 991.14
<i>E. coli</i>	<1 CFU /10g	USP
<i>Salmonella</i> species	<1 CFU /10g	USP
Yeast	<10 CFU/g	USP
Mold	<10 CFU/g	USP

D. Manufacturing Processes

The manufacturing process for freeze-dried Gac powder comprises the following steps.

The Gac fruit is harvested and washed.

The fruit is cut open and the fruit pulp including the red oily aril is separated from the skins and the seeds.

The fruit pulp including the red oily aril is frozen and dried under vacuum.

The dried powder is mixed, ground, sieved and packaged.

The manufacture of freeze-dried Gac fruit powder complies with the requirements of current Good Manufacturing Practices.

The manufacturer is ISO-9001 certified, has appropriate Hazard Analysis and Critical Control Point and current Good Manufacturing Practices in place and verified by independent audits and is certified to produce products eligible for Halal and Kosher dietary certification.

E. Product Specifications & Supporting Methods

The specifications for the freeze-dried Gac fruit powder are as follows.

A. Overall Composition

Component	Specification	Method
Total Fat	5 - 7%	AOAC 996.06
Total Protein	<1%	AOAC 984.13
Total Carbohydrate	84 - 89%	By Difference
Moisture	3 - 6%	AOAC 984.25
Ash	3 - 5%	AOAC 923.03

B. Detailed Fat Composition

Component	Specification	Method
Trans-Fat	<0.1%	AOAC 996.06
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Sodium	<10 mg/100g	AOAC 984.27
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Arsenic	<1 mg/kg	AOAC 993.14M
Lead	<1 mg/kg	AOAC 993.14M

D. Vitamins and Related Substances

Component	Specification	Method
Vitamin A as retinol	<10 mg/100g	Ultraviolet Spectroscopy
Vitamin C	80 - 100 mg/100g	Ultraviolet Spectroscopy
β -carotene	0.9 - 1.8 g/100g	Ultraviolet Spectroscopy
Lycopene	3 - 5 g/100g	Ultraviolet Spectroscopy

E. Microbiological		
Component	Specification	Method
Total Aerobic Plate Count	<10 CFU/g	USP
Coliforms	<10 CFU/g	AOAC 991.14
<i>E. coli</i>	<1 CFU /10g	USP
<i>Salmonella</i> species	<1 CFU /10g	USP
Yeast	<10 CFU/g	USP
Mold	<10 CFU/g	USP

F. Stability Data for Freeze-Dried Gac Fruit Powder

The Gac fruit is promptly processed and freeze-dried. VitaGac has not performed stability studies on the freeze-dried Gac fruit powder on the powder after it has been formulated in food. The stability of the lycopene and β -carotene in the freeze-dried Gac fruit powder is expected to be identical to that of synthetic lycopene and β -carotene in the particular matrix.

IV. INTENDED DIETARY USES

A. Intended Uses

Conditions of use, levels, purpose and population

VitaGac concludes that the freeze-dried Gac fruit powder is generally recognized as safe when used as follows.

Conditions of Use, Levels, Purpose and Population

Foods in which the substance is to be used	Levels of use in such foods Gac powder/kg food	Purposes for which the substance is used	Population expected to consume the substance
Juice Mixture or Beverage	Not more than 20 mg/kg	Source of lycopene and β -carotene	All ages and sexes, no restriction for pregnancy or nursing
Nutritional bars	Not more than 10 mg/kg	Source of lycopene and β -carotene	All ages and sexes, no restriction for pregnancy or nursing
Dietary Supplement	Not more than 20 mg/dose	Source of lycopene and β -carotene	All ages and sexes, no restriction for pregnancy or nursing
Functional Food	Not more than 20 mg/dose	Source of lycopene and β -carotene	All ages and sexes, no restriction for pregnancy or nursing

The freeze-dried Gac fruit is used to provide β -carotene and lycopene. β -Carotene conversion to retinol is regulated by the body's need for vitamin A and does not evoke the toxicity seen with high doses of vitamin A (retinol).

The Daily Value for vitamin A (retinol) is 5,000 IU. There is no established Daily Value for lycopene or β -carotene.

