GRAS ASSOCIATES, LLC

GRAS Associates, LLC
27499 Riverview Center Blvd.
Bonita Springs, FL 34134
T: 239.444.1724 | F: 239.444.1723
www.gras-associates.com

#850

March 01, 2019

Food and Drug Administration
Center for Food Safety & Applied Nutrition
Office of Food Additive Safety (HFS-255)
5001 Campus Drive
College Park, MD 20740-3835

Attention: Dr. Paulette Gaynor
Re: GRAS Notification – Shea Olein

Dear Dr. Gaynor:

GRAS Associates, LLC, acting as the Agent for BUNGE Loders Croklaan BV (Netherlands), is submitting for FDA review Form 3667 and the enclosed CD, free of viruses, containing a GRAS Notification for *Shea Olein*. Along with BUNGE's determination of safety, an Expert Panel of qualified persons was assembled to assess the composite safety information of the subject substance with the intended use in conventional foods as a replacement of animal fats and vegetable fats rich in palmitic, myristic and lauric fatty acids at levels determined by Current Good Manufacturing Practices. The attached documentation contains the specific information that addresses the safe human food uses for the subject notified substance as discussed in the GRAS guidance document.

If additional information or clarification is needed as you and your colleagues proceed with the review, please feel free to contact me via telephone or email.

We look forward to your feedback.

Sincerely,

William J. Rowe

President
Agent for BUNGE Loders Croklaan BV
GRAS Associates, LLC
27499 Riverview Center Blvd., Suite 212
Bonita Springs, FL 34134
wrowe@nutrasource.ca
Enclosure: GRAS Notification for BUNGE Loders Croklaan BV – Shea Olein

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

GENERALLY RECOGNIZED AS SAFE *(GRAS)* NOTICE (Subpart E of Part 170)

Form Approved: OMB No. 0910-0342; Expiration Date: 09/30/2019
(See last page for OMB Statement)

FDA USE ONLY

GRN NUMBER	DATE OF RECEIPT
000850	3/13/2019
ESTIMATED DAILY INTAKE	INTENDED USE FOR INTERNET
NAME FOR INTERNET	
KEYWORDS	

Transmit completed form and attachments electronically via the Electronic Submission Gateway *(see Instructions)*; OR Transmit completed form and attachments in paper format or on physical media to: Office of Food Additive Safety *(HFS-200)*, Center for Food Safety and Applied Nutrition, Food and Drug Administration,5001 Campus Drive, College Park, MD 20740-3835.

SECTION A – INTRODUCTORY INFORMATION ABOUT THE SUBMISSION

1. Type of Submission *(Check one)*
☒ New ☐ Amendment to GRN No. _____ ☐ Supplement to GRN No. _____

2. ☒ All electronic files included in this submission have been checked and found to be virus free. *(Check box to verify)*

3 Most recent presubmission meeting *(if any)* with FDA on the subject substance *(yyyy/mm/dd)*: N/A

4 For Amendments or Supplements: Is your amendment or supplement submitted in response to a communication from FDA? *(Check one)* ☐ Yes ☐ No If yes, enter the date of communication *(yyyy/mm/dd)*: _____

SECTION B – INFORMATION ABOUT THE NOTIFIER

1a. Notifier

Name of Contact Person	Position or Title
Dr. Luisa Gambelli	Regulatory and Nutritional Affairs Manager

Organization *(if applicable)*: BUNGE Loders Croklaan BV

Mailing Address *(number and street)*: Hogeweg 1

City	State or Province	Zip Code/Postal Code	Country
Wormerveer		1521 AZ	Netherlands

Telephone Number	Fax Number	E-Mail Address
+31 (0)75 629 29 11	+31 (0) 75 628 9455	Luisa.Gambelli@bunge.com

1b. Agent or Attorney *(if applicable)*

Name of Contact Person	Position or Title
William J. Rowe	President

Organization *(if applicable)*: GRAS Associates, LLC

Mailing Address *(number and street)*: 27499 Riverview Center Blvd., Suite 212

City	State or Province	Zip Code/Postal Code	Country
Bonita Springs	Florida	34134	United States of America

Telephone Number	Fax Number	E-Mail Address
239-444-1724	239-444-1723	wrowe@nutrasource.ca

SECTION C – GENERAL ADMINISTRATIVE INFORMATION

1. Name of notified substance, using an appropriately descriptive term

Shea olein

2. Submission Format: *(Check appropriate box(es))*

☐ Electronic Submission Gateway

☒ Electronic files on physical media

☐ Paper

If applicable give number and type of physical media

_____

3. For paper submissions only:

Number of volumes _____

Total number of pages _____

4. Does this submission incorporate any information in CFSAN's files? *(Check one)*

☐ Yes *(Proceed to Item 5)* ☒ No *(Proceed to Item 6)*

5. The submission incorporates information from a previous submission to FDA as indicated below *(Check all that apply)*

☐ a) GRAS Notice No. GRN _____

☐ b) GRAS Affirmation Petition No. GRP _____

☐ c) Food Additive Petition No. FAP _____

☐ d) Food Master File No. FMF _____

☐ e) Other or Additional *(describe or enter information as above)* _____

6. Statutory basis for conclusions of GRAS status *(Check one)*

☒ Scientific procedures *(21 CFR 170.30(a) and (b))* ☐ Experience based on common use in food *(21 CFR 170.30(a) and (c))*

7. Does the submission (including information that you are incorporating) contain information that you view as trade secret or as confidential commercial or financial information? (see 21 CFR 170.225(c)(8))

☐ Yes *(Proceed to Item 8*

☒ No *(Proceed to Section D)*

8. Have you designated information in your submission that you view as trade secret or as confidential commercial or financial information *(Check all that apply)*

☐ Yes, information is designated at the place where it occurs in the submission

☐ No

9. Have you attached a redacted copy of some or all of the submission? *(Check one)*

☐ Yes, a redacted copy of the complete submission

☐ Yes, a redacted copy of part(s) of the submission

☐ No

SECTION D – INTENDED USE

1. Describe the intended conditions of use of the notified substance, including the foods in which the substance will be used, the levels of use in such foods, and the purposes for which the substance will be used, including, when appropriate, a description of a subpopulation expected to consume the notified substance.

Intended to be used in conventional foods as a replacement for animal fats and vegetable fats rich in palmitic, myristic and lauric fatty acids at levels within Current Good Manufacturing Practices and principles.

2. Does the intended use of the notified substance include any use in product(s) subject to regulation by the Food Safety and Inspection Service (FSIS) of the U.S. Department of Agriculture?

(Check one)

☐ Yes ☒ No

3. If your submission contains trade secrets, do you authorize FDA to provide this information to the Food Safety and Inspection Service of the U.S. Department of Agriculture?

(Check one)

☐ Yes ☐ No , you ask us to exclude trade secrets from the information FDA will send to FSIS.

SECTION E – PARTS 2 -7 OF YOUR GRAS NOTICE

(check list to help ensure your submission is complete – PART 1 is addressed in other sections of this form)

☒ PART 2 of a GRAS notice: Identity, method of manufacture, specifications, and physical or technical effect (170.230).

☒ PART 3 of a GRAS notice: Dietary exposure (170.235).

☒ PART 4 of a GRAS notice: Self-limiting levels of use (170.240).

☒ PART 5 of a GRAS notice: Experience based on common use in foods before 1958 (170.245).

☒ PART 6 of a GRAS notice: Narrative (170.250).

☒ PART 7 of a GRAS notice: List of supporting data and information in your GRAS notice (170.255)

Other Information

Did you include any other information that you want FDA to consider in evaluating your GRAS notice?

☒ Yes ☐ No

Did you include this other information in the list of attachments?

☒ Yes ☐ No

SECTION F – SIGNATURE AND CERTIFICATION STATEMENTS

1. The undersigned is informing FDA that BUNGE Loders Croklaan BV
(name of notifier)

has concluded that the intended use(s) of Shea olein
(name of notified substance)

described on this form, as discussed in the attached notice, is (are) not subject to the premarket approval requirements of the Federal Food, Drug, and Cosmetic Act based on your conclusion that the substance is generally recognized as safe recognized as safe under the conditions of its intended use in accordance with § 170.30.

2. BUNGE Loders Croklaan BV
(name of notifier)
agrees to make the data and information that are the basis for the conclusion of GRAS status available to FDA if FDA asks to see them; agrees to allow FDA to review and copy these data and information during customary business hours at the following location if FDA asks to do so; agrees to send these data and information to FDA if FDA asks to do so.

Hogeweg 1, 1521AZ Wormerveer, The Netherlands
(address of notifier or other location)

The notifying party certifies that this GRAS notice is a complete, representative, and balanced submission that includes unfavorable, as well as favorable information, pertinent to the evaluation of the safety and GRAS status of the use of the substance.The notifying party certifies that the information provided herein is accurate and complete to the best or his/her knowledge. Any knowing and willful misinterpretation is subject to criminal penalty pursuant to 18 U.S.C. 1001.

3. Signature of Responsible Official, Agent, or Attorney	Printed Name and Title	Date (mm/dd/yyyy)
[redacted]	Ginny Bank on behalf of William Rowe	2/27/2019

SECTION G – LIST OF ATTACHMENTS

List your attached files or documents containing your submission, forms, amendments or supplements, and other pertinent information. Clearly identify the attachment with appropriate descriptive file names (or titles for paper documents), preferably as suggested in the guidance associated with this form. Number your attachments consecutively. When submitting paper documents, enter the inclusive page numbers of each portion of the document below.

Attachment Number	Attachment Name	Folder Location (select from menu) (Page Number(s) for paper Copy Only)
	Multiple Appendices --- Appendices 1-7	

OMB Statement: Public reporting burden for this collection of information is estimated to average 170 hours per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to: Department of Health and Human Services,Food and Drug Administration, Office of Chief Information Officer, PRAStaff@fda.hhs.gov. (Please do NOT return the form to this address.). An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number.

GRAS Notification

for

Shea Olein

Food Usage Conditions for General Recognition of Safety

on behalf of

BUNGE Loders Croklaan BV
Hogeweg 1
1521AZ Wormerveer
The Netherlands

March 1, 2019

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FIGURES

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FOREWORD

BUNGE Loders Croklaan BV (hereinafter "BUNGE") based its GRAS assessment primarily on the composite safety information, i.e., scientific procedures considering the safety/toxicity of shea olein, and compositional details, specifications, and method of preparation of the subject ingredient. History of safe use was considered secondarily. A search of the scientific and regulatory literature was conducted through September 1, 2018, with particular attention paid to adverse reports, as well as those that supported conclusions of safety. References that were deemed pertinent to this review are listed in Part 7. The totality of information about the composition, safety/toxicity, and dietary exposure, provide the scientific foundation for the GRAS conclusion.

At BUNGE's request, GRAS Associates, LLC convened an Expert Panel to complete an independent safety evaluation of BUNGE's shea olein. The purpose of the evaluation is to ascertain whether BUNGE's conclusion that the intended food uses of shea olein as described in Part 3 are generally recognized as safe, i.e., GRAS, under the intended conditions of use. In addition, BUNGE has asked that GRAS Associates act as Agent for the submission of this GRAS notification.

PART 1. SIGNED STATEMENTS AND CERTIFICATION

A. Basis of Exclusion from the Requirement for Premarket Approval Pursuant to Subpart E of 170[1]

BUNGE has concluded that its shea olein is Generally Recognized As Safe (GRAS) in accordance with Section 201(s) of the Federal Food, Drug, and Cosmetic Act (FD&C Act). This determination was made in concert with an appropriately convened panel of experts who are qualified by scientific training and experience. The GRAS determination is based on scientific procedures as described in the following sections, with supporting evidence from history of safe use. The evaluation accurately reflects the intended conditions of food use for the designated shea olein.

Signed:

Agent for BUNGE

William J. Rowe Date: 3/1/19
President

[1] See 81 FR 54960, 17 August 2016. Accessible at: https://www.gpo.gov/fdsys/pkg/FR-2016-08-17/pdf/2016-19164.pdf (Accessed 12/5/17).

GRAS Associates, LLC
27499 Riverview Center Blvd.
Suite 212
Bonita Springs, FL 34134

B. Name and Address of Responsible Party

Dr. Luisa Gambelli
Regulatory and Nutritional Affairs Manager
BUNGE Loders Croklaan BV
Hogeweg 1
1521AZ Wormerveer
The Netherlands

As the Responsible Party, BUNGE accepts responsibility for the GRAS conclusion that has been made for its shea olein as described in the subject safety evaluation; consequently, the shea olein which meet the conditions described herein are not subject to the premarket approval requirements for food ingredients.

C. Common Name and Identity of Notified Substance

The common name of the ingredient to be used on food labels is “shea olein.”

D. Conditions of Intended Use in Food

BUNGE’s shea olein is intended for use in conventional foods as a replacement for animal fats and vegetable fats rich in palmitic, myristic and lauric fatty acids at levels within current good manufacturing practices (CGMPs).

E. Basis for GRAS Conclusion

Pursuant to 21 CFR 170.30(a) and (b), BUNGE’s shea olein has been concluded to be GRAS on the basis of scientific procedures as discussed in the detailed description provided below.

Shea olein is not subject to premarket approval requirements of the FD&C Act based on BUNGE’s conclusion that the substance is GRAS under the conditions of its intended food use.

BUNGE certifies, to the best of its knowledge, that this GRAS notice is a complete, representative, and balanced assessment that includes all relevant information available---both favorable and unfavorable---that is pertinent to the evaluation of safety and the GRAS status of shea olein when used as proposed. This safety evaluation included a comprehensive literature search through September 1, 2018.

F. Availability of Information

The data and information that serve as the basis for this GRAS notice will be maintained at the offices of BUNGE Loders Croklaan BV at Hogeweg 1, 1521AZ Wormerveer, The Netherlands, and will be made available during customary business hours.

BUNGE certifies that no data or information contained herein are exempt from disclosure under the Freedom of Information Act (FOIA). No non-public, safety-related data were used by the GRAS Panel to reach the GRAS conclusion.

PART 2. IDENTITY, METHOD OF MANUFACTURE, SPECIFICATIONS, AND PHYSICAL OR TECHNICAL EFFECT

A. Chemical Identity of Ingredient

Common or Usual Name:	Shea olein
Chemical Name:	Shea olein
Synonyms:	Shea oleine, shea tree extract, oleins, glycerides C16-18 and C18 unsaturated
Chemical Abstracts Service (CAS) Number:	93348-6-9
Molecular Formula:	Not applicable
Molecular Weight:	833-889 g/mol (predominantly)

B. Historical Background on Shea Olein

The shea tree (*Vitellaria paradoxa*, formerly *Butyrospermum parkii*), is indigenous, agro-managed tree crop growing in parklands in large parts of Sub-Saharan Africa and savannah ecosystems of northern Ghana. The tree bears a berry-like fruit consisting of a thin epicarp and a soft mesocarp enclosing usually a single seed (kernel or shea nut). The pulp of the fruit is widely consumed in areas where it grows and has a high fat content. The shea nut is extracted for its fat, which is called shea butter. Shea butter is widely used for cooking and is an important export commodity. Shea butter is composed of triglycerides (of primarily oleic, stearic, linoleic and palmitic acids), and unsaponifiable matter, which includes triterpenes, phenols, tocopherol and sterols. Shea butter is also used in cosmetics (Honfo et al., 2014).

Another product from shea butter, sheanut oil, is an approved food ingredient by FDA (21 CFR§184.1702) and is commercialized in the United States for use as a cocoa butter substitute in confections and frosting, coatings of soft candy and sweet sauces and toppings.

C. Chemistry of Shea Olein

Shea olein is a refined vegetable oil. It is the product of the fractionation and refining of shea butter (Baldrick et al., 2001, Zhang et al., 2017). As is the case for other food-grade vegetable oils, shea

olein predominantly consists of fat (average 92% w/w), consisting of mainly triglycerides (>90% w/w), unsaponifiable matter (average 8% w/w) and traces of monoglycerides. The triglycerides present in shea olein are found in common vegetable oils and fats (Gunstone et al., 2007, Padley et al., 1986). Like other vegetable oils, the unsaponifiable matter in shea olein consists almost exclusively of phytosterols (Baldrick et al., 2001).

1. Identity of Main Components of Shea Olein

The triglycerides (>80%) present in shea olein are predominantly 1-stearoyl-2,3-dioleoylglycerol (StOO), triolein (OOO), 1-stearoyl-2-linoleoyl-3-oleoylglycerol (StLiO), 1,3-distearoyl-2-oleoylglycerol (StOSt), 1-palmitoyl-2-oleoyl-3-stearoylglycerol (POSt), 1,2-dioleoyl-3-palmitoylglycerol (POO), and 1-myristoyl-2-oleoyl-3-palmitoyl-rac-glycerol (MOP) (Zhang et al., 2017). They are further described below.

a. 1-Stearoyl-2,3-dioleoylglycerol (StOO)

Chemical Name: 1-stearoyl-2,3-dioleoylglycerol (StOO)
Synonyms: 1,2-dioleoyl-3-stearoyl-rac-glycerol,1,2-di(cis-9-octadecenoyl)-3-octadecanoyl-rac-glycerol, glycerol 1,2-di-(9Z-octadecenoate)-3-octadecanoate, 1-O-stearoyl-2-O,3-O-bis[I-9-octadecenoyl]glycerol
CAS Number: 2410-28-8 and 1138-10-0
Molecular Formula: $C_{57}H_{106}O_6$
Molecular Weight: 887.45 g/mol

Figure 1. Structure of StOO (ChemSrc, 2018b)

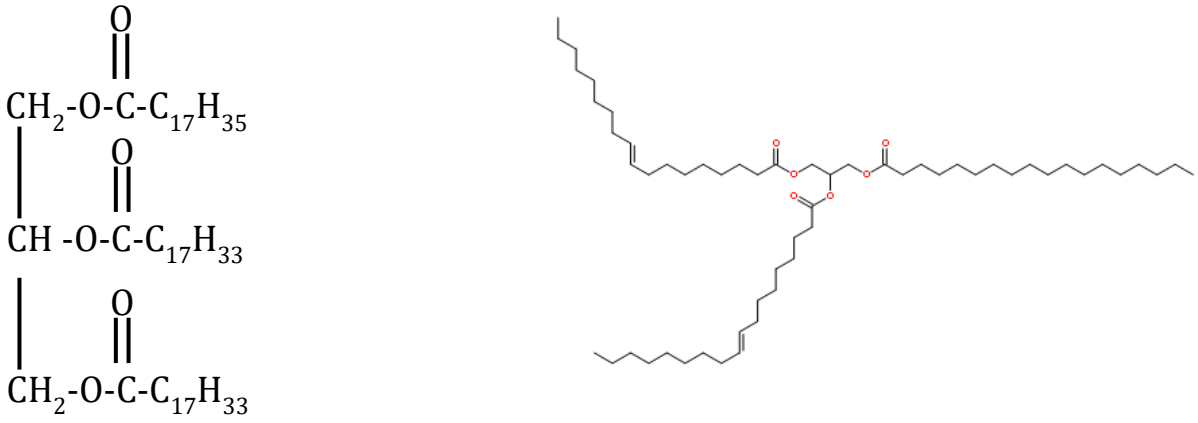


Table 1. Physical Characteristics of StOO (ChemSrc, 2018b)

Property	Value
Physical state at 20 °C and 101.3 KPa	Liquid
Melting/freezing point	No data available
Color	Colorless to very faint yellow
Density	0.917 g/cm^3
Boiling point	819.5°C at 760 mmHg

StOO is found in other fats and oils (in mole %): shea butter (26.8%), illipe fat (6.0%), tallow (5.9%), lard (6.1%), olive oil (3-7%), cocoa butter (4.9%), and butter (1.2%) (Gunstone et al., 2007, Di Vincenzo et al., 2005).

b. Triolein (OOO)

Chemical Name: triolein (OOO)
Synonyms: 1,2,3-propanetriyl (9Z,9'Z,9''Z)tris(-9-octadecenoate), 1,2,3-tri-(9Z-octadecenoyl)-sn-glycerol,1,2,3-Tri(cis-9-octadecenoyl)glycerol, glycerin trioleate
CAS Number: 122-32-7
Molecular Formula: $C_{57}H_{104}O_6$
Molecular Weight: 885.43 g/mol

Figure 2. Structure of OOO (Budavari, 1996)