The acceptable daily intake (ADI) for lycopene is 0.5 mg/kg body weight-day and 5 mg/kg body weight-day.

Lycopene is not converted into vitamin A. Lycopene has been assigned a retinol equivalent value. We assume, for the purpose of risk assessment as Vitamin A, that the maximum proposed levels of β -carotene and lycopene can be converted to retinol equivalents (RE) or International Units (IU) of vitamin A. The conversion factor is 1 IU of vitamin A is equal to 0.1 retinol equivalent or 0.6 μ g of β -carotene or 1.2 μ g of lycopene. The β -carotene and lycopene are also converted to an equivalent IU vitamin A in the table below to provide basis for estimating the maximum vitamin A potential of a dose of lycopene and β -carotene for the freeze-dried Gac fruit powder.

The maximum doses of lycopene and β -carotene from daily consumption of one 12 fluid ounce juice mixture or beverage, one 100g nutritional bar, one dose of dietary supplement or one dose of functional food bar are given in the table below.

Maximum Dose of β -Carotene and Lycopene at Maximum Level of Use

Foods in which the substance is to be used	Level of Freeze-dried Gac powder in food	Serving Size	Maximum Dose of Lycopene mg and [Vitamin A Equivalents]	Maximum Dose of β -carotene mg and [Vitamin A Equivalents]
Juice Mixture or Beverage	Not more than 50 mg/kg food	12 fl oz, or 354 g	0.885 mg [737 IU]	0.32 mg [533 IU]
Nutritional bar	Not more than 100 mg/kg food	100g	0.5 mg [417 IU]	0.18 mg [300 IU]
Dietary Supplement	Not more than 35 mg/dose	1 dose	1.75 mg [1458 IU]	0.63 mg [1050 IU]
Functional Food	Not more than 35 mg/dose	1 dose	1.75 mg [1458 IU]	0.63 mg [1050 IU]

Cumulative consumption of lycopene and β -carotene

The estimated 95th percentile total intake of lycopene is 30 mg of lycopene/person-day. The estimated total daily intake of β -carotene is up to 7 mg of β -carotene/person-day.

B. Estimated Daily Intake

The freeze-dried Gac fruit is used to provide β -carotene and lycopene. β -Carotene conversion to retinol is regulated by the body's need for vitamin A and does not evoke the toxicity seen with high doses of vitamin A (retinol).

The Daily Value for vitamin A (retinol) is 5,000 IU. There is no established Daily Value for lycopene or β -carotene.

The acceptable daily intake (ADI) for lycopene is 0.5 mg/kg body weight-day and 5 mg/kg body weight-day.

Lycopene is not converted into vitamin A. Lycopene has been assigned a retinol equivalent value. We assume, for the purpose of risk assessment as Vitamin A, that the maximum proposed levels of β -carotene and lycopene can be converted to retinol equivalents (RE) or International Units (IU) of vitamin A. The conversion factor is 1 IU of vitamin A is equal to 0.1 retinol equivalent or 0.6 μ g of β -carotene or 1.2 μ g of lycopene. The β -carotene and lycopene are also converted to an equivalent IU vitamin A in the table below to provide basis for estimating the maximum vitamin A potential of a dose of lycopene and β -carotene for the freeze-dried Gac fruit powder.

The maximum doses of lycopene and β -carotene from daily consumption of one 12 fluid ounce juice mixture or beverage, one 100g nutritional bar, one dose of dietary supplement or one dose of functional food bar are given in the table below.