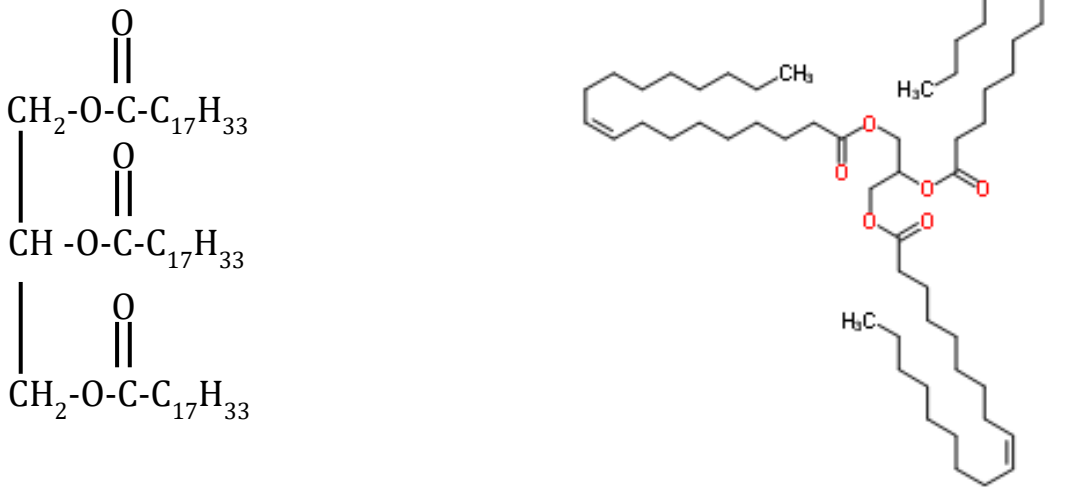


Table 2. Physical Characteristics of OOO (Budavari, 1996)

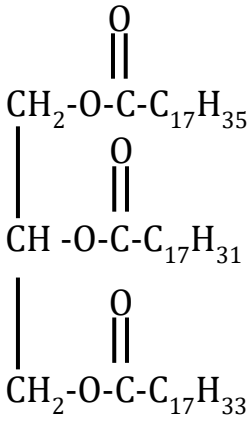
Property	Value
Physical state at 20 °C and 101.3 KPa	Liquid
Melting/freezing point	-4° C to 5° C
Color	Colorless to very faint yellow
Density	0.915 g/cm^3 (15 °C)
Boiling point	235-240°C at 15 mmHg

OOO is found in other fats and oils (in mole %): olive oil (40-59%), rapeseed oil (22.4%), and shea butter (10.8%) (Gunstone et al., 2007, Di Vincenzo et al., 2005).

c. 1-Stearoyl-2-linoleoyl-3-oleoylglycerol (StLiO)

Chemical Name: 1-stearoyl-2-linoleoyl-3-oleoylglycerol (StLiO)
Synonyms: [(2S)-2-[(9Z,12Z)-octadeca-9,12-dienoyl]oxy-3-[(Z)-octadec-9-enoyl]oxypropyl] octadecanoate, TG(18:0/18:2(9Z,12Z)/18:1(9Z)); 1-Octadecanoyl-2-(9Z,12Z-octadecadienoyl)-3-(9Z-octadecenoyl)-glycerol
CAS Number: Not available
Molecular Formula: $C_{57}H_{104}O_6$
Molecular Weight: 885.45 g/mol

Figure 3. Structure of StLiO (National Center for Biotechnology Information, 2018b)



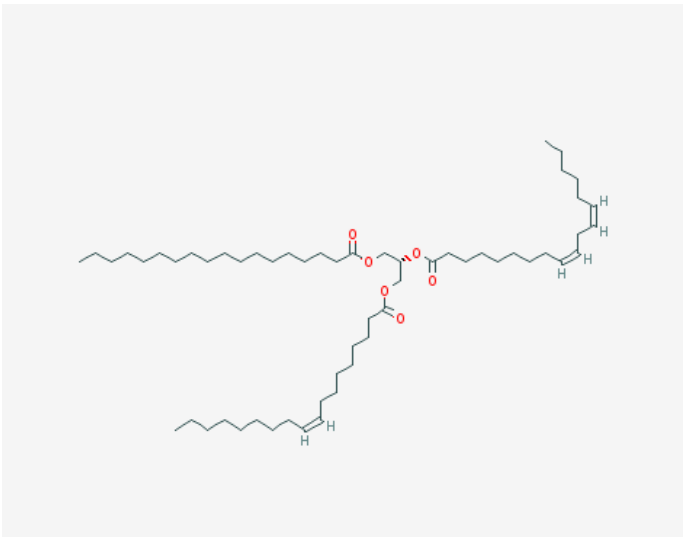


Table 3. Physical Characteristics of StLiO (National Center for Biotechnology Information, 2018b)

Property	Value
Physical state at 20 °C and 101.3 KPa	Liquid
Melting/freezing point	No data available
Color	No data available
Density	No data available
Boiling point	No data available

StLiO is found in other fats and oils (in mole %): shea butter (up to 5.2%), olive oil (3%), cocoa butter (0.3%), and palm oil (0.6%) (Di Vincenzo et al., 2005).

d. 1,3-Distearoyl-2-oleoylglycerol (StOSt)

Chemical Name: 1,3-distearoyl-2-oleoylglycerol (StOSt)
Synonyms: 1,3-bis(octadecanoyloxy)propan-2-yl (9Z)-octadec-9-enoate, 1,3 bis(stearoyloxy)-2-propanyl (9Z)-9-octadecenoate, 1,3 bis(stearoyloxy)propan-2-yl (9Z)-octadec-9-enoate, 1,3-distearo-2-olein.
CAS Number: 2846-04-0
Molecular Formula: $C_{57}H_{108}O_6$
Molecular Weight: 889.464 g/mol

Figure 4. Structure of StOSt (ChemSpider, 2018)

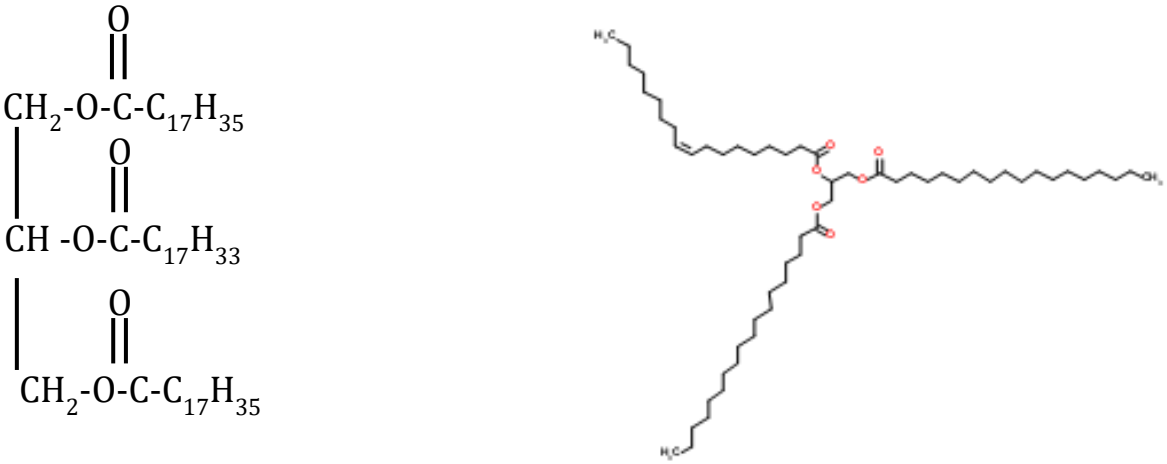


Table 4. Physical Characteristics of StOSt (ChemSpider, 2018)

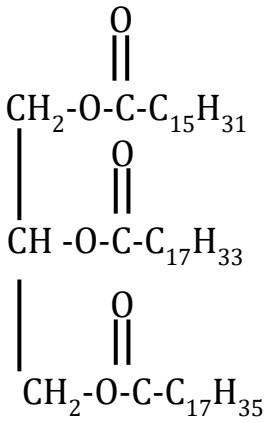
Property	Value
Physical state at 20 °C and 101.3 KPa	Solid
Melting/freezing point	36.5 °C (β'-form)
Color	White to very faint yellow
Density	0.9±0.1 g/cm^3
Boiling point	817.6±35.0°C at 760 mmHg

StOSt is found in other fats and oils (in mole %): shea butter (40.9%), cocoa butter (25.2%), illipe fat (44%), and tallow (4.8%) (Di Vincenzo et al., 2005, Padley et al., 1986).

e. 1-Palmitoyl-2-oleoyl-3-stearoylglycerol (POSt)

Chemical Name: 1-palmitoyl-2-oleoyl-3-stearoylglycerol (POSt)
Synonyms: 1-palmito-3-stearo-2-olein; 1-(((1-oxohexadecyl)oxy)methyl)-2-((1-oxooctadecyl)oxy)ethyl (Z)-9-octadecenoate; 1-palmitoyl-2-oleoyl-3-stearin; 2-oleo-3-palmito-1-stearin; 2-oleo-3-stearo-1-palmitin; 2-oleopalmitostearin; 9-octadecenoic acid (Z)-, 1-(((1-oxohexadecyl)oxy)methyl)-2-((1-oxooctadecyl)oxy)ethyl ester.
CAS Number: 2190-27-4
Molecular Formula: $C_{55}H_{104}O_6$
Molecular Weight: 861.41 g/mol

Figure 5. Structure of POSt (ChemSrc, 2018a)



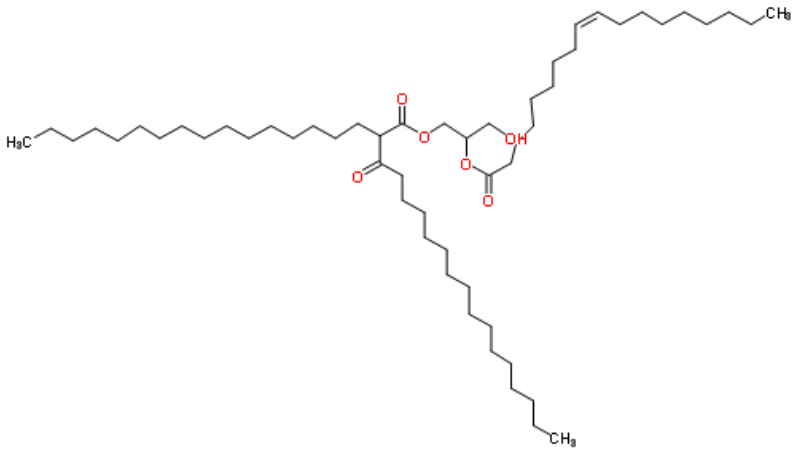


Table 5. Physical Characteristics of POSt (ChemSrc, 2018a)

Property	Value
Physical state at 20 °C and 101.3 KPa	Solid
Melting/freezing poi	39 °C (β-form)
Color	White to very faint yellow
Density	0.915 g/cm^3
Boiling point	800.3°C at 760 mmHg

POSt is found in other fats and oils (in mole %): cocoa butter (46%), shea butter (5.3%), and palm oil (5.1%) (Di Vincenzo et al., 2005, Padley et al., 1986).

f. 1,2-Dioleoyl-3-palmitoyl-rac-glycerol (POO)

Chemical Name: 1,2-dioleoyl-3-palmitoyl-rac-glycerol (POO)
Synonyms: 1,2-Di(cis-9-octadecenoyl)-3-hexadecanoyl-rac-glycerol, 3-(hexadecanoyloxy)propane-1,2-diyl (9Z,9'Z)bis-octadec-9-enoate, 3-(palmitoyloxy)-1,2-propanediyl (9Z,9'Z)bis(-9-octadecenoate).
CAS Number: 2190-30-9
Molecular Formula: $C_{55}H_{102}O_6$
Molecular Weight: 859.39 g/mol

Figure 6. Structure of POO (ChemSrc, 2018b)

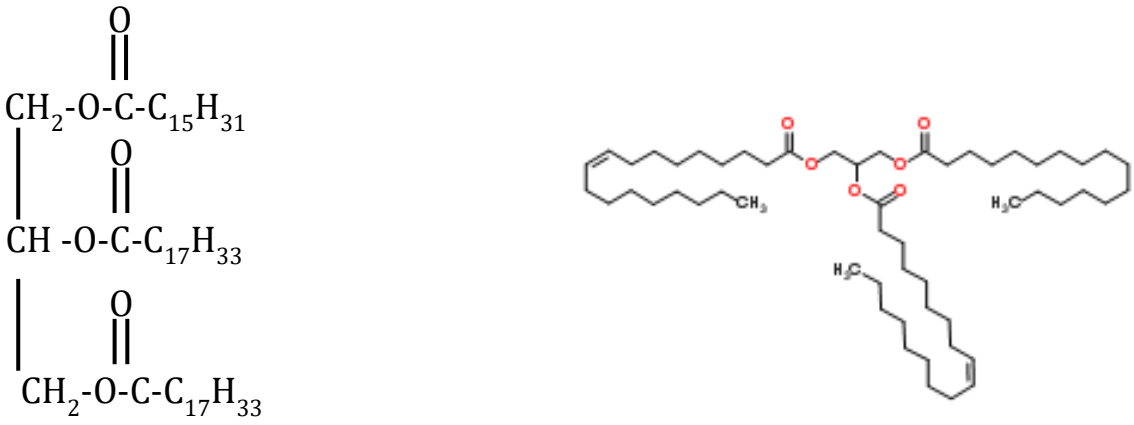


Table 6. Physical Characteristics of POO (ChemSrc, 2018b)

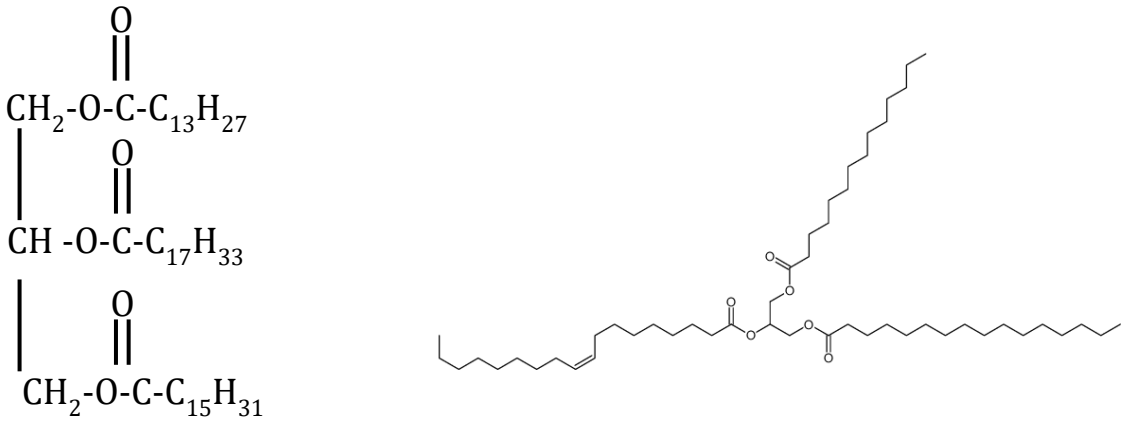
Property	Value
Physical state at 20 °C and 101.3 KPa	Liquid
Melting/freezing point	No data available
Color	Colorless to very faint yellow
Density	0.9±0.1 g/cm^3
Boiling point	802.2±45.0°C at 760 mmHg

POO is found in other fats and oils (in mole %): palm oil (22.8%), olive oil (20.1%), and shea butter (3.1%) (Di Vincenzo et al., 2005, Gunstone et al., 2007, Ollivier et al., 2006).

g. 1-Myristoyl-2-oleoyl-3-palmitoyl-rac-glycerol (MOP)

Chemical Name: 1-myristoyl-2-oleoyl-3-palmitoyl-rac-glycerol (MOP)
Synonyms: glycerol 1-myristate 2-oleate 3-palmitate; 1-Myristoyl-2-oleoyl-3-palmitoyl-rac-glycerol; 1-Tetradecanoyl-2-(cis-9-octadecenoyl)-3-hexadecanoyl-rac-glycerol; 1-(Hexadecanoyloxy)-3-(tetradecanoyloxy)propan-2-yl (9E)-octadec-9-enoate .
CAS Number: 134907-95-2
Molecular Formula: $C_{51}H_{96}O_6$
Molecular Weight: 805.32 g/mol

Figure 7. Structure of MOP (National Center for Biotechnology Information, 2018a)



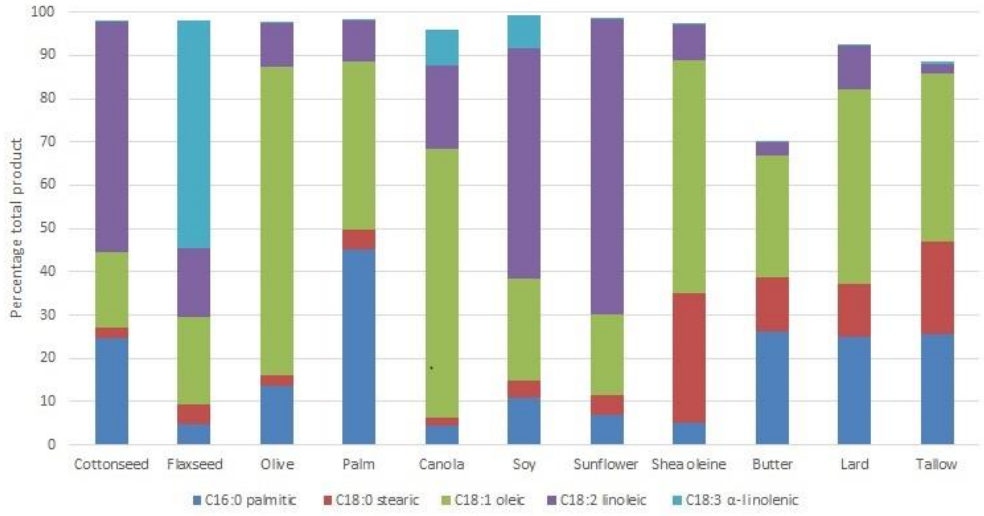
No references that describe the physical characteristics of MOP were found.

MOP is found in other fats and oils (in mole %): palm oil (1.3%), cocoa butter (0.9 %), and shea butter (3.1%) (Di Vincenzo et al., 2005, Gunstone et al., 2007, Ollivier et al., 2006).

2. Typical Fatty Acid Profile of Shea Olein

The typical fatty acid composition of shea olein (Zhang et al., 2017) along with the composition of vegetable oils and fats commonly consumed in the United States (Codex Alimentarius, 1981a, Woodgate and van der Veen, 2014) are shown in Figure 8. Only the comparison of the main fatty acids is given.

Figure 8. Percentage of Typical Fatty Acids in Shea Olein and of Oils and Fats Commonly Consumed in the United States



Oleic acid is the predominant fatty acid in shea olein, accounting for typically 54% of total fatty acids (based on total fatty acid methyl esters [FAME]). Approximately 30% of fatty acids in shea olein is stearic acid.

A summary of the typical fatty acid profile of BUNGE's shea olein is shown in Table 7**,** along with the fatty acids composition of three production batches of BUNGE's shea olein.

Table 7. Typical Fatty Acid Profile of BUNGE's Shea Olein and of Three Production Batches of BUNGE's Shea Olein

Fatty Acid	Percentage of Total FAME[1]			
C16:0 (Palmitic)	5	5.5	5.5	5.9
C18:0 (Stearic)	30	29.1	29.1	29.2
C18:1 (Oleic)	54	53.8	54.2	52.9
C18:2 (Linoleic)	8	8.6	8.4	7.9
C18:3 (α-Linolenic)	<1	0.3	0.3	0.4
C20:0 (Arachidonic)	<3.5	1.3	1.2	1.2
Others	<3	1.4	1.3	2.5

[1]Fatty Acid Methyl Esters

3. Identity of Minor Components (Unsaponifiable Matter) of Shea Olein

BUNGE's shea olein contains up to 9% w/w unsaponifiable matter, of which about 8% is phytosterols and less than 1% is tocopherols. Ninety-seven percent of phytosterols is 4,4-dimethylsterols (also known as triterpene alcohols), 2.5% is 4-desmethylsterols and 0.5% is 4-α-methylsterols. A detailed compositional analysis of the normalized percentage values of individual 4,4-dimethylsterols (typical and from two representative lots of BUNGE's shea olein) is given in Table 8 (original reports are found in Appendix 1). The 4,4-dimethylsterols composition of shea olein is similar to that reported in the literature for the unsaponifiable matter of shea butter. These phytosterols exist as esters and in free form (Akihisa et al., 2011, Akihisa et al., 2010).

Table 8. Normalized Percentage Values of the 4,4-Dimethylsterols in BUNGE's Shea Olein

4,4 Dimethylsterol	Typical Value (%)	[redacted]	[redacted]
α-Amyrin/cycloartenol	40.6	38.5	38.7
Butyrospermol	21.1	22.2	22.1
Lupeol	19.0	19.7	19.6
β-Amyrin	7.9	7.0	6.9
24-Methylene cycloartanol/cyclobranol	3.2	1.1	1.1
Others	8.2	11.5	11.6

The 4,4-dimethylsterol composition of different oils from the literature compared with that of shea olein can be found in Table 9. Shea olein phytosterol composition is very similar to that of shea butter since almost all the phytosterols remain with the shea olein fraction after acetone fractionation. 4,4-Dimethylsterols account for a greater fraction of shea butter and shea olein than other vegetable oils; however, the most represented phytosterols in shea products can also be found in other edible vegetable oils.

Table 9. 4,4-Dimethylsterol Composition of Some Vegetable Oils Compared to Shea Olein[1] (mg/kg)

	β Amyrin	Butyrospermol	α Amyrin	Lupeol	Cyclobranol	Others
BUNGE's Shea Olein	3896	12362	21411	10971	590	6365
Olive oil	216	101	-	302	144	677
Palm kernel oil	29	65	209	94	-	324
Safflower oil	84	-	78	-	20	471
Shea butter	3060	9945	17595	6120	383	1148
Soybean oil	126	139	-	235	-	345
Wheat germ oil	403	-	179	-	-	1479

[1]Data adapted from Gunstone et al. (2007) with exception of shea olein (data from batch [redacted])

4-Desmethylsterols are commonly found in vegetable oils in concentrations ranging from 300 mg/kg in palm oil to as high as 26,000 mg/kg in wheat germ oil (Gomez-Coca et al., 2015). The predominant 4-desmethylsterol in seed oils is normally β-sitosterol, but other 4-desmethylsterols can also be found in significant amounts in specific plants. A detailed comparison of 4-desmethylsterols of different oils has been reported in the literature and can be found in Table 10**.** For comparison purposes, shea olein phytosterol composition can be seen as very similar to that of shea butter since, as mentioned above, almost all the phytosterols remain with the shea olein fraction after acetone fractionation. Table 10 shows that most 4-desmethylsterols in shea butter, and consequently shea olein, are also commonly found in other edible vegetable oils.

Table 10. 4-Desmethylsterol Composition of Some Common Vegetable Oils[1] (mg/kg)

	Campesterol	Stigmasterol	β Sitosterol	β Stigmasterol	Δ7 Stigmastenol	Δ7 Avenasterol	Unknown
Peanut oil	360	2160	2160	1536	72	24	-
Rice bran oil	5056	2709	2709	8849	180	361	-
Safflower oil	576	313	313	1809	696	104	69
Shea butter	-	-	-	-	944	281	132
Soybean oil	720	720	720	1908	108	36	-
Sunflower oil	313	313	313	2352	588	156	39
Wheat germ oil	5702	-	-	17336	777	518	-

[1]Adapted from Gunstone et al. (2007)

D. Manufacturing Processes

1. Incoming Raw Material (Shea Nuts and Crude Shea Butter) Specifications

Incoming shea butter and shea nuts must comply with BUNGE's specifications shown in Table 11. When nuts are purchased, visual assessment for the presence of molds and estimation of moisture with a moisture meter is carried out, as advised by the Global Shea Alliance. Attention is also paid to the type of bags in which they have been transported, which should be of natural fiber (jute) and free of mineral oils, and to the stacking of the bags to favor ventilation, limiting formation of condensation and vapor to avoid mold growth.

When shea butter is purchased, the solid fat content (SFC) is determined. The SFC is of prime importance since it gives an indication of the melting profile of shea butter and, consequently, is linked to fatty acid and triglycerides compositions of shea butter and shea olein.

The free fatty acid content is also an important parameter for the estimation of the expected losses during processing since fatty acids are all removed during refining.

Table 11. BUNGE's Specifications For Shea Nuts and Crude Shea Butter

Parameter	Limit
Shea Nuts	
Visual assessment	Absence of molds
Moisture (moisture meter) (%)	<7
Shea Butter	
Free fatty acid as oleic (%)	Max 9.0
Impurities (%)	Max 0.1
Moisture (%)	Max 0.2
Refractive index (nD) at 50°C	<1.45995 and >1.45945

2. Manufacturing Process

BUNGE's shea olein is produced consistent with standard procedures used in the production of fractionated and refined vegetable edible oils. Shea (*Vitellaria paradoxa,* Fam Saponaceae) is an agro-managed tree crop, which is found in the wild, growing in parklands in large parts of Sub-Saharan Africa and savannah ecosystems of northern Ghana.

For the extraction of shea butter, the nuts are crushed, boiled and physically pressed. The remaining cake is further washed and pressed with hexane to extract any remaining oil from the cake, similar to olive oil.

After the extraction, crude shea butter is de-gummed in a reactor. The process involves a single-stage acetone treatment, followed by continuous removal of the hydrated gums by centrifugation. The de-gummed shea butter is then fractionated into shea olein and shea stearine in a filterbed with the aid of acetone.

The de-gummed shea olein is then physically refined. Neutralization is carried out in a "fatty acid stripper" (fatty acid thin film evaporator) at about 220-230°C under vacuum to remove free-fatty acids. Effective neutralization results in enhanced effectiveness of subsequent steps (i.e., bleaching and deodorization) and furthermore results in high yields of a quality product (Addaquay, 2004).

The neutral, washed and dried shea olein still contains some color bodies that have to be removed. Bleaching is carried out with food-grade bleaching earth in combination with the food-grade activated carbon to remove any potential residual contaminants present in the oil. The shea olein is mixed with metered quantities of bleaching earth and thereafter pumped to a bleaching chamber operating under vacuum where an adequate retention time is provided to ensure effective bleaching. The oil/earth slurry is further pumped through hermetic leaf filters operating in sequence to enable continuous bleached shea olein (filtrate) discharge.

Prior to deodorization, the bleaching earth is removed via several filtration steps with 10 µm food-grade polyester filters in the presence of food-grade perlite, a filter aid. Deodorization represents

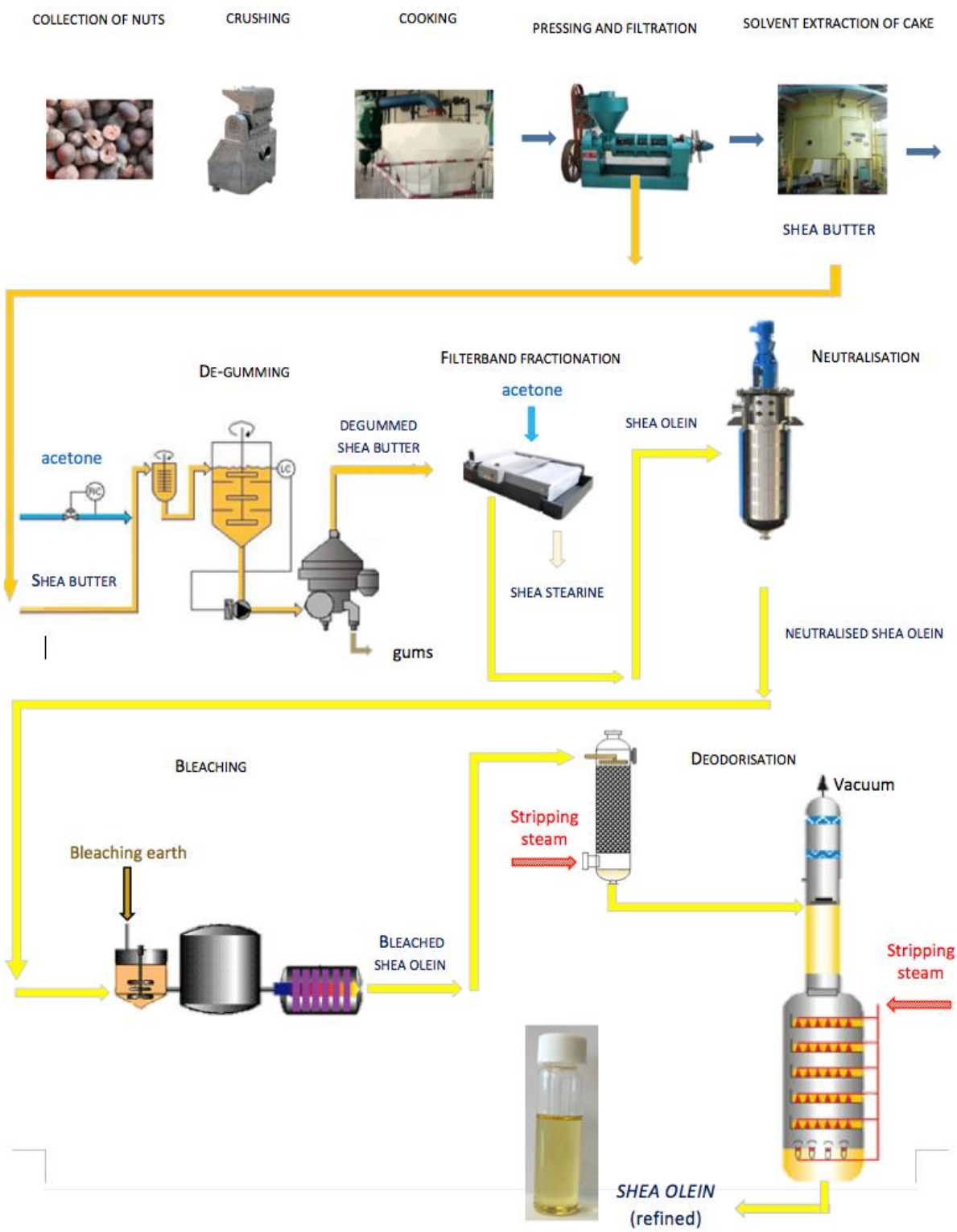
the last major processing step in refining of shea olein and removes compounds that cause undesirable odor, flavor and color. It removes fatty acids and monoglycerides, esters, oxidative reaction products (aldehydes, ketones and peroxides) and many unsaponifiable compounds, such as hydrocarbons (Addaquay, 2004).

Deodorization is by steam distillation under vacuum. The bleached shea olein passes through a de-aerator where the oil is degassed. The oil is heated to the stripping temperature in a pre-heater. The oil then flows to a flash chamber and descends counter-current to the stripping steam in the form of a very thin film and becomes completely deodorized. The fully refined shea olein from the bottom is further filtered and cooled down (Addaquay, 2004).

After deodorization, prior to loading for transport, shea olein is filtered using a food-grade polyester filter to make sure that no particles are present in the oil.

A schematic representation of the production of shea olein is shown in Figure 9. All processing aids and chemicals used in the manufacture of shea olein are of food-grade quality. BUNGE uses GMP certified production processes. Certificates of the location where shea olein is produced can be found in Appendix 2, entitled “BUNGE Loders Croklaan quality certificates”. Certificates are: Lloyd’s Register LRQA Food Safety Certification Scheme 22000, Bureau Veritas ISO 14001:2004, and Halal and Kosher certificates.

Figure 9. Flow Chart of Manufacturing Process for BUNGE's Shea Olein



E. Product Specifications

Food grade specifications for BUNGE's shea olein have been established by BUNGE and are summarized in Table 12.

Shea olein is a viscous pale yellow liquid at room temperature, similar in appearance to refined olive oil.

Table 12. BUNGE Shea Olein Specifications

Parameter	Limit	Method
Color	Max 7	Lovibond color red (5.25" cell) ISO 27608
Odor and taste	Neutral	In house panel
Peroxide value (PV) (mEq/kg)	Max 10	ISO 3960:2001
Free fatty acid as oleic (%)	Max 1.0	ISO 660
Unsaponifiable matter (%)[1]	Max 9	ISO 3596:2000*
Oleic acid (%)	Min 44	ISO 5508:1990
Stearic acid (%)	Max 44	ISO 5508:1990
Trans fatty acids (%)	Max 1.0	ISO 5508:1990
Iron (Fe) (mg/kg)	Max 2.5	AOAC 999.11[2]
Copper (Cu) (mg/kg)	Max 0.1	AgroLab in house method: QMP 504 VW 201[2]
Lead (Pb) (mg/kg)	Max 0.1	AgroLab in house method: QMP 504 VW 201[2]
Arsenic (Ar) (mg/kg)	Max 0.1	AgroLab in house method: QMP 504 VW 201[2]

[1]Because of the method used, the unsaponifiable material measured consists of free, unesterified phytosterols and tocopherols. The phytosterols that exist in the shea olein under consideration are esterified (Earl et al., 2002a, Peers and Agriculture, 1977).
[2]Tested by AgroLab Group

Table 13 shows that three lots of BUNGE's shea olein meet these specifications. Certificates of analyses for three lots of shea olein can be found in Appendix 3.

Table 13. Analysis of Three Production Lots for BUNGE's Shea Olein Meeting Specifications

Parameter	Limits			
Color	Max 7	3.8	4.9	6.6
Odor and taste	Neutral	Neutral	Neutral	Neutral
Peroxide value (mEq/kg)	Max 10	0.1	0.5	0.9
Free fatty acid as oleic (%)	Max 1.0	0.12	0.15	0.12
Unsaponifiable matter (%)	Max 9	6.06	6.15	6.89
Oleic acid (%)	Min 44	53.8	54.2	54.6
Stearic acid (%)	Max 44	29.1	29.1	29.4
Trans fatty acids (%)	Max 1.0	0.2	0.2	0.2
Iron (Fe) (mg/kg)	Max 2.5	<0.1	<0.1	0.4
Copper (Cu) (mg/kg)	Max 0.1	<0.05	<0.05	<0.05
Lead (Pb) (mg/kg)	Max 0.1	<0.05	<0.05	<0.05
Arsenic (Ar) (mg/kg)	Max 0.1	<0.02	<0.02	<0.02

Furthermore, shea olein meets the quality, chemical and physical criteria specified in the CODEX STAN 19-1981 entitled “Standard for edible fats and oils not covered by individual standards” (Codex Alimentarius, 1981b) and quality criteria specified in the CXS 325R-2017 entitled “Regional standard for unrefined shea butter” (Codex Alimentarius, 2017), as shown in Table 14.

Table 14. Analysis of Three Production Batches of Shea Olein Meeting Quality, Chemical and Physical Criteria in the CODEX STAN 19-1981 and in the CXS 325R-2017

Parameter	CODEX STAN 19 1981	CXS 325R 2017			
Quality Criteria					
Color	Off-white	Not listed	Off-white	Off-white	Off-white
Odor and taste	Characteristic	Not listed	Characteristic	Characteristic	Characteristic
Matter volatile at 105°C (% w/w)	Max 0.2	Not listed	0.01	0.02	0.01
Insoluble impurities (% w/w)	Max 0.05	Max 0.09	0.05	0.03	0.01
Soap content (% w/w)	Max 0.005	Not listed	<0.0005	<0.0005	<0.0005
Iron (Fe) (mg/kg)	Max 2.5	Not listed	<0.1	<0.1	0.4
Copper (Cu) (mg/kg)	Max 0.1	Not listed	<0.05	<0.05	<0.05
Acid value (mg KOH/g)	Max 0.6	Not listed	0.28	0.28	0.20
Peroxide value (mEq/kg)	Max 10	Max 10	0.1	0.5	0.9
Water content (% w/w)	Not listed	Max 0.05	0.00	0.01	0.01
Free fatty acids (% w/w)	Not listed	1	0.12	0.15	0.12
Chemical and Physical Criteria					
Relative density at 20°C	Not listed	0.91-0.98	0.9223	0.9225	0.9226
Density at 40°C (g/mL)	Not listed	0.89-0.93	0.9073	0.9074	0.9092
Saponification value (mg KOH/g)	Not listed	160-195	179.3	179.7	182.9
Iodine Value (g I_2/100g)	Not listed	30-75	69.0	69.2	64.2
Unsaponifiable matter (% w/w)	Not listed	1-19	6.04	6.15	6.89
Refractive index at 44 C	Not listed	1.4620-1.4650	1.466	1.466	1.466
Melting point (°C)	Not listed	35-40	30	32	30

Minor differences in the refractive index and in the melting point of BUNGE’s shea olein compared with the quality criteria specified in the CXS 325R-2017 may be due to the fact that specifications of CXS 325R-2017 relate to unrefined shea butter whereas BUNGE’s shea olein is the liquid fraction of fully refined shea butter. A refractive index higher than the upper range indicated in the CXS 325R-2017 is not uncommon and has been reported in the literature (Okullo et al., 2010).

F. Nutritional Profile of BUNGE’s Shea Olein

Shea olein is a vegetable oil, composed of fatty acids primarily in the form of triglycerides with up to 9% of unasaponifiable matter. Shea olein fatty acids are compositionally similar to other vegetable oils with a medium content of saturated fat. An individual consuming shea olein in the diet in place of palm oil or another commonly consumed vegetable oil or fat in the food categories proposed, will therefore not change the total SAFA intake. However, the quality of the SAFA is

improved, since stearic acid, the major saturated fatty acid in shea olein, is neutral on blood total and LDL cholesterol levels compared with shorter-chain fatty acids found in other oils (see below).

The typical nutritional composition of shea olein is given in Table 15**.** Typically shea olein consists of about 54% monounsaturated fatty acids (MUFA), 37% saturated fatty acids (SAFA) and 8% polyunsaturated fatty acids (PUFA).

Table 15. Typical Nutritional Composition of BUNGE's Shea Olein

Nutrition Facts (per 100g)		
	CALCULATED	MEASURED
Calories	830	
Calories from fat	830	
Calories from carbohydrates	0	
Total fatty acids		
Saturated fatty acids		37 g
Monounsaturated fatty acids		54 g
Polyunsaturated fatty acids		8 g
Trans fatty acids		<1 g
Insoluble fiber (g)	0	
Potassium (mg)	0	
Folic acid (mcg)	0	
Cholesterol (mg)	0	
Sodium (mg)	0	
Carbohydrates (polyols) (g)	0	
Dietary fiber (g)	0	
Sugar (g)	0	
Protein (g)	0	
Vitamin A (IU)	0	
Vitamin C (mg)	0	
Calcium (mg)	0	
Iron (mg)	0	

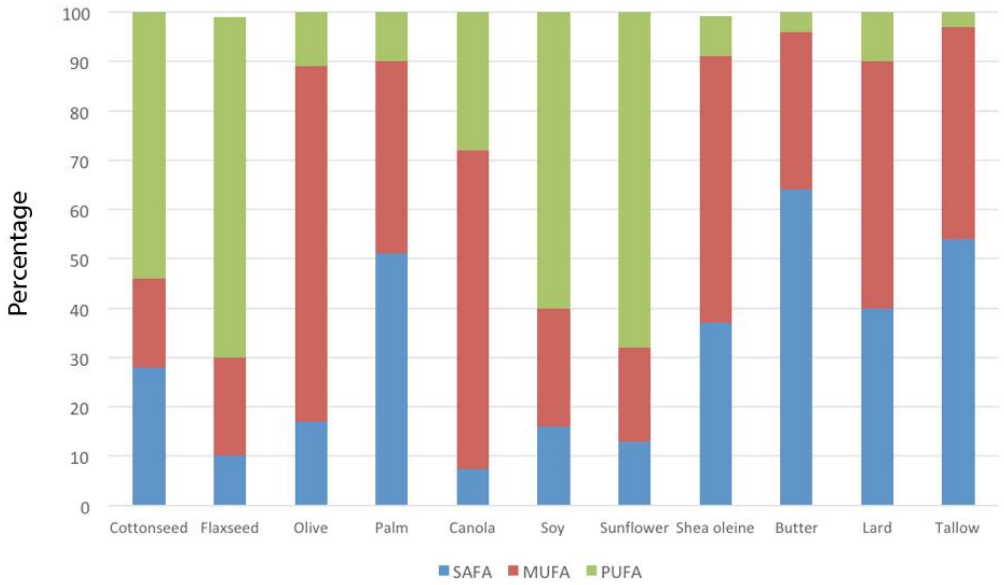
Except for palm oil, compared with other common vegetable oils, shea olein is richer in saturated fatty acids as shown in Figure 10. In fact, it is more comparable to palm oil, cottonseed and lard in terms of SAFA concentrations. Nevertheless, compared with these oils and fats, shea olein contains almost exclusively stearic acid as source of saturated fatty acids instead of palmitic acid.

Data accumulated during the past fifty years indicate that stearic acid (C18:0) is unique among the SAFA. Unlike other common long-chain SAFA (palmitic (C16:0), myristic (C14:0), and lauric (C12:0) acids), stearic acid has neutral effect on blood total and low-density lipoprotein (LDL) cholesterol levels when carbohydrates are used as a reference (Kris-Etherton et al., 2005, Mensink, 2016).

The neutral effect of stearic acid on blood total and LDL cholesterol levels implies that this long-chain SAFA may not increase the risk for cardiovascular disease. For this reason, it may represent

a better option than other fats rich in palmitic, lauric and/or myristic fatty acids and might be a suitable replacer for trans fat for several applications.

Figure 10. Percentages of Common SAFA, MUFA and PUFA Concentrations in Common Edible Oils and Fats (EUFIC, 2014)



Like other oils rich in saturated fat, shea olein has the following advantages:

- it is stable at high cooking temperatures;
- it is suitable for use in products needing solidity and consistency such as crispy and crunchy products with a long shelf life;
- it provides smooth and creamy texture and spreadability in margarine and chocolate spreads; and
- it could serve as blending base oil for preparing specialty fats (Zhang et al., 2017).

G. Physical or Technical Effect

BUNGE's shea olein is intended for use in conventional foods as a replacement of animal fats and vegetable fats rich in palmitic, myristic and lauric fatty acids at levels determined by CGMPs.

The proposed amount of shea olein to be used for each category of food products described in Part 3 is based on the expectation that replacement of the fat in the product with shea olein will not change the overall saturated fat intake.

H. Stability

Edible fats and oils are not highly perishable ingredients because of the absence of water. Nevertheless, fats and oils have minor changes to their sensory characteristics due to rancidity. Two types of rancidity can occur: hydrolytic rancidity and oxidative rancidity.