Maximum Dose of β -Carotene and Lycopene at Maximum Level of Use

Foods in which the substance is to be used	Level of Freeze-dried Gac powder in food	Serving Size	Maximum Dose of Lycopene mg and [Vitamin A Equivalents]	Maximum Dose of β -carotene mg and [Vitamin A Equivalents]
Juice Mixture or Beverage	Not more than 50 mg/kg food	12 fl oz, or 354 g	0.885 mg [737 IU]	0.32 mg [533 IU]
Nutritional bar	Not more than 100 mg/kg food	100g	0.5 mg [417 IU]	0.18 mg [300 IU]
Dietary Supplement	Not more than 35 mg/dose	1 dose	1.75 mg [1458 IU]	0.63 mg [1050 IU]
Functional Food	Not more than 35 mg/dose	1 dose	1.75 mg [1458 IU]	0.63 mg [1050 IU]

C. Risk assessment as Vitamin A intake

The proposed level of use in juice mixture or beverage would have not more than 0.885 mg of lycopene and not more than 0.32 mg of β -carotene per 12 fluid ounces. This is equivalent to not more than 1,270 IU of vitamin A or 25% of the Daily Value of Vitamin A if all of the lycopene and β -carotene were converted to vitamin A.

The proposed level of use in nutritional bars would have not more than 0.5 mg of lycopene and not more than 0.18 mg of β -carotene per 100 gram bar. This is equivalent to not more than 717 IU of vitamin A or 14% of the Daily Value of Vitamin A if all of the lycopene and β -carotene were converted to vitamin A.

The proposed level of use in a dietary supplement would have not more than 1.75 mg of lycopene and not more than 0.63 mg of β -carotene per dose. This is equivalent to not more than 2,508 IU of vitamin A or 50% of the Daily Value of Vitamin A if all of the lycopene and β -carotene were converted to vitamin A.

The proposed level of use in a functional food would have not more than 1.75 mg of lycopene and not more than 0.63 mg of β -carotene per dose. This is equivalent to not more than 2,508 IU of vitamin A or 50% of the Daily Value of Vitamin A if all of the lycopene and β -carotene were converted to vitamin A.

The proposed maximum levels of lycopene and β -carotene provide 14-25% of the Daily Value of vitamin A as pro-vitamin A carotenoids. Foods with this level of freeze-dried Gac powder will provide a significant source of vitamin A yet not result in vitamin A levels that exceed the Daily Value if consumed as part of a normal diet.

The proposed maximum levels of lycopene and β -carotene in dietary supplement or functional food provide 50% of the Daily Value of vitamin A as pro-vitamin A carotenoids. The potential for overdose is more likely with these foods, however, as the foods provide pro-vitamin A carotenoids that are recognized as non-toxic at these doses, there is little risk to individuals who deliberately or accidentally consume more than the recommended dose.

D. Risk assessment of lycopene and β -carotene

The generally available data and information that establish safety, including evidence of a substantial history of consumption of the substance by a significant number of consumers.

Lycopene and β -carotene are normal constituents in the human diet. They have been consumed by millions of humans with few side effects. The Agency has recognized levels for both that are generally recognized as safe. We are not aware of adverse consumer complaints for lycopene and β -carotene other than the skin discoloration seen in individuals who consume large amounts of these compounds over extended periods of time. These rare adverse events are reported in the medical literature and cited in the Agency determinations of the safety of lycopene and β -carotene.

Lycopene is the ingredient present at the highest concentration in the freeze-dried Gac powder. The dose limits are set based on acceptable daily intake of lycopene levels when lycopene is a food colorant or food additive of 0 to 0.5 mg/kg body weight-day.

Lycopene

Lycopene is available from a wide variety of natural and synthetic sources. The freeze-dried Gac powder contains natural lycopene.

The Agency has published information that lycopene levels of 10 mg/kg in a wide variety of food products [GRAS Notice No. GRN 000156] and 20 ppm or mg/kg in non-alcoholic beverages [GRAS Notice No. GRN 000185] are generally recognized as safe.

VitaGac proposes that the use of freeze dried Gac powder to supplement the lycopene levels in foods up to 2.5 mg lycopene/kg for juice mixtures and non-alcoholic beverages and up to 5 mg/kg lycopene for nutritional bars. The dose for dietary supplement and functional food is not more than 1.75 mg lycopene per dose.

These proposed usage levels are below the GRAS levels of lycopene in other naturally derived food additives.