Hydrolytic rancidity results in the formation of free fatty acids and soaps (salts of free fatty acids). It is caused by either the reaction of lipid and water in the presence of heavy metals or by the action of lipase enzymes. Low levels of free fatty acids are not necessarily objectionable, particularly if they are sixteen or eighteen carbon fatty acids as commonly found in shea olein, since these fatty acids have negligible odor and taste characteristics. The acid value in fat is used to check progress of hydrolytic rancidity during storage by either of two methods, IUPAC 2.201 or ISO 660:1996.

Oxidative rancidity occurs in fats and oils that contain unsaturated fatty acids, as unsaturated fats are less stable than saturated fats. Oxidation produces aldehydes and ketones, which are compounds that are responsible for unfavorable flavors and odors. One of the most widely used tests for oxidative rancidity is the measure of the peroxide value (AOCS cd.8b-90 or IUPAC 2.501 or ISO 3960:2001). It gives a measure of the extent to which an oil sample has undergone primary oxidation. The extent of secondary oxidation may be determined from the p-anisidine test (AOCS Official Method Cd 18-90). The anisidine value (AV) method measures secondary oxidation compounds, primarily 2-alkenals and 2,4-alkadienals, generated due to hydroperoxide decomposition. Since AV represents the content of secondary oxidation products, it is used instead of, or with, peroxide value (PV) to evaluate quality of fats and oils.

Storage trial data for BUNGE's shea olein can be found in Table 16.

Table 16. Storage Trial Data for Two Production Batches of BUNGE's Shea Olein at Ambient Temperatures

Production batch code								
	t = 0	t = 4 months	t = 7 months	t = 9 months	t = 0	t = 4 months	t = 7 months	t 9 months
FFA oil (As oleic)	0.12	0.13	0.12	0.14	0.15	0.13	0.12	0.12
Peroxide Value (PV) (mEq/kg)	0.1	1.5	0.8	3.0	0.5	1.8	0.6	2.0
Anisidine value (AV)	Not measured	2.4	3.7	2.3	Not measured	3.9	1.0	2.0
Color (R5¼")[1]	3.8	3.7	3.9	3.6	4.9	4.9	4.9	5.0
Color (Y5¼")[2]	44	43	45	42	56	56	56	62

[1]Color red measured in 5 ¼ inch cuvette
[2]Color yellow measured in 5 ¼ inch cuvette

Storage data for shea olein show that no relevant oxidative changes are seen based on AV, which measures the secondary stage of oxidation, in shea olein after nine months storage at ambient temperature and that samples are well within the specifications.

PART 3. DIETARY EXPOSURE

A. Estimate of Dietary Exposure to the Notified Substance

The proposed shea olein use level per product category is given in Table 17. A summary of the proposed food uses based on Reference Amounts Customarily Consumed (RACC) is given in Table 18.

Table 17. Proposed Food Use of Shea Olein

Food category	Proposed food use[1]	Shea Olein typical use level (per 100g product)	Serving size
Baked goods and baking mixes	Biscuits, croissants, bagels	8	55g
	Bread rolls	4	50g
	Cakes (light and medium weight)	7	55-80g
	Coffee cakes, crumb cakes, doughnuts, Danish sweet rolls, brownies	14	55g
	Cookies	23	30g
	Waffles	6	85g
Breakfast cereals	Any variety	3	15-55g
Condiments and relishes	Sauces	4	60g
Confections and frosting	Candy and flavored frosting	29	2 tbsp (30-35g)
	Baking chocolate	60	15g
Fats and oils	Margarines and shortening	50	15g
	Mayonnaise, sandwich spreads	16	15g
	Salad dressings	12	15g
Frozen dairy desserts and mixes	Ice Cream (surrogate for frozen desserts)	14	85g
Gravies and sauces	Minor condiments and sauces	4	60g
Nuts and nut products[2]	Nut and seed butters, pastes and creams	4	60g
Snack foods	All varieties	14	30g
Soft candy	Candy bars	35	40-53g
	Fudge	17	22g
Soups and soup mixes[3]	All varieties	1.5	245 g
Sweet sauces	Chocolate topping	5	2 tbsp (30-35g)

[1]May be used in a standardized food only if it is permitted by the applicable standard of identity
[2]As baking medium
[3]As consumed

Table 18. Summary of the Individual Proposed Food Uses and Use Levels for Shea Olein in the U.S.

Food Category (21 CFR 170.3)	Proposed Food Uses	RACC1 (g or mL)	Shea Olein Use Levels (%)
Baked goods and baking mixes	Biscuits, croissants, bagels	55 g	8
	Bread rolls	50 g	4
	Cakes (light and medium weight)	55-80 g	7
	Coffee cakes, crumb cakes, doughnuts, Danish sweet rolls, brownies	55 g	14
	Cookies	30 g	23
	Waffles	85 g	6
Breakfast cereals	Breakfast cereals	15-55 g	3
Condiments and relishes; Gravies and sauces	Minor condiments and sauces	30-60 g	4
Confections and frostings	Candy and flavored frostings	30 mL	29
	Chocolate topping sauce	30 mL	5
Fats and oils	Margarines, shortenings	15 mL	50
	Mayonnaise, sandwich spreads	15 g	16
	Salad dressings	30 g	12
Desserts	Frozen desserts	160 mL	14
Nuts and nut products	Nut and seed butters, paste and creams	30 mL	4
Snack foods	Snack foods	30 g	14
Soft candy	Candy bars	30 g	35
	Baking chocolate	15 g	60
	Fudge	30 g	17
Soups and soup mixes	Soup and soup mixes	245 g, as consumed	1.5

CFR = Code of Federal Regulations; RACC = Reference Amounts Customarily Consumed per Eating Occasion
[1]RACC based on values established in 21 CFR §101.12. When a range of values is reported for a proposed food-use, particular foods within that food-use may differ with respect to their RACC. RACCs reported with household measure were converted to g or mL based on 21 CFR §101.9. RACCs are included in this table for reference. However, for the exposure assessment, the estimated intakes of shea olein were derived based on the use levels expressed on a % w/w basis.

1. Methodology

Shea olein is proposed for use in the United States in foods such as baked goods and baking mixes, breakfast cereals, condiments and relishes, gravies and sauces, confections and frostings, fats and oils, desserts, nuts and nut products, snack foods, soft candy, and soup and soup mixes.

Estimates for the intake of shea olein were based on the proposed food uses and use levels for this ingredient in conjunction with food consumption data included in the U.S. National Center for Health Statistics (NCHS)'s National Health and Nutrition Examination Surveys (NHANES) 2013-2014. Calculations for the mean and 90th percentile *per capita* and consumer-only intakes were performed for all proposed food uses of shea olein, and the percentage of consumers were determined. Similar calculations were used to estimate the intake of shea olein resulting from each individual proposed food-use, including the calculations of percent consumers. In both

cases, the per person and per kilogram body weight intakes were reported for the following population groups:

- Infants and young children, up to and including 2 years;
- Children, ages 3 to 11 years;
- Female teenagers, ages 12 to 19 years;
- Male teenagers, ages 12 to 19 years;
- Female adults, ages 20 years and up;
- Male adults, ages 20 years and up; and
- Total population (all ages and gender groups combined).

For the intake assessment, consumption data from individual dietary records, detailing food items ingested by each survey participant, were collated by computer and used to generate estimates for the intake of shea olein by the U.S. population[2]. Estimates for the daily intake of shea olein represent projected 2-day averages for each individual from Day 1 and Day 2 of NHANES 2013-2014; these average amounts comprised the distribution from which mean and percentile intake estimates were determined. Mean and percentile estimates were generated incorporating survey weights in order to provide representative intakes for the entire U.S. population. "*Per capita*" intake refers to the estimated intake of shea olein averaged over all individuals surveyed, regardless of whether they consumed food products in which shea olein is proposed for use, and therefore includes individuals with "zero" intakes (*i.e*., those who reported no intake of food products containing shea olein during the 2 survey days). "Consumer-only" intake refers to the estimated intake of shea olein by those individuals who reported consuming food products in which the use of shea olein is currently under consideration. Individuals were considered "consumers" if they reported consumption of 1 or more food products in which shea olein is proposed for use on either Day 1 or Day 2 of the survey.

Mean and 90th percentile intake estimates based on sample sizes of less than 30 and 80, respectively, may not be considered statistically reliable due to the limited sampling size (CDC, 2013). Since all samples sizes were greater than 80, the results for shea olein are statistically reliable.

[2] Statistical analysis and data management were conducted using subscriber-based DaDiet Software (Dazult Ltd., 2018). DaDiet Software is a web-based software tool that allows accurate estimate of exposure to nutrients and to substances added to foods, including contaminants, food additives and novel ingredients. The main input components are concentration (use-level) data and food consumption data. Data sets are combined in the software to provide accurate and efficient exposure assessments.

2. Estimated Daily Intake of Shea Olein and Constituents from All Proposed Food Uses in the U.S.

a. Estimates of Shea Olein Daily Intake

Estimates for the total daily intakes of shea olein from proposed food uses are provided in Table 19 (in g/person/day) and Table 20 (in mg/kg body weight (bw)/day). The percentage of consumers was high among all age groups evaluated in the current intake assessment. More than 72.8% of the population groups consisted of consumers of food products in which shea olein is proposed for use; this figure was higher when only individuals over 3 years were considered (>97.7%). Children had the greatest proportion of consumers at 99.9%. The consumer-only estimates are more relevant to risk assessments as they represent exposures in the target population; consequently, only the consumer-only intake results are discussed in detail herein.

Among the total consumer-only population (all ages), the mean and 90th percentile intakes of shea olein were determined to be 15.24 and 30.33 g/person/day, respectively. Of the individual population groups, male adults were determined to have the greatest mean and 90th percentile consumer-only intakes of shea olein on an absolute basis, at 17.07 and 34.27 g/person/day, respectively, while infants had the lowest mean and 90th percentile consumer-only intakes of 7.01 and 14.56 g/person/day, respectively.

Table 19. Summary of the Estimated Daily Intake of Shea Olein from Proposed Food Uses in the U.S. by Population Group (2013-2014 NHANES Data)

Population Group	Age Group (Years)	*Per Capita* Intake (g/day)		Consumer Only Intake (g/day)			
		Mean	90th Percentile	%	n	Mean	90th Percentile
Infants & Young Children	0 to 2	5.10	13.08	72.8	432	7.01	14.56
Children	3 to 11	15.42	29.00	99.9	1,282	15.44	29.00
Female Teenagers	12 to 19	13.95	28.59	99.5	572	14.01	28.59
Male Teenagers	12 to 19	16.31	30.45	98.7	550	16.53	30.45
Female Adults	20 and up	14.02	28.90	99.0	2,352	14.17	28.92
Male Adults	20 and up	16.67	34.21	97.7	2,043	17.07	34.27
Total Population	**All Ages**	**14.87**	**30.10**	**97.5**	**7,231**	**15.24**	**30.33**

On a body weight basis, the total consumer-only population (all ages) mean and 90th percentile intakes of shea olein were determined to be 0.26 and 0.56 g/kg body weight/day, respectively. Among the individual population groups, children were identified as having the highest mean and 90th percentile consumer-only intakes of any population group, of 0.58 and 1.18 g/kg body weight/day, respectively. Male and female adults had the lowest mean and 90th percentile consumer-only intakes of 0.20 and 0.40 g/kg body weight/day, respectively (Table 20).

Table 20. Summary of the Estimated Daily Per Kilogram Body Weight Intake of Shea Olein from Proposed Food Uses in the U.S. by Population Group (2013-2014 NHANES Data)

Population Group	Age Group (Years)	*Per Capita* Intake (g/kg bw/day)		Consumer Only Intake (g/kg bw/day)			
		Mean	90th Percentile	%	n	Mean	90th Percentile
Infants & Young Children	0 to 2	0.41	0.98	72.6	430	0.56	1.11
Children	3 to 11	0.58	1.18	100	1,274	0.58	1.18
Female Teenagers	12 to 19	0.23	0.53	99.6	563	0.23	0.53
Male Teenagers	12 to 19	0.25	0.52	98.7	548	0.25	0.52
Female Adults	20 and up	0.19	0.40	99.0	2,339	0.20	0.40
Male Adults	20 and up	0.20	0.40	97.6	2034	0.20	0.40
Total Population	**All Ages**	**0.25**	**0.55**	**97.5**	**7188**	**0.26**	**0.56**

The major contributors to shea olein intake have been estimated to be snack foods, ice-cream and cookies, as shown in Table 21.

Table 21. Top Contributors to Mean Population Intake of Shea Olein

Food Group	% Contribution to Mean Population Intakes
Snack foods	17.5
Frozen desserts (based on ice cream intake)	17.0
Cookies	16.2
Coffee cakes, crumb cakes, doughnuts, Danish sweet rolls, brownies	7.2
Breakfast cereals	5.9
Salad dressings	5.2

b. Intake Considerations

Despite the fact that there is the wish to use shea olein in a broad range of applications, it is extremely unlikely that any consumer ever will be exposed to maximum amounts of shea olein described above. This is because of agronomic and economic reasons.

Shea olein is a vegetable fat extracted from the kernel of the fruit of the shea tree (*Vitellaria paradoxa*). The tree is the main indigenous oil-producing wild plant growing in Africa and occasionally in plantations. The yield is maximum 17.4 kg of fresh fruit per tree (Aleza et al., 2018). Even by optimizing plantation practices and by planting more shea trees, total potential production of sheanut is only 4.04 metric tons (Lovett, 2013). In contrast, a palm oil tree can produce over 400 kg fruits per tree per year (Palm Plantations of Australia, 2018). Currently, palm oil production is 72,259 metric tons per year (Index Mundi, 2018). Therefore, there will never be enough shea fruits to provide even 6% of oil provided by palm fruits.

Against the backdrop of the multi-million ton vegetable oils and fats industry, shea butter production currently represents less than 0.1% of the total edible oils market (Global Shea Alliance, 2018). According to the Global Shea Alliance (Lovett, 2013), the estimated total export of shea butter is currently around 118,000 metric tons per year, with a total estimated shea export, including the contribution of the export of shea nuts, of 350,00 metric tons. In comparison, palm oil production is around 60,000,000 metric tons per year, as shown in Figure 11 and Figure 12. Since fractionation of shea butter produces 33-40% shea stearine ("sheanut oil") and 60-67%% shea olein, the total available amount of shea olein in the market is not expected to be more than 87,750 metric tons.

Figure 11. World Production of the Major Vegetable Oils and Fats for 2014 (x1000 metric tons) (Statista.com, 2018)

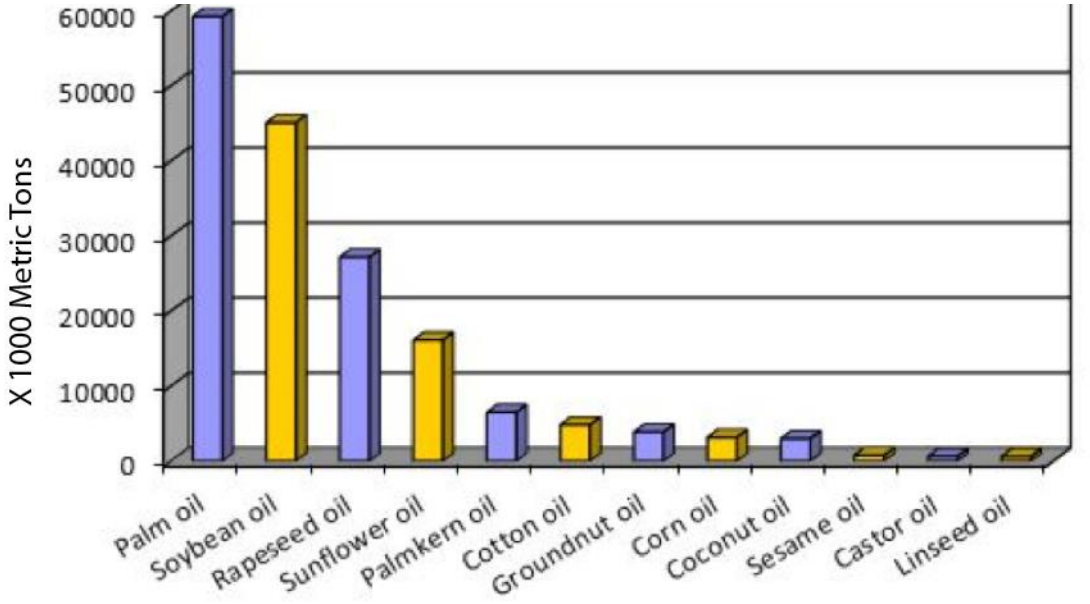
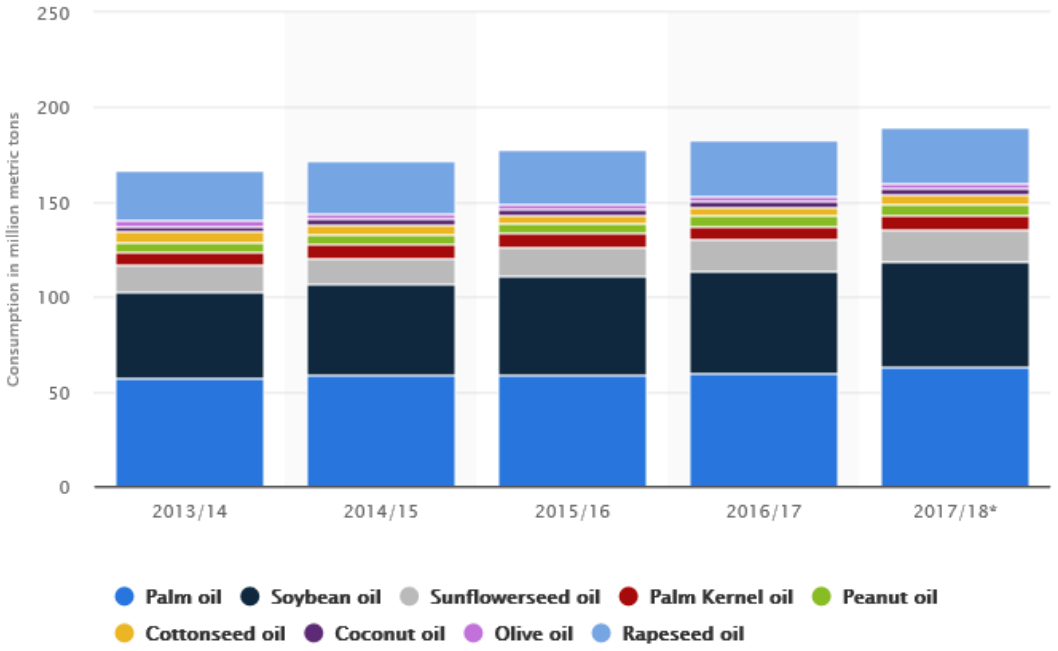


Figure 12. Consumption of Vegetable Oils Worldwide from 2013/2014 to 2017/2018 by Oil Type (in million metric tons) (Statista.com, 2018)



Even if all shea olein available were to be eaten in the U.S., in view of the USA total population (~325,000,000), that would be on average 0.74 g of shea olein per person per day. That would even be an overestimation of average consumption per person per day since a good proportion of shea butter is also used in cosmetics.

c. Estimates of Phytosterol Daily Intake

The consumption of shea olein from a high-intake scenario using the NHANES approach is 35 g/day. With 8% sterols, this is 2.8 g sterols/day, equivalent to 40 mg/kg bw for a 70 kg person.

As explained above, the intake of shea olein estimated using NHANES data will almost certainly never occur because there is not enough shea produced in the world to fill all the proposed uses. A more realistic estimate of shea sterol intake is provided by production data from BUNGE. If the mean intake of shea olein is conservatively estimated at 0.74 g/person/day, and a high intake is estimated to be three times that, then a high intake yields an estimate of 2.2 g/person per day (31.7 mg/kg bw/day) for shea olein and 0.2 g/person/day (2.9 mg/kg bw per day) of the sterol fraction as a more reasonable estimate of maximum exposure.

B. Estimated Dietary Exposure to Any Other Substance That is Expected to be Formed In or On Food

Edible oils may oxidize and form primary oxidation products, such as lipid hydroperoxides, which are relatively stable at room temperature . In the presence of metals or at high temperature (such as baking) they are readily decomposed to alkoxy radicals and then form aldehydes, ketones, acids, esters, alcohols, and short-chain hydrocarbons (Choe et al., 2006). Phytosterols and their fatty acid esters are quite stable compounds and undergo only limited degradation during oil processing (Cantrill, 2008). There is no reason to believe that shea olein is any less stable than any other edible oil under conditions of use.

C. Dietary Exposure to Contaminants or Byproducts

Potential contaminants of BUNGE's shea olein include solvent residue (hexane and acetone), heavy metals, mycotoxins, polychlorinated biphenyls, environmental persistent organic pollutants (POPs), polycyclic aromatic hydrocarbons (PAHs) and pesticides. In order to minimize potential exposure to contaminants, specifications set by BUNGE are in line with those of Codex Alimentarius and of EU Legislation, (EC) No 1881/2006[3]. Contaminants analyses of three batches of shea olein carried out in an independent laboratory show that BUNGE's shea olein is within the contaminants specifications and is appropriate for food use. The contaminants specifications, as given in Appendix 4, apply to the shea olein commercialized by BUNGE and are tested biannually.

As described in Part 2H, edible fats and oils have insufficient water present for the growth of microorganisms. Testing of three samples of shea olein for the presence of microbiological contamination, as shown in Table 22, also demonstrate that the oil has no contamination from microorganisms and is appropriate for food use.

Table 22. Microbiology Analysis of Three Production Batches of BUNGE's Shea Olein

				Method
Salmonella (Vidas) in 25g	absent	absent	absent	ISO 6579
Escherichia coli (CFU/g)	<1. (LOD)	<1.0 (LOD)	<1.0 (LOD)	DIN ISO 16649-2 (KI)
Aerobic mesophilic bacteria (CFU/g)	<100 (LOD)	<100 (LOD)	<100 (LOD)	VDLUFA III, 28.1.2 (KI)
Molds (CFU/)g	<10 (LOD)	<10 (LOD)	<10 (LOD)	DIN ISO 21527-2 (KI)
Yeasts (CFU/g)	<100 (LOD)	<100 (LOD)	<100 (LOD)	VDLUFA III, 28.1.2 (KI)
Enterobacteriacea (CFU/g)	<10 (LOD)	<10 (LOD)	<10 (LOD)	DIN ISO 21528-2 (KI)

CFU: colony forming units; DIN: Deutsches Institut für Normung e. V. (German institute for Standardisation; ISO: International Standards Organization; LOD: limit of detection; VDLUFA:Verband Deutscher Landwirtschaftlicher Untersuchungs- und Forschungsanstalten (Association of the German Agricultural Bureaus of Investigation and Research)

[3] Available at https://eur-lex.europa.eu/legal-content/EN/ALL/?uri=celex%3A32006R1881

PART 4. SELF-LIMITING LEVELS OF USE

Higher amounts of shea than the typical amounts indicated in Table 17 would affect the rheological properties of the final product. As a result, it is consequently not recommended/feasible in several food applications.

For applications such as mayonnaise or salad dressings, the limiting factor is taste. Shea olein has a characteristic taste which does not allow use when there is a need for oils and fats with neutral taste. Consequently, it is likely that in mayonnaise and salad dressings the amount of shea olein used will be even lower than the potential typical value given.

Finally, following the WHO guidelines (WHO, 2018), manufacturers are asked to reformulate their products by replacing, when possible, saturated fat with monounsaturated fat and polyunsaturated fat, independent of the type of saturated fat. Consequently, in all applications where shea olein would not pose any taste or technological issue, the limiting factor is going to be the typical total saturated fat of the product. Manufacturers are unlikely to replace an existing fat blend with another with a higher SAFA content.

PART 5. EXPERIENCE BASED ON COMMON USE IN FOOD BEFORE 1958

In 1984, FDA affirmed sheanut oil as GRAS in response to a petition filed by Fuji Oil Co., Ltd. FDA noted that the petitioner provided several published articles that document that sheanut oil has a history of common use in food prior to 1958. Sheanut oil has been used in Africa for food purposes since the 1800's (Murray, 1933) and in Europe as a cooking oil, a cocoa butter substitute, and for making margarine (Hefter, 1908, Jamieson, 1943, Schwitzer, 1956, Commonwealth Economic Committee, 1952, Anderson and Williams, 1965). It is likely that shea olein or most of its constituents were also consumed prior to 1958.

PART 6. NARRATIVE

A. Regulatory History

1. U.S. Regulatory History

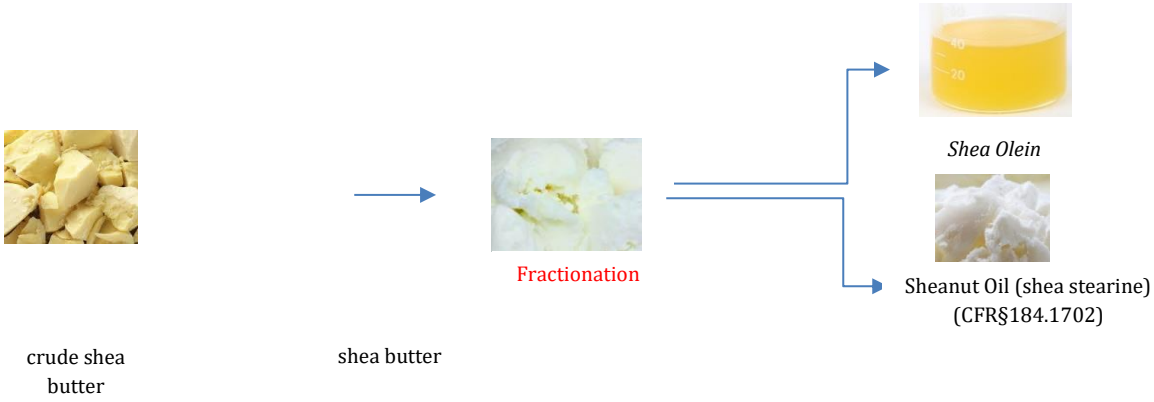
According to 21CFR§184.1702, sheanut oil is affirmed as GRAS for use in confections and frostings, coatings of soft candy, sweet sauces and toppings, at levels not to exceed CGMPs.

It is important to highlight that the approved material is actually the stearine fraction of shea butter. The Generally Recognized as Safe Petition (GRASP) 8G0343[4] uses the term "Refined Sheanut Oil" to describe the product of fractionation and refining of crude shea butter; however, a more

[4] See Federal Register, 63(101) May 27, 1998 (available at https://www.gpo.gov/fdsys/pkg/FR-1998-05-27/pdf/98-13917.pdf)

appropriate name for this product would have been refined shea stearine. Despite the fact that for labeling purposes there is no distinction between a fractionated or non-fractionated oil, there are differences in the fatty acid compositions of shea stearine (richer in saturated fatty acids) and shea olein (richer in oleic acid). Furthermore, shea olein contains a higher amount of unsaponifiable matter (up to 9%) as compared to shea stearine (<1.5%).

Figure 13. Fractionation of Shea Butter and Relative Fractions



A search of the FDA GRAS Notices inventory for "shea" yielded no returns. Other edible plant-based oils (including further refined oils) have received a "no questions" response from the FDA. These are listed in Table 23.

Table 23. GRAS Notice Inventory Search Results

Material	GRN #/ Closure Date	Intended Use	Use Rate	Company	FDA No Questions Response
Gamma Linolenic Acid Safflower	GRN 652/December 16, 2016	As an ingredient in nutritional beverages, medical foods, salad dressings, mayonnaise and yogurt	0.05 to 4 g of gamma linolenic acid per serving.	Arcadia Biosciences (2016)	FDA (2016b)
Camelina Oil	GRN 642/October 12, 2016	As a replacement for other edible oils in baked goods and baking mixes, beverages and beverage bases, breakfast cereals, dairy replacements, fats and oils, grain products and pasta, milk and milk products, processed fruits and fruit juices, processed vegetables and vegetable juices, snack foods, soft candy, and soup and soup mixes	3 g per serving	CamStar LLC. (2016)	FDA (2016a)
Sacha Inchi Oil	GRN 506/March 26, 2014	As an ingredient in baked goods, cereals, condiments, soft candy, fats and oils, dressings, mayonnaise, margarines, gravies and sauces, nuts and nut products, and snack foods	100% in salad oil, up to 17% in other applications	Agroindustries Amasonicas et al. (2014)	FDA (2014b)
Refined Buglossoides Oil	GRN 486/December	As a source of fatty acids in baked goods, cereals, grains, cheeses, dairy product	375 mg stearidonic acid per serving	Technology Crops	FDA (2014a)

Material	GRN #/ Closure Date	Intended Use	Use Rate	Company	FDA No Questions Response
	23, 2014	analogs, fats and oils, fish products, frozen dairy desserts, grain products and pastas, gravies and sauces, meat products, milk products, nut and nut products, poultry products, process fruit juices, processed vegetable products, puddings and fillings, snack foods, soft candy, soup and soup mixes	(1250 – 2500 mg oil)	International (2013)	
Low Saturated, High Oleic, Low Linoleic Soybean Oil	GRN 306/April 7, 2010	For frying and spraying applications in a variety of food products including meat, poultry, and fish dishes (commercial and restaurant), fried eggs (commercial and restaurant), French fries, potato chips and puffs, creamy salad dressings, salty snacks, and grain mixture dishes	100% replacement in oil blends except for crackers (50%)	Monsanto Company (2009)	FDA (2010a)
Korean Pine Nut Oil	GRN 332/September 24, 2010	As a replacement for other in baked goods and baking mixes, beverages and beverage bases, breakfast cereals, dairy product analogs, fats and oils, grain products and pasta, milk and milk products, nuts and nut products, processed fruit and fruit juices, processed vegetables and vegetable juices, snack foods, soft candy, and soups and soup mixes; does not include any meat or meat-containing products	3 g/serving	Lipid Nutrition (2010)	FDA (2010b)
Low Linoleic Acid Flaxseed Oil	GRN 256/Jan 16, 2009	Use as a source of fatty acids in baked goods, alcoholic and non- alcoholic beverages, cereals, cheeses, chewing gums, coffee and tea, condiments, confections and frostings, dairy product analogs, egg products, fats and oils, fish products, frozen dairy desserts, fruit and water ices,, gelatins, puddings and fillings, grain products and pastas, gravies and sauces, hard candy, jams and jellies, meat products, milk products, nut and nut products, poultry products, plant protein products, poultry products, processed fruits and juices, processed vegetables and vegetable products, snack foods, soft candy, soup and soup mixes, sugar, sugar substitutes, sweet sauces and syrups	0.86-17% depending on application up to 36 g/day	Polar Foods Inc. (2008)	FDA (2009)
Solin Oil (low linolenic acid flaxseed oil or low linolenic acid linseed oil)	GRN 2/May 27, 1998	Use as a general purpose cooking, frying, and salad oil; and as an ingredient in margarines, shortenings, and other food products	Substitute for other vegetable oils	United Grain Growers LTD (1998)	FDA (1998)

2. Canadian Regulatory History

A search of the Health Canada website for the term “shea olein” or “sheanut oil” yielded no results. Health Canada lists shea butter and shea butter extract as approved herbal substances for topical use (Health Canada, 2018a, Health Canada, 2018b).

3. European Regulatory History

According to Directive 2000/36/EC[5], shea is one of the vegetable fats derived from six species currently allowed as an ingredient in non-cocoa butter fats. The EU allows the use of cocoa butter alternatives to a maximum of 5% of the chocolate product.

4. Chinese Regulatory History

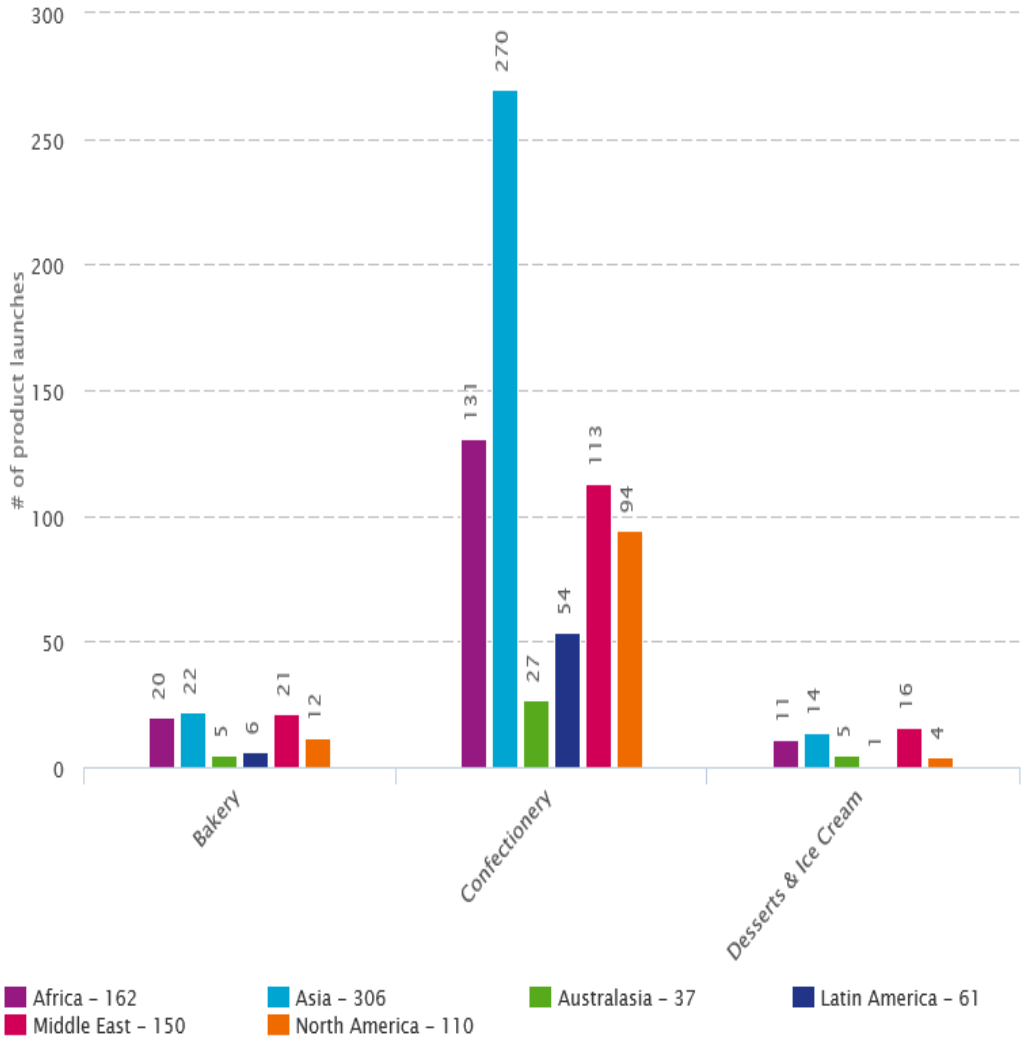
On May 31, 2017, the National Health and Family Planning Commission of China released the announcement that “sheanut oil”, i.e. shea butter, shea stearine and shea olein were approved for food use. Specifically, any shea fat material with ≥ 25% oleic acid and ≥ 25% stearic acid was approved. Although they were being used in cosmetics in China, shea butter, shea stearine and shea olein were previously not allowed in food. According to the latest announcement, shea butter, shea stearine and shea olein are listed as new food raw materials and could be used in chocolate, candy, ice-cream, bakery products, frying oil, excluding infant food (Chemlinked, 2017). The document entitled “Chinese Approval Document Sheanut Oil” is translated from Chinese in Appendix 5.

5. Other Regulatory History

Figure 14 shows the products launched in the world between January 2013 and December 2015 containing shea butter (and/or shea olein). The graph shows that shea butter (and/or shea olein) is well represented in the bakery, confectionary and desserts and ice cream food categories in several parts of the world.[6]

[5] https://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2000:197:0019:0025:EN:PDF
[6] Subscriber search done at https://www.innovadatabase.com

Figure 14. Products Launched Globally Between January 2013 and December 2015 Containing Shea Butter (and/or Shea Olein) as an Ingredient[6]



B. Safety Discussion for Shea Olein

Shea olein, the subject of this safety evaluation, is a vegetable oil composed of fatty acids primarily in the form of triglycerides with up to 9% of unsaponifiable matter.

Shea olein is compositionally similar to other vegetable oils with a medium content (45-55%) of saturated fat. A person consuming shea olein in the diet in place of palm oil or another commonly consumed vegetable oil or fat in the food categories proposed will therefore not change the total SAFA intake. However, the quality of the SAFA will be improved since shea olein contains mainly stearic acid, which is neutral on blood total and LDL cholesterol levels.

The safety of shea olein was evaluated by the following:

- a review of the safety of constituents of shea olein, namely the main triglycerides;

- studies addressing the safety of the unsaponifiable matter (phytosterols) of shea olein;
- a review of pre-clinical and clinical trials in which the test article was shea olein produced by BUNGE;
- a review of the safety of shea derivatives, including shea olein, carried out by Cosmetic Ingredient Review (CIR) in 2016 for the use of the shea derivatives in the cosmetic industry;
- the current and historical use of shea butter; and
- the allergenicity of shea butter.

1. Current and Historical Uses of Shea Olein for Human Food Use

In the petition to FDA for the GRAS status of sheanut oil (Fuji Oil Company Ltd, GRASP 8G0343), it is reported that shea butter has been used extensively in Africa as cooking oil since at least the 19th century (Fuji Oil Co., 1988). For more recent consumption estimates, Lovett (2013) estimates 40% of African people living in the shea tree growing zone (approx. 42.8 million people) consume crude shea butter on a daily basis for an equivalent of about 21 g of crude shea butter per day (approximately 12.6-14.7 g of shea olein).

2. Absorption, Distribution, Metabolism and Excretion (ADME) Studies of Shea Olein and its Constituents

The ADME of triglycerides, which make up approximately 90% of shea olein, is well understood and not relevant to discuss in a safety analysis.

a. ADME of Shea Olein Unsaponifiables

In an oral absorption and excretion study, groups of male Wistar rats were fed shea olein in a semisynthetic diet. The shea olein was produced by BUNGE. In a low-dose experiment, groups of 24 rats received control feed, feed containing 0.5% shea olein or feed containing 5% shea olein for one week, with control feed administered to all rats the week prior and the week following the exposure week. In a high-dose experiment, 2 groups of 15 male and 15 female rats received either 10% or 20% shea olein in the feed for 3 weeks. Shea olein contained approximately 8% unsaponifiable matter (phytosterols) (Earl et al., 2002b).

In the first experiment, feces were collected and pooled weekly for each treatment group throughout weeks 2 and 3. In the second experiment, feces were collected and pooled for each treatment group in week 3 only. The dried fecal matter of the rats was then analyzed with thin-layer and gas-liquid chromatography for fecal lipid, total sterol, differential sterol levels, and 4,4-dimethylsterols (4,4-DMS), the main components of the unsaponifiable matter of shea olein. Excretion of 4,4-DMS increased with the consumption of shea olein. Apparent absorption was

estimated from the disappearance of 4,4-DMS. The majority of the 4,4-DMS was excreted unchanged (Earl et al., 2002b).

Earl et al. (2002b) also examined the oral absorption and excretion of shea olein in four men. On day 3 of an 8-day study, the subjects consumed a single 25 g portion (approximately 0.4 g/kg of shea olein; 2 g of unsaponifiable matter or 28 mg/kg) of shea olein in mayonnaise. No other vegetable fats were consumed during the course of the study.

Feces were collected on days 3 to 8 inclusively, freeze-dried and weighed. The dried fecal matter was analyzed in the manner described above. Excretion of 4,4-DMS increased with the consumption of shea olein, with a marked increase from baseline on days 4 and 5 and a return to approximate baseline on day 8. Absorption of 4,4-DMS was estimated to be 13% to 49%. The majority of the 4,4-DMS was excreted unchanged.

3. Safety of Metabolites of Shea Olein (Fatty Acids and Monoglycerides)

During digestion, shea olein releases mainly oleic acid, stearic acid, linoleic acid, palmitic acid and 2-monoglycerides. These are naturally found as part of glycerides, lipids, lipoproteins, and membranes of both plants and animals. Moreover, they are the same fatty acids, monoglycerides and glycerol components as are found in a broad range of edible fats, oils, and emulsifiers that are GRAS. They are consequently part of the everyday normal child and adult diet.

Evaluations of the safety and the roles of oleic, stearic, linoleic, palmitic acids, and vegetable oils in human nutrition are extensive and ongoing.

a. Acute Oral Toxicity Studies

The acute oral toxicity of oleic, palmitic and stearic acids was tested in rats (sex not reported) (CIR, 1987). Doses of up to 21.5 mL/kg bw (equivalent to 19.1 g/kg bw) of oleic acid and up to 10 g/kg bw of palmitic acid by gavage to albino rats resulted in no deaths and no significant gross lesions at necropsy. One rat died when a dose of 25% (w/v) stearic acid in corn oil was administered. At necropsy of the rat, congested lungs and kidneys and advanced autolytic changes were observed. No significant gross lesions were found at necropsy of 2 rats of the 0.464 and 4.64 g/kg bw/day triple-pressed stearic acid (40-47% stearic acid/40-60% palmitic acid fat) dose group. Transient signs of toxicity were observed in rats at doses of 10 g/kg 25 % stearic acid in corn oil and 4.64 and 10.0 g/kg bw/day triple-pressed stearic acid. Signs of toxicity included slight depression, depressed righting and placement reflexes, oily and unkempt fur, mucoid diarrhea, excessive salivation, and sero-sanguineous discharge from the muzzle. A summary of the chemical safety information of palmitic and stearic acid can be found in the ECHA website (European Chemicals Authority, 2015a, European Chemicals Authority, 2015b). Additional safety studies were carried out in the 1970s and 1980s mainly with cosmetic formulations. In 1987, CIR published a summary of the studies (CIR, 1987) and results are given in Appendix 6 entitled “Acute oral toxicity studies for oleic, palmitic and stearic acids”.

b. Subacute Toxicity Studies

CIR (1987) also reported that feeding of 5% oleic acid or 50% stearic acid diets to chicks for 4 weeks had no adverse effects. Rats fed diets containing 4.6 g/kg bw/day palmitic acid for 6 weeks developed hyperlipemia. A diet containing 50% stearic acid fed to rats for 8 weeks resulted in microscopic “foreign body-type reaction” in adipose tissue. Feeding 15% oleic acid diets to rats for 10-16 weeks had no adverse effects on growth or general health. Of 4 female weanling rats fed the diet for 16 weeks, all were able to become pregnant; however, 2 died at parturition, a litter was eaten at birth, and the remaining litter died within 3 days of birth. Mating of 7 adult female rats fed the diet for 16 weeks resulted in production of 52 young, 44 of which survived 1 week and 11 of which survived 3 weeks. Mammary development was retarded, and a few rats had ovarian cysts. No lesions were found in other organs (CIR, 1987).