Maximum Dose of β -Carotene and Lycopene at Maximum Level of Use

Foods in which the substance is to be used	Level of Freeze-dried Gac powder in food	Lycopene Level
Juice Mixture or Beverage	Not more than 50 mg/kg food	Not more than 2.5 mg/kg
Nutritional bar	Not more than 100 mg/kg food	Not more than 5 mg/kg
Dietary Supplement	Not more than 35 mg/dose	Not more than 1.75 mg/dose
Functional Food	Not more than 35 mg/dose	Not more than 1.75 mg/dose

β-Carotene

β-Carotene is available from a wide variety of natural and synthetic sources. The freeze-dried Gac powder contains natural β-carotene. The Agency has published an evaluation of the safety of β-carotene in the Database of Select Committee on GRAS Substances (SCOGS) Reviews. The following is taken from the database.

Carotene (beta - carotene)

Report No.: 111

Type of Conclusion: 1

ID Code: 7235-40-7

Year: 1979

CFR Section: 21CFR184.1245

SCOGS Opinion: Carotene is a general term describing certain polyene hydrocarbons containing 40 carbon atoms. Three of these, α-, β-, and γ-carotene, as well as some closely related oxygen-containing carotenoids, exhibit provitamin A activity. β-carotene is the most active of the carotenes and the only one that is available commercially. It is added to food, chiefly margarine, both as a coloring agent, and for its vitamin A potential. Early studies of the health aspects of "carotene" were performed with preparations of uncertain composition and purity. However, it is apparent from the sources of carotene utilized and the purification procedures adopted, that the active principle in these studies was largely β-carotene, so that the results are relevant to the present review. Since the development of synthetic β-carotene for commercial use in 1954, nearly all research on "carotene" has employed a crystalline and well-defined product.

The average daily intake of carotene from natural sources is estimated to be about 2 mg per day which is equivalent to approximately 3300 IU of vitamin A. Substantially larger amounts may be ingested in diets rich in colored vegetables. The Recommended Dietary Allowance of vitamin A from all sources is 5000 IU for adults. Consumption information from various sources, suggests that the per capita daily intake of β -carotene added to foods is 0.2 to 0.3 mg.

Doses several orders of magnitude greater than would conceivably be used as additives in food have proved nontoxic to various animal species given β -carotene orally in acute, short and long term studies. A single study suggested some impairment in neonatal skeletal development when 180 mg per kg or more of carotene were administered, daily to rats, but this study has not been confirmed.

When given in moderate amounts, carotene is readily converted to vitamin A. However, this conversion is limited when large amounts of carotene are administered. The regulatory mechanism has not been elucidated. Doses of 180 mg (300,000 IU) daily for 2 or more years have been taken orally by patients suffering from certain types of photosensitivity with no evidence of hypervitaminosis A or other harmful effects. In the light of these considerations, the Select Committee concludes that: There is no evidence in the available information on carotene (β -carotene) that demonstrates, or suggests reasonable grounds to suspect, a hazard to the public when it is used at levels that are now current or that might reasonably be expected in the future.

The estimated dietary intake of β -carotene is 2-5 mg/day from dietary sources and 1-2 mg/day from additives for a total daily intake of 3-7 mg β -carotene/day. The VitaGac proposed uses would produce a daily maximum consumption of less than 1 mg of β -carotene in any of the designated food forms, which is in the range that is generally recognized as safe.

V. SAFETY DATA FOR FREEZE-DRIED GAC FRUIT POWDER

A. Safety Data Reviews by Expert Bodies

The freeze-dried Gac fruit is used to provide β -carotene and lycopene. β -Carotene conversion to retinol is regulated by the body's need for vitamin A and does not evoke the toxicity seen with high doses of vitamin A (retinol).

The Daily Value for vitamin A (retinol) is 5,000 IU. There is no established Daily Value for lycopene or β -carotene.

The acceptable daily intake (ADI) for lycopene is 0.5 mg/kg body weight-day and 5 mg/kg body weight-day.

The Agency has published GRAS notices for vitamin A, lycopene and β -carotene that carefully considered the toxicity information for these dietary components. The Agency and others have established recommended maximum daily intakes for these components of freeze-dried Gac fruit powder. Vita-Gac, LLC intends that the uses of freeze-dried Gac fruit powder will be at levels that are at or below the recommended values.