4. Toxicology of BUNGE’s Shea Olein

a. Genotoxicity Studies

Bacterial Reverse Mutation Test

An independent laboratory (Triskelion B.V.) carried out an Ames test with BUNGE’s shea olein that adhered to Organization for Economic Co-operation and Development (OECD) 471 guidelines. In this unpublished study (van der Wijngaard, 2018), BUNGE’s shea olein was examined for possible mutagenic activity in the bacterial reverse mutation test using the histidine-requiring *Salmonella typhimurium* strains TA 1535, TA 1537, TA 98, TA 100 and the tryptophan-requiring *Escherichia coli* strain WP2 uvrA, in the absence and presence of a liver fraction of Aroclor 1254-induced rats for metabolic activation (S9-mix). A single test was performed. All strains, both in the absence and presence of S9-mix, were exposed to five concentrations of BUNGE’s shea olein, ranging from 62 to 5000 µg/plate. A stock solution of the test substance of 50 mg/mL in acetone was prepared, resulting in a slightly turbid, homogeneous solution. Negative controls (solvent) and positive controls were run simultaneously. An additional negative control (milli-Q water) was tested to demonstrate that no deleterious or mutagenic effects were induced by the solvent (acetone).

No toxicity was observed in any strain, which was evidenced by absence of a clearing of the background lawn of bacterial growth compared to the negative controls, absence of a decrease in the mean number of revertants and an absence of pinpoint colonies. Precipitation of the test substance was observed in the final treatment mix at and above 185 µg/plate. Precipitation was observed by microscope at and above 62 µg/plate and at and above 1667 µg/plates by naked eye. The test substance did not induce a more than 2-fold and/or dose related increase in the mean number of revertant colonies compared with the background spontaneous reversion rate observed with the negative control with strains TA 1535, TA 1537, TA 98, TA 100 and WP2 uvrA, in both the absence and presence of S9-mix.

It was concluded that the results obtained in *Salmonella typhimurium* strains TA 1535, TA 1537, TA 98 and TA 100, and in *Escherichia coli* strain WP2 uvrA, in both the absence and presence of

the S9-mix, show that the test substance, shea olein, is not mutagenic under the conditions used in this study (van der Wijngaard, 2018).

In Vitro Micronucleus Test

An independent laboratory (Triskelion B.V.) also performed an *in vitro* micronucleus test with BUNGE's shea olein in cultured human lymphocytes following the OECD 487 guidelines. In this unpublished study (Usta, 2018), BUNGE's shea olein was examined for its potential to induce micronuclei in cultured binucleated human lymphocytes in the absence and presence of a liver fraction of Aroclor 1254-induced rats for metabolic activation (S9-mix).

Two independent experiments were performed. In the first experiment, the treatment/recovery time was 4/20 hours (pulse treatment), both in the presence and absence of S9-mix. In the second experiment, the treatment/recovery time was 24/0 hours in the absence of S9-mix (continuous treatment). Ethanol was used as a solvent for the test substance. The maximum concentration of the test substance was limited by solubility. In both experiments, the final concentrations of BUNGE's shea olein tested ranged from 500 to 1 µg/mL. Duplicate cultures were used. Cytotoxicity was determined from the Cytokinesis-Block Proliferation Index (CBPI). Negative controls (solvent) and positive controls were run simultaneously with the test substance.

In both experiments, the solvent controls were within the range for historical data of the test facility. Treatment with the positive controls, cyclophosphamide and vinblastine sulphate, resulted in statistically significant increases in the numbers of binucleated cells containing micronuclei when compared with the numbers observed in the concurrent solvent control cultures. Therefore, the test was considered valid.

In both experiments, no clear cytotoxicity was observed at any concentration analyzed when compared with the concurrent solvent control cultures in both experiments.

In the first and second experiments, three test substance concentrations (i.e., 500, 250 and 125 µg/mL) and four test substance concentrations (i.e., 500, 250, 125 and 31.3 µg/mL), respectively, together with the solvent and positive control cultures were selected for micronuclei analysis.

In both experiments, BUNGE's shea olein did not show a statistically significant increase in the number of binucleated cells containing micronuclei at any of the concentrations analyzed when compared with the concurrent solvent control cultures.

It was concluded that the test substance, shea olein, is not clastogenic and/or aneugenic to cultured human lymphocytes under the conditions used in this study (Usta, 2018).

b. Subchronic Toxicity Study

In a 13-week rat feeding study reported by Earl et al. (2002a), the biological effects of BUNGE's shea olein in growing rats were compared with two common vegetable oils, soy and palm oils.

Wistar rats were fed a diet containing 20% wt palm oil, soybean oil, or shea olein for 13 consecutive weeks (approximately 10 to 15 g/kg bw/day for all test products). Each group comprised 15 male and 15 female rats. During the exposure period, body weight, food and water consumption, urine chemistry, and clinical pathology were assessed. Gross necropsy and microscopic examination of select tissues and organs were performed at study completion. The following tissues were studied: adrenals, aorta, urinary bladder, brain, heart, liver, spleen, kidneys, muscle, caecum, lung, thymus, pancreas, thyroid, esophagus, colon, pituitary, tongue, ovaries, stomach, rectum, cervical lymph node, mesenteric lymph node, uterus, sciatic nerve, duodenum, epididymis, testes, eyes with harderian gland, femur bone, spinal cord, salivary glands, vagina, and seminal vesicles.

Shea olein and the common vegetable oils were well tolerated and did not produce any adverse effects when fed to rats at a dietary level of 20% for 13 weeks. The lack of biological effects in rats fed a palm oil diet is consistent with the good safety profiles with various palm oils administered at 15% in rat diet (Cohen et al., 1983, Owu et al., 1998). Generally, slight, but statistically significant greater body weight gains for male rats treated with palm and soybean oil diets were noted compared with the shea olein diet, which were reflected in slightly higher final body weights for these animals. There were also slight, but statistically significant lower mean total cholesterol levels and higher aspartate aminotransferase (AST) levels with the shea olein and soybean oil diets when compared with the palm oil diet. Other significant clinical chemistry changes were minor and considered by the authors to be of no biological significance.

Diets containing shea olein resulted in a slight, but statistically significant reduction in heart weight for female rats in comparison with palm and soybean diets. None of the diets was associated with histological changes in the heart. Overall, shea olein produced a similar biological profile to palm and soybean oil diets.

Based on these findings, the authors concluded that shea olein given at 20% of the diet (10 to 15 g/kg bw/day) was well tolerated and appeared to have no adverse effect on the growing rat.

c. Reproductive Toxicology Studies

Baldrick et al. (2001) investigated the reproductive toxicity of BUNGE's shea olein in two dietary studies in rats during pre-mating, mating, pregnancy and offspring weaning.

In Study 1, groups of Colworth-Wistar rats (20 males and 20 females) received diets containing 7% wt of shea olein, 7 wt % hardened (hydrogenated) shea olein or 7 wt % of cocoa butter for 20 consecutive weeks. During week 12, the rats were mated, and following gestation, all dams were allowed to litter. At weaning, the offspring were fed the parental diet for 7 to 10 days prior to sacrifice. In addition, 12 male and 12 female parental animals from each group were sacrificed following the 20-week treatment period (after weaning) for examination. Parental animals were assessed for general condition and health, body weight and food consumption were measured, clinical pathology and gross necropsy examinations were conducted and selected organs were

weighed. The assessment of pups included a clinical chemistry evaluation, as well as skeletal (using X-ray) and macroscopic examinations.

In Study 2, groups of Colworth-Wistar rats were fed diets containing 15% wt shea olein (approximately equivalent to 7.5 g/kg bw/day) or palm oil for 10 consecutive weeks. Experimental diets were introduced 2 weeks prior to mating. Dams were allowed to litter and at weaning, offspring were fed the parental diet. Endpoints observed included assessment of general health and measurement of litter and weaning parameters. In addition, at the end of the 10-week treatment period, liver, lymph glands, serum and red blood cells were examined for fatty acid composition, and livers and mesenteric lymph nodes were examined for evidence of lipogranulomas in F_0 animals.

For parental animals, Study 1 showed no differences in the general conditions of animals fed the two diets. None of the animals was found to have diarrhea. The actual test material intake ranged from 3 to 6 g/kg bw/day across the groups. Compared with male and female rats fed the cocoa butter diet, a statistically significant reduction in mean body weight gain was observed in males fed shea olein. The authors attributed the observed reduction in body weight gain to a decreased calorific value of the shea olein diets. A marginal, but statistically significant increase in mean body weight gain occurred in females fed the shea olein diet. Administration of hardened shea olein produced no effect on body weight gain. The authors did not consider the body weight changes to be toxicologically significant.

No differences in hematological parameters were noted among the groups after 20 weeks of treatment. Results of clinical chemistry analyses showed a trend for reduced mean cholesterol in both sexes fed the shea olein and hardened shea olein compared with those fed cocoa butter. Increased mean alkaline phosphatase (ALP) values were also observed in both sexes of the hydrogenated shea olein group. The authors suggest that both findings resulted from the feeding of high fat diets (Young et al., 1981). With respect to organ weights, an increase in the absolute, but not relative, mean heart weights of females fed the shea olein and hydrogenated shea olein diet, compared with those receiving the cocoa butter diet, was observed. In offspring, none of the diets had an effect on the number of litters born or weaned. Litter size, number of pups at birth and weaning, survival and body weight at weaning were similar among groups. Macroscopic and x-ray examination of animals showed no findings related to the test materials. The authors state that none of these findings is of toxicological significance.

For parental animals in Study 2, no unusual health problems were noted. Fatty acid analyses of the liver, lymph node and blood serum, as well as membrane phosphatidyl choline (PC) analyses showed no unexpected results for the diets administered. Likewise, histopathological examination of the liver and mesenteric lymph nodes showed no evidence of lipogranulomas in any of the groups. For offspring, none of the diets had any effect on the number of litters born. No significant differences were noted in pup body weights at birth and weaning among groups.

Based on the results of both studies, the authors concluded that there was no evidence of reproductive toxicity for shea olein in the rat at levels equating to approximately 7.5 g/kg bw/day.

d. Carcinogenicity Studies

The carcinogenic potential of BUNGE's shea olein was evaluated in a dietary study in Wistar rats for 104 weeks (Carthew et al., 2001). The study also evaluated palm oil and crude sheanut oil. The free fatty acid compositions of sheanut oil, shea olein and palm oil were 11.3, 0.2, and 0.2% respectively and the unsaponifiable material contents were 5.0, 6.4, and 0.1%, respectively. Groups of 50 male and 50 female rats received diets containing 15 wt % (approximately equivalent to 7.5 g/kg bw/day) shea olein or 15 wt % palm oil. The rats were the offspring of the animals used in the reproduction study described above (Study 2) and the test diets began at weaning (21 days of age). The following parameters were assessed: mortality, clinical signs of toxicity, body weight, food intake, clinical pathology, organ weights and macroscopic and histopathological changes plus tumor type and incidence evaluation. Importantly, this study compared the two oils and did not include a "control" chow diet group.

Shea olein containing diet was well tolerated and did not produce any signs of adverse toxicity or carcinogenic potential when fed to rats at a dietary level of 15% for 104 weeks. Shea olein's safety profile was essentially similar to that of commercially available palm oil. The authors state that satisfactory survival was found for both diets used in the study with slightly higher mortality for palm oil (40%) compared to shea olein and (28-30%). Reduced body weight gain (notably for males during the early part of the study) and increased food intake (notably with the shea olein diet) were recorded for both sexes fed the shea olein diet in comparison with palm oil diet. The authors reported that this is consistent with the comparatively lower caloric value of shea olein reported in the literature by Thomasson (1955). Reduced cholesterol concentrations and raised ALP concentrations with the shea olein diet were recorded for both sexes in comparison with palm oil diet. Other findings were increased AST values for both sexes fed the shea olein diet and reduced pseudocholinesterase levels for females fed the shea olein diet, as noted in the previous 13-week rat study.

Reduced heart weight with the shea olein diet was seen for both sexes in comparison with palm oil diet. Increases in liver weight were consistent with the feeding of a high fat diet. Histopathological examination showed a much greater incidence and severity of pulmonary lipidosis in both sexes fed shea olein compared to palm oil diet. This finding, which is characterized by accumulation of lipid-laden alveolar macrophages, is a background finding in aged rats (Greaves and Faccini, 1984). The authors reported that the accumulation of lipids within the macrophages may be due to an impairment of lipid catabolism and reported data showing that also 7.5% sunflower seed oil gave similar values to those seen with shea olein in a contemporary lifetime study performed in Wistar rats. No evidence of an effect on macrophage aggregation in the mesenteric lymph nodes was seen.

Histopathological examination showed a much greater incidence and severity of pulmonary lipidosis in both sexes fed shea olein compared to palm oil diet. This finding, which is characterized by accumulation of lipid-laden alveolar macrophages, is a background finding in aged rats (Greaves and Faccini, 1984). The authors reported that the accumulation of lipids within the macrophages may be due to an impairment of lipid catabolism and reported data showing that also 7.5% sunflower seed oil gave similar values to those seen with shea olein in a contemporary lifetime study performed in Wistar rats. No evidence of an effect on macrophage aggregation in the mesenteric lymph nodes was seen.

The authors also reported that no unexpected types of tumors were found for any other diet treatments and the tumor incidences compared favorably with those in the published literature for studies with Wistar rats (Bomhard and Rinke, 1994, Bomhard et al., 1986, Walsh and Poteracki, 1994, Poteracki and Walsh, 1998).

Overall, the authors concluded that none of the findings was considered to be adverse and, in comparison to palm oil, shea olein showed no tumorigenic potential following dietary administration of 7.5 g/kg bw/day (Carthew et al., 2001).

5. Toxicology Studies of Other Shea Olein Products and its Constituents

a. Acute Toxicity Studies

Unpublished toxicology studies on the unsaponifiable matter of shea olein were submitted by Cantox Health Sciences International as part of a Premarket Notification for a new dietary ingredient (NDI) derived from shea (BSP Pharma A/S, 2004). An acute toxicity trial in Wistar rats was carried out using an extract of shea oil standardized to 50% unsaponifiables (phytosterols). In accordance with OECD 420 guidelines for acute toxicity studies, single gavage doses of 2000 mg of shea olein per kg body weight were administered to male and female rats (5/sex). The animals were observed for at least 1, 3, and 6 hours after dosing and daily thereafter for 14 consecutive days. There were no deaths or other signs of toxicity and body weight gains were normal during the study period. Piloerection was observed in 3 animals 1 hour after treatment and in five animals 3 hours after treatment, though the authors suggested this may have been related to treatment and handling procedures. During gross necropsy examination, erythema was observed in the intestine of one male and discoloration of the liver, spleen, and lungs was seen in one female. The authors concluded that the minimal lethal dose was above 2000 mg of the test substance per kg bw, or 1000 mg unsaponifiable matter per kg body weight, which would then be equivalent to 12.5 g/kg bw shea olein.

b. Genotoxicity Studies

Unpublished toxicology studies on the unsaponifiable matter of shea olein included an Ames assay and *in vivo* mouse micronucleus test (BSP Pharma A/S, 2004). In the Ames assay, which was conducted in accordance with OECD 471 guidelines, the unsaponifiable matter of shea olein dissolved in dimethylsulfoxide (DMSO) was not toxic to *Salmonella typhimurium* strains TA102,

TA100, TA98, TA1537, or TA1535 at levels of 50, 160, 500, 1600 and 5000 µg/plate (equivalent to 25, 80, 250, 800, and 2500 µg unsaponifiable matter/plate). In addition, no biologically or statistically significant increases in the number of revertant colonies were observed in any tester train after treatment with the test substance at any dose level, either in the presence or absence of rat liver metabolic fraction (S-9), as compared with negative controls.

In an *in vivo* mouse micronucleus assay, male mice were treated with a single 2000 mg/kg bw dose of the test substance, equivalent to 1000 mg of shea olein unsaponifiable material/kg bw, or negative controls by oral gavage. Five mice from each group were sacrificed 24 hours after dosing and five additional mice from the test group and the negative control groups were sacrificed 48 hours after dosing. No adverse reactions to treatment with the test substance were observed, nor were any biologically or statistically significant increases in the frequency of micronucleated polychromatic erythrocytes in mice treated with the shea butter extract as compared with negative controls. It was concluded that the test substance was not genotoxic under the conditions of this study.

6. Additional Animal Studies with Shea-derived Material

An additional study was reported by BSP Pharma A/S (2004) as part of a Premarket Notification for new supplements derived from shea. The animal study compared the gastric effects of ibuprofen to an 80% enriched sample of the unsaponifiable matter of shea olein (Weidner, 2003), known as SheaFlex70™ in Japan and Taiwan and FlexNow in United States. Twelve Sprague-Dawley rats were administered 2000 mg/kg doses of SheaFlex75™ dissolved in peanut oil by oral gavage daily for four days. Other rats were administered the control vehicle or 200 mg/kg of ibuprofen, which served as a positive control. Following an overnight fast, the rats were given intravenous injections of 1 mL of % Evans blue saline 30 minutes prior to sacrifice. The stomach and small intestines were scored for lesions. No adverse clinical signs were recorded, and no adverse effects on body weight were seen with the exception of one rat treated with ibuprofen. No gastrointestinal lesions were observed in negative control rats or in rats treated with the test material. In contrast, a significant number of lesions was observed in rats treated with ibuprofen as compared with those in the control group. The majority of these small intestinal lesions were seen in the aboral part of the jejunum and in the ileum. SheaFlex75™, at oral doses of 2000 mg/kg bw/day administered for 4 days, was found to have no ulcerogenic effect in the rat. This lack of gastrointestinal effects, along with the absence of treatment-related adverse clinical signs, supports the safety of short-term (4 day) intake of up to 1500 mg/kg of unsaponifiable matter of shea olein.

In a study reported by Kao et al. (2016), an anterior cruciate ligament transection with medial meniscectomy was used to induce osteoarthritis in 40 male Wistar rats. Different doses of SheaFlex75™ (111.6 mg/kg, 223.2 mg/kg, and 446.4 mg/kg) were then intragastrically administered daily for 12 weeks after surgery. Body weight and the width of the knee joint were measured weekly. Additionally, incapacitance tests were performed at weeks 2, 4, 6, 8, 10 and 12 to measure the weight bearing of the hind limbs, and the morphology and histopathology of the medial femoral condyles were examined and evaluated using the Osteoarthritis Research Society

International (OARSI) scoring system. This study showed that SheaFlex75™ reduced the swelling of the knee joint with osteoarthritis and rectified its weight bearing after anterior cruciate ligament transaction with medial meniscectomy surgery in rats. No abnormal behavior or alteration of body weight of the rats was seen. All rats survived for 12 weeks until sacrifice.

7. Toxicology Summary

There is a long history of safe use of shea butter and its refined byproducts. This was demonstrated in FDA's assessment of Fuji Oil Company's petition for the GRAS status of sheanut oil (*Fed. Reg*., Vol. 63, No. 101, page 28894, 1998)[7]. Further, the fats and fatty acids making up the triglycerides of shea olein are commonly consumed in the diet through other fats and oils, meaning they are safe. The unsaponifiables in shea olein, mainly 4,4-DMS, are consumed from various oils already in the diet, although generally not in amounts that could be encountered when consuming shea olein. This is addressed below.

Unpublished genotoxicity studies with BUNGE'S shea olein showed no indication of point mutations or chromosomal aberrations.

Pivotal subchronic, reproduction, and carcinogenicity studies in rats were published in the open, peer-reviewed literature (Baldrick et al., 2001, Carthew et al., 2001, Earl et al., 2002a). While all showed random differences from controls, the authors of each study concluded that the high-fat diets were well tolerated and showed no adverse effects that could be attributed to BUNGE'S shea olein. Based on these findings, shea olein given at up to 20% of the diet (ranging from 7.5 to 15 g/kg bw per day, depending on the study) has no adverse effect on rats throughout their life spans. Additionally, 4,4-DMS, constituting up to 8% of the shea olein, is also well tolerated and has no adverse effect on rats when consumed in amounts ranging from approximately 400 to 1200 mg/kg bw/day, depending on the study.

Information from unpublished but publicly available studies submitted to FDA for a new dietary ingredient derived from shea having high levels of unsaponifiables shows a lack of genotoxicity and acute toxicity. A published study (Kao et al. (2016) shows that daily intragastric doses of a dietary supplement with 50-70% shea unsaponifiables, mainly 4,4-DMS, for 12 weeks did not cause gross indications of toxicity.

The totality of evidence from the reported toxicology studies, unpublished and published, BUNGE believes that the data support the safety of shea olein and the unsaponifiable material in it at high levels in well conducted toxicologic studies.

8. Human Studies with Sheanut Unsaponifiables

In a randomized double-blind, placebo-controlled, balanced, incomplete, Latin square design study, 95 healthy, non-obese, normocholesterolemic and mildly hypercholesterolemic volunteers

[7] Available at https://www.govinfo.gov/content/pkg/FR-1998-05-27/pdf/98-13917.pdf

received, in four consecutive periods of 24 or 25 days (3.5 weeks), 30 g/day of a spread in a coded tub for consumption at lunch and dinner. The spread was meant to replace the spreads habitually used by the volunteers. Five types of spread were investigated: spreads enriched with sterols from soybean, shea butter, or rice bran oil, or with sitostanol-ester were compared to a non-enriched control spread. Sterol intake was 1.5±3.3 g/day. The shea butter sterol extract, an enriched sterol extract derived from shea butter and used in the trial, was comparable to the sterol fraction of the BUNGE shea olein since the main identified sterols consisted of 32% α-amyrin, 17.8% of butyrospermol,14.9% lupeol, and 5.7% β-amyrin. None of the spreads induced adverse changes in blood clinical chemistry, serum total bile acids or hematology. All sterol-enriched spreads reduced lipid-standardized plasma α- plus β-carotene levels. Blood chemistry and hematological variables were monitored and no evidence was found for adverse effects of consumption of the sterol-enriched spreads on plasma AST, alanine aminotransferase (ALT), ALP, and L-γ-glutamyltransferase activities, serum total bilirubin concentration and plasma total bile acids concentrations, nor on plasma concentrations of urea, creatinine, albumin or glucose. The levels of hematological variables indicated no adverse response of the blood to exposure of the spreads; white blood cell, red blood cell, platelet counts, hemoglobin concentration and hematocrit were all within normal ranges (Weststrate and Meijer, 1998)

A single-site, 15-week randomized, double-blind, parallel, placebo-controlled study examined a range of biomarkers in 89 patients with osteoarthritis of the knees and/or hips to determine potential modes of action of SheaFlex70™, as described in patent application by Weidner (2003) (70% triterpenes derived from the seed of the shea tree, BSP Pharma). After a minimum washout period of 3 weeks, participants were randomized to either placebo or SheaFlex70™ once daily for 15 weeks. Blood and urine samples for safety and biomarker assays were taken at baseline, weeks 1, 10, and 15, and the conclusion of the study. The treatment comprised either 100% SheaFlex70™ or placebo, which was 100% canola oil. The daily dosage was three 750 mg soft gel capsules (2.25 g of SheaFlex70™) taken in the morning. In the group of participants with levels of osteoarthritis biomarkers in the upper quartile at baseline, there were significant decreases in inflammation and cartilage breakdown and trend level decreases in bone remodeling in the SheaFlex70™ group versus placebo between commencement and completion of the study. The inflammation marker, TNF-alpha, fell 23.9% vs. 6% (treatment vs. placebo) and the cartilage degradation marker C-terminal crosslinked telopeptide type II collagen (CTX-II) fell 28.7% vs. an increase of 17.6 % (treatment vs placebo). This marker was significantly reduced across the entire study group, 10.6% vs. an increase of 11.6%, (treatment vs. placebo). Osteocalcin levels fell 9.2%, (treatment) vs 1.2%, ns (placebo). These findings, coupled with the finding of decreased pain in the treatment group, point toward a group of potentially beneficial pharmacological effects on the part of SheaFlex70™ in key areas associated with arthritis pathophysiology. Adverse effects were not discussed (Cheras et al., 2010).

In the non-randomized control intervention study published by Chen et al. (2013) on the effects of SheaFlex75™ on quadriceps strength, which is typically reduced in osteoarthritis patients, 33 patients were given six pills of SheaFlex75™ /day for 16 weeks, equivalent to 2,160 mg of

SheaFlex75™ per day. The morphological changes of muscles around the knees and the ability to control muscles in different tasks were examined at baseline, after 8 weeks and after 16 weeks of treatment. Improved muscle function was observed, including greater control and an increase in-muscle strength to achieve a functional goal; nevertheless, the subjective feeling of improvement in the activities of daily living was not significant. Adverse effects were not discussed.

In the study reported by Sierksma et al. (1999) that investigated the effect of spreads enriched with plant sterols on plasma total- and LDL-cholesterol in humans, 76 healthy adults received a total of three different table spreads for personal use. Two spreads were fortified either with free (non-esterified) vegetable-oil sterols, mainly from soybean oil (31 g sterol equivalents/kg; 0.8 g/day) or sheanut-oil sterols (133 g sterol equivalents/kg; 3.3 g/day unsaponifiables). The sheanut oil sterols used, an enriched sterol extract derived from shea butter and used in the trial, was comparable to the sterol fraction of the BUNGE shea olein since the main identified sterols consisted of 95.5% 4,4-dimethylsterols, 2.8% 4-desmethylsterols and 0.7% 4-α-methylsterols. One spread was not fortified (control). The average intake of spread was 25 g/day for 3 weeks. The spread enriched with shea unsaponifiable matter did not lower plasma total, LDL- and HDL-cholesterol levels. None of the spreads induced changes in blood clinical chemistry or hematology. A small reduction in beta-carotene absorption was observed for all sterol diets. No other adverse effects were mentioned.

In a double-blind crossover trial, Vissers et al. (2000) studied the effects of plant sterols from rice bran oil and 4,4-dimethylsterols (also known as triterpene alcohols) from shea butter on cholesterol concentrations in healthy, normolipemic volunteers. Sixty subjects (32 females, 28 males) consumed 29 g/day of 3 margarines for 3 weeks each. Concentrates of plant sterols from rice bran oil or phytosterols from shea butter were added so that each margarine had the same fatty acid composition. The sheanut oil sterol concentrate used, which was an enriched sterol extract derived from shea butter and used in the trial, was comparable to the sterol fraction of the BUNGE shea olein since the main identified sterols consisted of 95.7% 4,4-dimethylsterols and 4.3% 4-desmethylsterols. The mean intake of total plant sterols (in free sterol equivalents) was 0.06 g/day from the control margarine, 2.6 g/day from sheanut oil and 2.1 g/day from the rice bran oil. Phytosterols from sheanut oil did not significantly affect lipoprotein concentrations in all subjects combined. No adverse effects were mentioned.

9. Summary of Human Studies

Three clinical trials have been completed using spreads enriched with shea sterols that were comparable to the sterol fraction of BUNGE's shea olein. Weststrate and Meijer (1998) reported that consumption of a spread enriched with shea sterol extract at 1.5±3.3 g/day did not induce adverse changes in blood clinical chemistry, serum total bile acids, hematology, plasma AST, ALT, ALP or L-γ-glutamyltransferase activities, serum total bilirubin level or plasma total bile acids concentrations, nor on plasma levels of urea, creatinine, albumin or glucose. Sierksma et al. (1999) also showed no changes in blood clinical chemistry or hematology or adverse effects (with the exception of a small reduction in beta-carotene absorption) at dosages of 3.3 g/day sheanut oil

sterols. Lastly, Vissers et al. (2000) did not report adverse effects of 2.6 g/day intake of 4,4-DMS from sheanut oil.

Two studies using SheaFlex products (containing 70-75% shea-derived 4,4-DMS) did not mention adverse effects at dosages of 2.25 g (1.575 g sterols) (Cheras et al., 2010) and 2.16 g/day (1.62 g sterols) (Chen et al., 2013).

These totality of evidence from the reported clinical studies, support the safety of shea olein and the unsaponifiable material at dosages ranging from 1.5 – 3.3 g/day of shea-derived sterols.

10. Studies Addressing the Safety of the Phytosterols of Other Oils

The Joint FAO/WHO Expert Committee on Food Additives (JECFA) summarized in 2009 the evaluation on the toxicological studies with a range of phytosterols, phytostanols and their esters (focusing on desmethylsterols), together with several double-blinded, placebo-controlled human studies, in which these substances were added to the diet. As phytosterol and phytostanol esters and mixtures of phytosterols and phytostanols generally show similar effect profiles, the Committee considered establishing a group acceptable daily intake (ADI) (WHO, 2009).

Using the combined evidence from several short-term (90-day) studies of toxicity, the Committee identified an overall no observed adverse effect level (NOAEL) of 4,200 mg/kg bw per day. The Committee established a group ADI of 0–40 mg/kg bw for the group of phytosterols, phytostanols and their esters, expressed as the sum of phytosterols and phytostanols in their free form, based on the overall NOAEL, to which a safety factor of 100 was applied. This safety factor incorporates a factor of 10 for interspecies differences and a factor of 10 for intraspecies differences. Based on the availability of a range of studies in humans, which includes two 1-year studies, the Committee considered the safety factor of 100 as sufficient to also account for deficiencies in the database, such as the absence of chronic studies in experimental animals. As there is no evidence for genotoxicity of phytosterols or phytostanols and their esters and no indication of potential for carcinogenicity from the available toxicity studies, the Committee did not see a need for a carcinogenicity study to be performed.

Based on available data, the Committee concluded that dietary exposure to phytosterols and phytostanols would typically be within the ADI range of 0–40 mg/kg bw.

11. Information on the Allergenicity of Shea Olein

When the U.S. Congress passed the Food Allergen Labeling & Consumer Protection Act in 2004, they appropriately designated tree nuts as among the most commonly allergenic foods in the U.S. However, Congress failed to provide a list of tree nuts when they passed this law. Later in October 2006, the U.S. Food & Drug Administration provided a list of tree nuts in an attempt to clarify the uncertainty left by Congress. That list included shea nuts and consequently the FDA requires listing of shea nut or shea butter as an ingredient. It is consequently assumed that also shea olein will have to be labeled as a potential allergen.

In Europe, shea nuts are not listed among the nuts that are subject to mandatory allergen labeling.

An exhaustive search of the worldwide clinical literature provided no evidence to indicate that any allergic reactions have ever been reported to shea butter and shea olein. Allergic reactions to shea nuts have not been described either.

Furthermore, research by Chawla et al. (2011) indicates that refined shea butter does not contain any detectable protein residues and does not contain detectable residues of proteins from peanut or various known allergenic tree nuts (walnut, almond, pecan, hazelnut). Since allergens are proteins, this research indicates the absence of detectable allergens in refined shea butter.

A material containing shea butter and shea butter unsaponifiables (70:30) was non-irritating in an EpiSkin™ assay when tested undiluted and in a human primary cutaneous tolerance tested at a 30% dilution in paraffin oil. The same material was considered non-sensitizing in a Direct Peptide Reactivity Assay when tested undiluted and non-phototoxic in a 3T3 Neural Red Uptake assay when tested at 0.005 to 1 mg/mL. Shea butter unsaponifiable matter was non-sensitizing in human patch tests at up to 5% in formulation (CIR, 2016).

A balm containing 1.5% of the mixture shea butter and shea butter unsaponifiables (70:30) was considered non-irritating in a Skinethic™ reconstituted mucous membrane model (CIR, 2016).

Overall there is no indication in the literature that there is an allergenic risk to consumers, including individuals with pre-existing peanut or tree nut allergies. Refining shea butter to make shea olein reduces the risk even more since it is established that full refining eliminates protein from the oil (Health Canada, 2013).

C. 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.”[8]

Amplification is provided in that the conclusion of safety is to include probable consumption of the substance in question, the cumulative effect of the substance and appropriate safety factors. It is FDA’s operational definition of safety that serves as the framework against which this evaluation is provided.

Furthermore, in discussing GRAS criteria, FDA notes that:

> “…General recognition of safety requires common knowledge, throughout the expert scientific community knowledgeable about the safety of substances directly

[8] See 21 CFR 170.3 (e)(i) and 81 FR 54959 Available at: https://www.federalregister.gov/documents/2016/08/17/2016-19164/substances-generally-recognized-as-safe (Accessed on 4/15/17).

> or indirectly added to food, that there is reasonable certainty that the substance is not harmful under the conditions of its intended use."
>
> "'Common knowledge' can be based on either "scientific procedures" or on experience based on common use of a substance in food prior to January 1, 1958." [9]

FDA discusses in more detail what is meant by the requirement of general knowledge and acceptance of pertinent information within the scientific community, i.e., the so-called "common knowledge element," in terms of the two following component elements:[10]

- Data and information relied upon to establish safety must be generally available, and this is most commonly established by utilizing published, peer-reviewed scientific journals; and
- There must be a basis to conclude that there is consensus (but not unanimity) among qualified scientists about the safety of the substance for its intended use, and this is established by relying upon secondary scientific literature such as published review articles, textbooks, or compendia, or by obtaining opinions of expert panels or opinions from authoritative bodies, such as JECFA and the National Academy of Sciences.

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. General recognition of safety through scientific procedures shall be based upon the application of generally available and accepted scientific data, information, or methods, which ordinarily are published, as well as the application of scientific principles, and may be corroborated by the application of unpublished scientific data, information, or methods.

The apparent imprecision of the terms "appreciable," "at the time," and "reasonable certainty" demonstrates that the FDA recognizes the impossibility of providing absolute safety in this or any other area (Lu, 1988, Renwick, 1990, Rulis and Levitt, 2009).

As noted below, this safety assessment to ascertain GRAS status for shea olein for the specified food uses meets FDA criteria for reasonable certainty of no harm by considering both the technical and common knowledge elements.

D. Bunge's Findings on Safety of Shea Olein

Shea olein has been determined by BUNGE Loders Croklaan to be GRAS on the basis of scientific procedure in accordance with Section 201(s) of the Federal Food, Drug, and Cosmetic Act.

[9] See 81 FR 54959 Available at: https://www.federalregister.gov/documents/2016/08/17/2016-19164/substances-generally-recognized-as-safe (Accessed on 4/15/17).
[10] See Footnote 1.

The following considerations were also taken into account for the safety evaluation:

- The triglycerides and fatty acids present in shea olein are identical to those found in common edible vegetable oils and fat;
- Shea butter is one of the six vegetable fats (other than cocoa butter) that is permitted to be added to chocolate products (EU Directive 2000/36/EC);
- FDA has already established that sheanut oil, the stearine fraction of shea butter, is generally recognized as safe (21 CFR§184.1702);
- The production process of the shea olein is equivalent to the process commonly used for the fractionation and refining of vegetable oils and fats;
- The maximum level of 9% for unsaponifiables in shea olein is supported by the available toxicology data and the JECFA conclusion that up to 40 mg/kg bw/day of phytosterols is safe;
- Specifications for shea olein meet quality criteria for shea butter as laid down in the Codex Standards for unrefined shea butter that can be used for direct food consumption;
- The concentration of triglycerides, diglycerides, monoglycerides and free fatty acids is within the specifications of edible vegetable oils and fats;
- Contaminants analysis shows that values are within the specifications of other edible oils and fats;
- A comprehensive search of the scientific literature for safety and toxicity information on shea olein and toxicity studies carried out on shea olein and the available toxicology and human clinical studies show that shea olein is safe; and
- Unpublished studies provided corroborative evidence of safety.
- Unrefined and refined shea butter has been consumed for centuries without evidence of toxicity.

BUNGE Loders Croklaan is not in possession of unpublished information that is relevant to the subject of this determination.

Based on the availability of shea nut for oil production the actual consumption of shea olein by consumers in the United States in would be < 1 g per day. Based upon this review, the maximum estimated per user intake of shea olein from the proposed uses of shea olein is safe.

Furthermore, a shea olein daily intake of 35 g per day is below USDA recommendations for total fat intake (USDA, 2015).

It is therefore reasonable to conclude that the proposed uses of shea olein are safe and suitable, and meet the criteria for consideration of generally recognized as safe (GRAS) status.

E. Expert Panel Findings on Safety of BUNGE's Shea Olein

An evaluation of the safety and GRAS status of the intended use of BUNGE's shea olein has been conducted by an Expert Panel convened by GRAS Associates; the Panel consisted of Kara Lewis, Ph.D., as Panel Chair; Richard Kraska, Ph.D., and Richard Lane, Ph.D. The Expert Panel reviewed BUNGE's dossier as well as other publicly available information available to them. The individuals serving as Expert Panelists are qualified to evaluate the safety of foods and food ingredients by merit of their scientific training and experience.

The GRAS Expert Panel report is provided in Appendix 7.

F. Common Knowledge Elements for GRAS Conclusions

The first common knowledge element for a GRAS conclusion requires that data and information relied upon to establish safety must be generally available; this is most commonly established by utilizing studies published in peer-reviewed scientific journals. The second common knowledge element for a GRAS conclusion requires that consensus exists within the broader scientific community.

1. Public Availability of Scientific Information

The majority of the studies reviewed in this safety assessment have been published in the scientific literature as reported in Part 6. The safety conclusion was based solely on published studies and other publicly available information. Unpublished studies have been mentioned for completeness.

The pivotal studies by Earl et al. (2002a), Baldrick et al. (2001) and Carthew et al. (2001) investigating the subchronic and reproductive toxicities and carcinogenicity of shea olein in rats have been published in peer-reviewed journals that are readily available. The composite information thereby fulfills the general availability common knowledge element for GRAS determinations.

2. Scientific Consensus

The second common knowledge element for a GRAS conclusion requires that there must be a basis to conclude that consensus exists among qualified scientists about the safety of the substance for its intended use. BUNGE's shea olein is intended for use in conventional foods as a replacement of animal fats and vegetable fats rich in palmitic, myristic and lauric fatty acids. Considering the totality of evidence, experts would agree that:

- the scientific composition and biochemistry of Bunge's shea olein are similar to oils already on market;

- published toxicology studies do not indicate any safety concerns;
- unpublished, but publicly available, toxicology studies do not indicate any safety concerns;
- sheanut oil (stearin) is GRAS;
- shea butter, of which shea olein is a constituent, is used in foods in the EU; and
- shea butter is widely used in cosmetics globally.

BUNGE and the Expert Panel maintain that well-qualified scientists would conclude that BUNGE's shea olein is generally recognized as safe for use in food given the regulatory and safety data available and using well accepted toxicological principles.

G. Conclusion

In consideration of the aggregate safety information available on shea olein, as well as the report from the designated Expert Panel provided in Appendix 7, BUNGE concludes that the shea olein defined in the subject notification, and produced under Current Good Manufacturing Practices, is safe for the intended uses in foods as per Part 3, and is generally recognized as safe (GRAS) within the meaning of the Food, Drug, and Cosmetic Act.

This declaration has been made in accordance with FDA's standard for food ingredient safety, i.e., reasonable certainty of no harm under the intended conditions of use.

PART 7. LIST OF SUPPORTING DATA AND INFORMATION IN THE GRAS NOTICE.