The agency review included expert assessment of the extensive human and animal toxicity data for these materials. VitaGac, LLC feels that these toxicity assessments are adequate and that no further toxicology assessments are required.

VI. DISCUSSION OF GRAS CRITERIA & SAFETY FINDINGS

A. GRAS Criteria

FDA defines “safe” or “safety” as it applies to food ingredients as: “. . . reasonable certainty in the minds of competent scientists that the substance is not harmful under the intended conditions of use. It is impossible in the present state of scientific knowledge to establish with complete certainty the absolute harmlessness of the use of any substance. This safety assessment of the GRAS status for freeze-dried Gac fruit powder for the defined food uses meets FDA criteria for reasonable certainty of no harm by considering both the technical and common knowledge elements.

B. Findings on Safety Studies of Freeze-Dried Gac Fruit Powder.

The freeze-dried Gac fruit powder contains high levels of lycopene and β -carotene. The Agency and other regulatory authorities have comprehensively reviewed the safety of lycopene and β -carotene and have established acceptable daily intake values. IN addition, VitaGac, LLC has considered the potential toxicity as vitamin A. The intended use levels for the freeze-dried Gac fruit powder are less than the ADI.

The risk assessments for daily intake of lycopene and β -carotene at the maximum levels in this notification show no risk.

VII. CONCLUSIONS

Freeze-dried Gac Fruit powder, prepared under a process that conducted under current Good Manufacturing Practices and designed in accordance with the principles of Hazard Analysis and Critical Control Points and meeting the established specifications is Generally Recognized as Safe when used to supply lycopene and β -carotene at levels not to exceed 20 mg/kg. These limits were established by reference to prior Agency and other regulatory authority determinations and assessments that led to establishment of acceptable daily intake levels for these components as a part of a normal diet. VitaGac, LLC has established the use limits for the freeze-dried Gac fruit powder to conform to these ADIs. The use of freeze-dried Gac fruit powder at levels below the ADI is rational and should be generally recognized as safe.

DECLARATION

Freeze-dried Gac Fruit powder which are produced in accordance with FDA Good Manufacturing Practices requirements and which meet at a minimum the specifications are Generally Recognized As Safe when consumed as a component of nutritional bars at not more than 10 mg/kg and as a functional food, dietary supplement, beverage or juice mixture at not more than 20 mg/kg. In order to remain within the designated ADI, it is important to observe good manufacturing practices principles in that the quantity of a substance added to food should not exceed the amount reasonably required to accomplish its intended effect. This declaration has been made in accordance with the reasonable certainty standard for food ingredient safety (b) (6)

Charles M. Heldebrant, Ph.D.
June 14, 2010

References

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APPENDIX A

Credentials of Expert Panel

Charles M. Heldebrant, Ph.D.

Education

A.B. Biochemistry, 1969 University of California, Berkeley

Ph.D. Biochemistry, 1974 University of Minnesota, Minneapolis, Minnesota and Mayo Clinic, Rochester, Minnesota

Senior Fellow (Postdoctoral) 1974-1975, Department of Biochemistry, University of Washington, Seattle, Washington.

Experience

Consultant, PSC Biotech, February 2010-present. Responsible for analysis and execution of cGMP compliance, comprehensive validation programs and analytical methods design, implementation and validation.

Consultant, Agvania, Inc and VitaGac, LLC. 2009-present. Responsible for development and execution of GLP animal study protocols and grant applications, and toxicology assessments.

Consultant, Jim Henson Productions, November 2007-present. Scientific Consultant, Sid the Science Kid (Airs on PBS from September 2008). Consult on scientific issues related to development of science program for children. Review overall episode cycles and episode outlines, scripts, song lyrics, visual materials and program experiments.

Consultant, Shanbrom Technologies, May 2003-present. Consult on scientific issues, experimental plans and evaluations for projects in ST research areas. Prepare and submit grant applications. Prepare clinical protocols for grant submissions. Prepare and file financial and scientific reports on awarded NIH grants.

Vice President, Regulatory Affairs & Validation, National Genetics Institute, January 2007-August 3, 2007. Prepare, review and file FDA IND and NDA submissions, interactions, and responses to CBER. Prepare, review and file Plasma Masterfile regulatory information for European submissions. Prepare and file Annual Reports for INDs and NDAs. Perform regulatory maintenance of approved assays. Responsible for overall coordination of validation program, review and approval of protocols, programs and reports. Work with NGI Quality to improve quality systems, manage inspections and responses and responses to vendor and regulatory inspection findings.

Vice President, Post-PCR Operations, Regulatory Affairs & Validation, National Genetics Institute, May 2004-January 2007. Responsible for all day-to-day operations of the 24/7 Post-PCR facility. Relocated the Post-PCR facility without operational

discontinuity while obtaining FDA approvals for new facility and relocated equipment. Prepare, review and submit IND and NDA submissions and Annual Reports to FDA. Perform regulatory maintenance of approved assays. Responsible for preparation of validation master plan and overall coordination of validation program, review and approval of protocols, programs and reports.

Vice President, Research and Development, Regulatory Affairs & Validation, National Genetics Institute, September 2, 2003-May 2004. Responsible for research & development program development and operations. Prepare, review and submit IND and NDA submissions and Annual Reports to FDA. Perform regulatory maintenance of approved assays. Responsible for preparation of validation master plan and overall coordination of validation program, review and approval of protocols, programs and reports.

Director, Technology and Business Development, Alpha Therapeutic Corporation, Los Angeles, California, September 2002-June 2003.

Director, Development Services, Alpha Therapeutic Corporation, Los Angeles, California, April 2002-August 2002. Responsible for development of new production processes.

Vice President, Manufacturing Technical, Alpha Therapeutic Corporation, Los Angeles, California, July 2001-April 2002. Responsible for research and development, validation, engineering, facilities, maintenance and centralized manufacturing support activities.

Vice President, Research and Development, Alpha Therapeutic Corporation, Los Angeles, California, January 2001-July 2001. Responsible for research and development.

Director, Technical Affairs, Alpha Therapeutic Corporation, Los Angeles, California, 1997-January 2001. Responsible for intramural and extramural pharmaceutical product research and development, viral inactivation and validation, and nucleic acid technology programs.

Member of the Board of Directors, Consortium for Plasma Science, LLC January 1997-July 2000. Vice Chairman, July 1997 to December 1998; Chairman, January 1999-July 2000.

Director, Technical Affairs, Alpha Therapeutic Corporation, Los Angeles, California, May 1995-1997. Responsible for intramural and extramural pharmaceutical product research and development, viral inactivation and validation, nucleic acid technology and corporate quality assurance programs. Inspect and provide cGMP consulting services to contract radiopharmaceutical manufacturer and contract pharmaceutical manufacturer.

Scientific Director, Research and Development Department, Alpha Therapeutic Corporation, Los Angeles, California, October 1994-April 1995. Responsible for intramural and extramural pharmaceutical product research and development activities. Inspect and provide GLP and cGMP consulting services to contract pharmaceutical manufacturers.

Scientific Director, Research and Development Department, Pharmaceutical Division, Alpha Therapeutic Corporation, Los Angeles, California, March 1990-September 1994. Responsible for intramural and extramural product research and development activities.

Scientific Director, New Products Research, Research and Development Department, Alpha Therapeutic Corporation, Los Angeles, California, 1985-March 1990. Responsible for intramural and extramural new product research activities.

Director, New Products Research, Research and Development Department, Alpha Therapeutic Corporation, Los Angeles, California, January 1981-1985. Responsible for intramural and extramural new product research activities.

Manager, New Products and Analytical Services, Research and Development Department, Alpha Therapeutic Corporation, Los Angeles, California, August 1978-January 1981. Responsible for coagulation product research and pilot scale development.

Senior Biochemist, Research and Development, Abbott Scientific Products Division, Abbott Laboratories, Los Angeles, California, February 1975-August 1978.

Senior Fellow and National Hemophilia Foundation Postdoctoral Fellow, Department of Biochemistry, University of Washington, Seattle, Washington, August 1973-February, 1975. Conducted research on the subunit structure of bovine Factor VIII (laboratory of Dr. Earl Davie).

Visiting Research Fellow, Mayo Clinic Foundation, Rochester, Minnesota, June 1972-July 1973. Conducted research on the isolation, structure, and activation mechanisms of bovine prothrombin and thrombin (laboratory of Dr. Kenneth Mann).

Research Assistant, University of Minnesota, St. Paul, Minnesota, September 1969-June 1972. Conducted research toward doctoral degree on the isolation, structure, and activation mechanism of bovine prothrombin and thrombin (laboratory of Dr. Kenneth Mann).

Publications

KG Mann CM Heldebrant and DN Fass (1971) Multiple Active Forms of Thrombin. I. Partial Resolution, Differential Activities, and Sequential Formation *J Biol Chem* 246, 5994-6001.

KG Mann CM Heldebrant and DN Fass (1971) Multiple Active Forms of Thrombin. II. Mechanism of Production from Prothrombin *J Biol Chem* 246, 6106-14.

KG Mann R Yip CM Heldebrant and DN Fass (1971) Multiple Active Forms of Thrombin. III. Polypeptide Chain Location of Active Site Serine and Carbohydrate *J Biol Chem* 248, 1868-75.

CM Heldebrant and KG Mann (1973) The Activation of Prothrombin. I. Isolation and Preliminary Characterization of Intermediates *J Biol Chem* 248, 3642-52.

CM Heldebrant RJ Butkowski SP Bajaj and KG Mann (1973) The Activation of Prothrombin II. Partial Reactions, Physical and Chemical Characterization of Intermediates *J Biol Chem* 248, 7149-63.

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GN Vyas PK Bhatnagar HE Blum J Expose and CM Heldebrant (1983) Appraisal and Prospects of a Dimeric Synthetic Peptide Coupled with Tetanus Toxoid for a Bifunctional Vaccine against Hepatitis B Infection *Devel Biol Standards* 54, 93-102.

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RIF Smith CM Heldebrant (2000) Large Scale PCR Screening of Pooled Plasma Samples for HIV-1 and HCV Dev Biol Stds 102, 109-111.

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CM Heldebrant and K Yokoyama (1981) Phase I Report and Final Report, Contract N01-HB-9-2927 Formulation and Evaluation of Four New Perfluorochemicals.

CM Heldebrant H Okamoto M Watanabe AM McLaughlin and K Yokoyama (1982) Evaluation of Four New Perfluorochemicals as Oxygen Transporting Emulsions American Chemical Society, 183rd National Meeting, Las Vegas, Abs Fluo 4.

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PF Glidden JC Cavin M Nilsen L Mercado S Eubanks and CM Heldebrant (1993) Restriction of Diet and Administration of Heparin Result in Prolonged Time to Reperfusion and Greater Occurrence of Restenosis During Thrombolytic Treatment With and Without Fluosol® in Rabbits Int Cong Thromb Hemostas NY, abs.

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P Bhattacharya C Bunch C Ngo L Gayleard D Hwang Y Uemura CM Heldebrant (1996) Inactivation and Removal of Viruses During the Manufacturing Process of Human Albumin XXII International Congress of the World Federation of Hemophilia Dublin, Ireland.

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C Bunch C Kavanagh B Tran CM Heldebrant and WS Craig (1998) Investigation of the Conditions Affecting Virus Removal During Planova® 15N Filtrations of Albumin Spiked with EMC or PPV CHI Viral Clearance Conference, Philadelphia.

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Patents

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(b) (6)



SUBMISSION END

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AM



Mosley, Sylvester

From: Miriam Lewensztain [ml.nutra@gmail.com]

Sent: Friday, September 10, 2010 3:44 PM

To: Mosley, Sylvester

Subject: GRN 346

Hi Sylvester,

Please withdraw our application without prejudice at this time for GRN 346.

Please send copy of the issues discussed on our call of Sept 8, 2010, as agreed, to facilitate our resubmission in the near future.

Thank you for all of your help.

Miriam Lewensztain

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