A. List of Acronyms

ADI - Acceptable Daily Intake

ADME - Absorption, Distribution, Metabolism, and Excretion

AOAC - Association of Official Agricultural Chemists

AOCS - American Oil Chemists Society

ALP - Alkaline Phosphatase

ALT - Alanine Aminotransferase

AST - Aspartate Aminotransferase

ATP - Adenosine Triphosphate

AV - Anisidine Value

BUNGE - BUNGE Loders Croklaan BV

bw - body weight

C - Celsius

CAS - Chemical Abstracts Service

CBPI - Cytokinesis-Block Proliferation Index

CDC - Center for Disease Control

CFR - Code of Federal Regulations

CFU or cfu - colony forming unit

CGMP - Current Good Manufacturing Practice

CIR - Cosmetic Ingredient Review

cm - centimeter

COA - Certificate of Analysis

CTX-II - C-terminal crosslinked telopeptide type II collagen

CXS - Codex Alimentarius

DMS - 4,4-Dimethylsterols

DMSO - Dimethylsulfoxide

EC - European Commission

ECHA - European Chemicals Agency

EU - European Union

FAME - Fatty Acid Methyl Esters

FD&C Act - Federal Food, Drug, and Cosmetic Act

FDA - Food and Drug Administration

FFA - Free Fatty Acid

FOIA - Freedom of Information Act

g - gram

GMP - Good Manufacturing Practice

GRAS - Generally Recognized as Safe

GRASP - Generally Recognized as Safe Petition

GRN - GRAS Notice

HDL - High-Density Lipoprotein

IOM – Institute of Medicine

ISO - International Organization for Standardization

IU - International units

IUPAC - International Union of Pure and Applied Chemistry

JECFA - Joint FAO/WHO Expert Committee on Food Additives

kg - kilogram

KPa - kilopascal

LDL - Low-Density Lipoprotein

LLC - Limited Liability Corporation

LOD - Limit of Detection

LRQA - Lloyd’s Register Quality Assurance

mcg or µg - microgram

mg - milligram

mL - milliliter

mmHG - millimeter of mercury

mol - mole

mon - month

MOP - 1-myristoyl-2-oleoyl-3-palmitoyl-rac-glycerol

MUFA - Mono-Unsaturated Fatty Acids

NCHS - National Center for Health Statistics

NDI - New Dietary Ingredient

NOAEL - No Observed Adverse Effect Level

NHANES - National Health and Nutrition Examination Surveys

OARSI - Osteoarthritis Research Society International

OECD - Organization for Economic Co-operation and Development

OOO - Triolein

PAH - Polycyclic Aromatic Hydrocarbons

PC - Phosphatidyl Choline

pg - picogram

POO - 1,2-dioleoyl-3-palmitoylglycerol

POP - 1,3-dipalmitoyl-2-oleoylglycerol

POSt - 1-palmitoyl-2-oleoyl-3-stearoylglycerol

ppm - parts per million

PUFA - Poly-Unsaturated Fatty Acids

PV - peroxide value

QMP - Quantitative Method Procedure

RACC - Reference Amounts Customarily Consumed

SAFA - Saturated Fatty Acids

SFC - Solid Fat Content

StLiO -1-stearoyl-2-linoleoyl-3-oleoylglycerol

StOO - 1-stearoyl-2,3-dioleoylglecerol

StOSt - 1,3-distearoyl-2-oleoylglycerol

TNF - tumor necrosis factor,

tbsp - tablespoon

µm - micrometer

U.S. or USA - United States

VW - Verwey BV (previous name of analytical lab before being purchased by AgroLab)

WHO - World Health Organization

wt - weight

WWEIA - What We Eat In America

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C. Appendices

Appendix 1 Phytosterol Analyses of Batches of Shea Olein

mylnefield
lipid analysis

James Hutton Limited, Errol Road, Invergowrie, Dundee DD2 5DA, UK
claire.traynor@huttonltd.com www.lipid.co.uk +44 (0) 1382 568876

Designation of Sample - [redacted]
Submitted By - IOI Loders Croklaan
Our Number - MRSLU/2018/1140
Date Posted 17/04/2018
Date Received - 19/04/2018
Report Ref/Issue Number - 2-1

Sterol	Normalised A%	mg Sterol/100g Sample
Unknown	4.0	222.3
β-amyrin	6.9	381.7
Butyrospermol	22.1	1221.9
α-amyrin	38.7	2135.2
Lupeol	19.6	1084.7
D-7-stigmastenol	2.9	158.2
24-methylene cycloartenol	1.1	62.3
Taraxasterol	3.8	208.0
Psi-taraxasterol	0.9	49.1
Total Sterol Content (mg/100g Sample)		5523.4

Method Used: ATM019

	Name	Signature	Date
Written by	Amy Stewart	[redacted]	16/10/2018
Approved by	Claire Traynor	[redacted]	16/10/2018

SGS

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mylnefield
lipid analysis

James Hutton Limited, Errol Road, Invergowrie, Dundee DD2 5DA, UK
claire.traynor@huttonltd.com www.lipid.co.uk +44 (0) 1382 568876

Designation of Sample - [redacted]
Submitted By - IOI Loders Croklaan
Our Number - MRSLU/2018/1141
Date Posted 17/04/2018
Date Received - 19/04/2018
Report Ref/Issue Number - 2-1

Sterol	Normalised A%	mg Sterol/100g Sample
Unknown	4.0	222.8
β-amyrin	7.0	389.6
Butyrospermol	22.2	1236.2
α-amyrin	38.5	2141.1
Lupeol	19.7	1097.1
D-7-stigmastenol	2.9	160.2
24-methylene cycloartenol	1.1	59.0
Taraxasterol	3.9	215.6
Psi-taraxasterol	0.7	37.9
Total Sterol Content (mg/100g Sample)		5559.5

Method Used: ATM019

	Name	Signature	Date
Written by	Amy Stewart	[redacted]	16/10/2018
Approved by	Claire Traynor	[redacted]	16/10/2018

SGS

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Appendix 2 Loders Croklaan Quality Certificates

2-A ISO-14001 Certification

BUREAU VERITAS

BUREAU VERITAS 1828

Certification

Awarded to

Loders Croklaan B.V.

Hogeweg 1, 1521 AZ WORMERVEER, The Netherlands

Bureau Veritas Certification certifies that the Management System of the above organisation has been audited and found to be in accordance with the requirements of the management system standards detailed below

STANDARD

ISO 14001:2004

SCOPE OF SUPPLY

Marketing, sales, development, manufacturing and delivery of Speciality Oils and Fats.

Date of Initial Issue: **20 January 1998**

Subject to the continued satisfactory operation of the organisation's Management System, this certificate is valid until: **9 April 2018**

To check the validity of this certificate please call: +31 (0)88 450 5500.

Certificate Number: **NL013993-1** Date of Issue: **11 May 2015**

MGMT. SYS. RvA C 248

SCCM

Managing office: **Bureau Veritas Inspection & Certification Nederland** B.V., Computerweg 2, 3821 AB Amersfoort
Issuing office: **Bureau Veritas Inspection & Certification Nederland** B.V., Computerweg 2, 3821 AB Amersfoort

2-B ISO-14001 Halal Certification

HALAL VOEDING EN VOEDSEL KEURINGSDIENST
HALAL FEED AND FOOD INSPECTION AUTHORITY
مؤسسة الحلال الطيب
الخدمات ومراقبة المواد الغذائية قسم الرقابة على المواد الغذائية

Telephone: 00-31-(0)70-364 9191 **Fax:** 00-31-(0)70-364 5460// **E-mail**: certification@halal.nl
Address: Neherkade 3140 / 2521 VX The Hague // P.O. BOX 16786/ 2500BT The Hague/ The Netherlands

HALAL CERTIFICATE

Processing Plant	Plant code	Halal logo number
Loders Croklaan BV Hogeweg 1 1521 AZ Wormerveer The Netherlands	XXXXXXX	H00052-01412//A0046-ANL

Investigation:

1. The production of the below-mentioned product is taking place in a clean and Halal approved processing system. The ingredients, raw materials used to produce this product mentioned below are screened on Halal-being and Halal approved.
2. The processing plant Loders Croklaan BV Hogeweg 1, 1521 AZ Wormerveer, The Netherlands produces Halal products according to the HFFIA Halal protocols.
3. The following product(s) is/are Halal:

Article description (ranges)	Article description (ranges)
Betapol	DP-products
Biscuitine	Durkex
Centremelt	Fatmix FN
Clsp	Ines
Coberine	Ker
Cose	Kriskol
Couva	Parhiep
Creamelt	Presdough
Crokvitol (Incl. erES48)	Prestine
Clarinol	Revel Liquid
Cristal Green	Revel Flakes
Sheabutter	Crockcool

Confirmation:

The processing plant Loders Croklaan BV Hogeweg 1, 1521 AZ Wormerveer, The Netherlands is an approved plant under the supervision of the Majlis Al IFTA (Council of Theological Scholars in the Netherlands/EU). This product is Halal and suitable for the Muslim consumer.

This product is Halal as long as a HFFIA Halal certificate is attached to the consignment and/ or a HFFIA Halal logo is labelled on the packaging.

Validity	Registration Number	Expiry date of the Halal Certificate
13 Months	LC/17002a/H00052/046a	After// 30-04-2018 //new application is required.

The Hague, 30 March 2017
Halal Feed and Food Inspection Authority,

ANL
H00052
180430

[redacted]

Mohamed M'Hamdi, Director.
(official functionary of Halal Feed and Food Inspection Authority)

The products mentioned in this Halal Certificate are Halal Certified in conformity with the standards of the 1) ISO/IEC 17065:2012, 2) HAS 23000:1, LPPOM-MUI 2012 and 3) Malaysian Halal Standard (MS 1500:2009, second revision).

GHC LC 17002a - 046a - 30032017 - NA.docx

2-C Kosher Certification

DIGITALKOSHER

K-ID INFORMATION

Why go looking for certificates...?
They can be delivered directly to you.
click here for more information

Click on the 7 letter K-ID to view the Kosher Certification Letter. What is a K-ID?

K-ID:	MLM-FLPW
Ingredient Name:	Shea Olein
Vendor:	Loders Croklaan B.V.
Kosher Certifier:	OK Kosher Certification
Expires On:	September 30, 2018

To subscribe to this K-ID and get e-mail notifications of updates you must log in. What's this?

To view the Kosher Certificate Letter Adobe Reader 5 or higher is required. If you have problems viewing it, please download Adobe Reader by clicking here.

Get Adobe Reader

The K-ID is a digital "Kosher Certification Letter". It is the core of what makes a paperless certification process possible. For more information click on the K-ID link.

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2-D Food Safety Certification

Lloyd's Register
LRQA

CERTIFICATE OF APPROVAL

This is to certify that the Food Safety Management System of:

Loders Croklaan B.V.
Hogeweg 1
1521 AZ Wormerveer, The Netherlands

has been assessed by Lloyd's Register Quality Assurance
and complies with the requirements of:

FOOD SAFETY SYSTEM CERTIFICATION 22000

Certification scheme for food safety systems including:
ISO 22000:2005, ISO/TS 22002-1:2009
and additional FSSC 22000 requirements.

This certificate is applicable to:

Manufacturing by wet and dry fractionation, enzymatic re-arrangement, inter-esterification, hydrogenation, refining, packing and distribution of packed and bulk vegetable specialty oils and fats.
Category: E

This certificate is provided on the basis of the FSSC 22000 certification scheme version 3, published 10 April 2013. The certification system consists of a minimal annual audit of the food safety management system and a minimal annual verification of the PRP elements and additional requirements as included in the scheme and ISO/TS 22002-1:2009.

Approval Certificate No: RQA667033

Initial Certification Date	:	18 December 2013
Current Certificate	:	18 December 2016
Certificate Expiry	:	17 December 2019

[redacted]

Issued by: Lloyd's Register Nederland B.V. for and on behalf of Lloyd's Register Quality Assurance Limited

UKAS MANAGEMENT SYSTEMS 001

FSSC 22000

K.P. van der Mandelelaan 41a, 3062 MB Rotterdam, Nederland
For and on behalf of 1 Trinity Park, Bickenhill Lane, Birmingham, B37 7ES, United Kingdom
This approval is carried out in accordance with the LRQA assessment and certification procedures and monitored by LRQA.
The use of the UKAS Accreditation Mark indicates Accreditation in respect of those activities covered by the Accreditation Certificate Number 001.

Appendix 3 Certificates of Analyses for Shea Olein

BUNGE
Loders Croklaan

CERTIFICATE OF ANALYSIS

SHEA OLEINE

Production site : Wormerveer (NL)
Production date : 21-11-2017
Production code : PD-20171121-002

Analysis

Description	Results	Units	Method
Color	3.8		ISO 27608
Odor and taste	Neutral		IN HOUSE Bunge Loders Croklaan
Peroxide value	0.1	mEqO2/kg	ISO 3960
Free fatty acid (oleic)	0.12	%	ISO 660
Unsaponifiable matter	6.06	%	ISO 3596:2000
Oleic acid	53.8	%	ISO 5508:1990
Stearic acid %	29.1	%	ISO 5508:1990
Trans fatty acids	0.2	%	ISO 5508:1990
Iron (Fe)	<0.1	mg/kg	AOAC 999.11
Copper (Cu)	<0.05	mg/kg	IN HOUSE AgroLab
Lead (Pb)	<0.05	mg/kg	IN HOUSE AgroLab
Arsenic (Ar)	<0.02	mg/kg	IN HOUSE AgroLab

Shelf-life, unopened container, as recommended:
9 months from the date of production

A. Hutten
Head Quality Assurance

A.G. Hutten
Group QA/QC Manager

BUNGE
Loders Croklaan

Bunge Loders Croklaan B.V. - Bunge Loders Croklaan Oils B.V.
Hogeweg 1 - 1521 AZ Wormerveer - P.O. Box 4 - 1520 AA Wormerveer – The Netherlands
T. +31 (0)75 629 29 11 - F. +31 (0)75 628 94 55
Homepage: www. www.bungeloders.com
Bunge Loders Croklaan B.V. - VAT no: NL001197344B01 - Chamber of Commerce Amsterdam 35011263
Bunge Loders Croklaan Oils B.V. - VAT NL813000749B01 - Chamber of Commerce Amsterdam 34204984

BUNGE
Loders Croklaan

CERTIFICATE OF ANALYSIS

SHEA OLEINE

Production site : Wormerveer (NL)
Production date : 22-11-2017
Production code : PD-20171122-004

Analysis

Description	Results	Units	Method
Color	4.9		ISO 27608
Odor and taste	Neutral		IN HOUSE Bunge Loders Croklaan
Peroxide value	0.5	mEqO2/kg	ISO 3960
Free fatty acid (oleic)	0.15	%	ISO 660
Unsaponifiable matter	6.15	%	ISO 3596:2000
Oleic acid	54.2	%	ISO 5508:1990
Stearic acid %	29.1	%	ISO 5508:1990
Trans fatty acids	0.2	%	ISO 5508:1990
Iron (Fe)	<0.1	mg/kg	AOAC 999.11
Copper (Cu)	<0.05	mg/kg	IN HOUSE AgroLab
Lead (Pb)	<0.05	mg/kg	IN HOUSE AgroLab
Arsenic (Ar)	<0.02	mg/kg	IN HOUSE AgroLab

Shelf-life, unopened container, as recommended:
9 months from the date of production

A. Hutten
Head Quality Assurance

A.G. Hutten
Group QA/QC Manager

BUNGE
Loders Croklaan

Bunge Loders Croklaan B.V. – Bunge Loders Croklaan Oils B.V.
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T. +31 (0)75 629 29 11 - F. +31 (0)75 628 94 55
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Bunge Loders Croklaan B.V. - VAT no: NL001197344B01 - Chamber of Commerce Amsterdam 35011263
Bunge Loders Croklaan Oils B.V. – VAT NL813000749B01 - Chamber of Commerce Amsterdam 34204984

BUNGE
Loders Croklaan

CERTIFICATE OF ANALYSIS

SHEA OLEINE

Production site : Wormerveer (NL)
Production date : 01-05-2018
Production code : QC-20180509-001

Analysis

Description	Results	Units	Method
Color	6.6		ISO 27608
Odor and taste	Neutral		IN HOUSE Bunge Loders Croklaan
Peroxide value	0.9	$mEqO_2/kg$	ISO 3960
Free fatty acid (oleic)	0.12	%	ISO 660
Unsaponifiable matter	6.89	%	ISO 3596:2000
Oleic acid	54.6	%	ISO 5508:1990
Stearic acid %	29.4	%	ISO 5508:1990
Trans fatty acids	0.2	%	ISO 5508:1990
Iron (Fe)	0.4	mg/kg	AOAC 999.11
Copper (Cu)	<0.05	mg/kg	IN HOUSE AgroLab
Lead (Pb)	<0.05	mg/kg	IN HOUSE AgroLab
Arsenic (Ar)	<0.02	mg/kg	IN HOUSE AgroLab

Shelf-life, unopened container, as recommended:
9 months from the date of production

A. Hutten
Head Quality Assurance

A.G. Hutten
Group QA/QC Manager

BUNGE
Loders Croklaan

Bunge Loders Croklaan B.V. – Bunge Loders Croklaan Oils B.V.
Hogeweg 1 - 1521 AZ Wormerveer - P.O. Box 4 - 1520 AA Wormerveer – The Netherlands
T. +31 (0)75 629 29 11 - F. +31 (0)75 628 94 55
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Bunge Loders Croklaan Oils B.V. – VAT NL813000749B01 - Chamber of Commerce Amsterdam 34204984

Appendix 4 Standard Contaminants Specifications of Shea Olein and Contaminants Analysis of Three Production Batches of Shea Olein

Compound	Specifications			
ELEMENTS				
Iron (Fe) (mg/kg)	max. 0.50 mg/kg	<0.1	<0.1	0.4
Copper (Cu) (mg/kg)	max. 0.05 mg/kg	<0.05	<0.05	<0.05
Arsenic (As) (mg/kg)	max. 0.10 mg/kg	<0.02	<0.02	<0.02
Lead (Pb) (mg/kg)	max. 0.10 mg/kg	<0.05	<0.05	<0.05
Cadmium (Cd) (mg/kg)	max 0.02 mg/kg	<0.02	<0.02	<0.02
Mercury (Hg) (mg/kg)	max 0.10 mg/kg	<0.005	<0.005	<0.005
Nickel (Ni) (mg/kg)	max 0.10 mg/kg	<0.06	<0.06	<0.06
MYCOTOXINS				
B1 (µg/kg)	max. 2 µg/kg	<0.1	<0.1	<0.1
B1+B2+G1+G2 (µg/kg)	max. 4 µg/kg	<0.1	<0.1	<0.1
PCB S				
PCB28+52+101+153+180 (ICES 6) (µg/kg)	max. 40 µg/kg	0.6	0.6	0.6
DIOXIN, FURANS AND DIOXIN LIKE PCB S				
Dioxin (pg/kg)	max. 0.75 pg/g	0.189	0.174	0.168
Dioxin+furans+dioxin like PCB s (pg/kg)	max. 1.25 pg/g	0.328	0.313	0.307
PAH				
Benzo(a)pyrene (µg/kg)	max. 2 µg/kg	0.2	0.3	0.1
BaP+BaA+Chr+Bbf (µg/kg)	max. 10 µg/kg	<1.0	<1.0	<1.0
GLYCIDYL FATTY ACID ESTERS EXPRESSED AS GLYCIDOL				
Glycidyl fatty acid ester (mg/kg)	max. 1mg/kg	0.8	0.9	0.9
PESTICIDES				
CHLORINE PESTICIDES				
Captafol (mg/kg)	max. 0.02 mg/kg	<0.01	<0.01	<0.01
Chlordane (mg/kg)	max. 0.02 mg/kg	<0.005	<0.005	<0.005
Campheclor (toxaphene) (mg/kg)	max. 0.1 mg/kg	<0.01	<0.01	<0.01
DDT (mg/kg)	max. 0.05 mg/kg	<0.005	<0.005	<0.005
Dichlorbenil (mg/kg)	max. 0.05 mg/kg	<0.005	<0.005	<0.005
Dieldrin (mg/kg)	max. 0.02 mg/kg	<0.005	<0.005	<0.005
Endosulfan (mg/kg)	max. 0.10 mg/kg	<0.005	<0.005	<0.005
Endrin (mg/kg)	max. 0.01 mg/kg	<0.010	<0.010	<0.010
Heptachlor (mg/kg)	max. 0.01 mg/kg	<0.005	<0.005	<0.005
Heptachlorociclohexane (mg/kg)	max. 0.01 mg/kg	<0.001	<0.001	<0.001
Hexachlorobenzene (mg/kg)	max. 0.01 mg/kg	<0.001	<0.001	<0.001
Lindane (mg/kg)	max. 0.01 mg/kg	<0.001	<0.001	<0.001
Methoxychlor (mg/kg)	max. 0.01 mg/kg	<0.005	<0.005	<0.005
Nitrofen (mg/kg)	max. 0.02 mg/kg	<0.01	<0.01	<0.01
NITROGEN PESTICIDES				
Amitraz (mg/kg)	max. 0.05 mg/kg	<0.01	<0.01	<0.01
Diclofop methyl (mg/kg)	max. 0.05 mg/kg	<0.01	<0.01	<0.01
Captan (mg/kg)	max. 0.02 mg/kg	<0.01	<0.01	<0.01
Carbaryl (mg/kg)	max. 0.05 mg/kg	<0.01	<0.01	<0.01
Procymidone (mg/kg)	max. 0.05 mg/kg	<0.01	<0.01	<0.01
Propoxur (mg/kg)	max. 0.05 mg/kg	<0.01	<0.01	<0.01
Vinclozolin (mg/kg)	max. 0.05 mg/kg	<0.01	<0.01	<0.01

Compound	Specifications	PD 20171122 002	PD 20171122 004	20180331 076
PYRETHORIDES				
Cypemethrin (mg/kg)	max. 0.05 mg/kg	<0.01	<0.01	<0.01
Deltamethrin (mg/kg)	max. 0.05 mg/kg	<0.01	<0.01	<0.01
Fenvalerate (mg/kg)	max. 0.05 mg/kg	<0.01	<0.01	<0.01
Permethrin (mg/kg)	max. 0.10 mg/kg	<0.01	<0.01	<0.01
PHOSPHOR PESTICIDES				
Azinphos methyl (mg/kg)	max. 0.05 mg/kg	<0.01	<0.01	<0.01
Acephate (mg/kg)	max. 0.05 mg/kg	<0.01	<0.01	<0.01
Bromphos ethyl (mg/kg)	max. 0.05 mg/kg	<0.01	<0.01	<0.01
Chlorphyrifos ethyl (mg/kg)	max. 0.05 mg/kg	<0.01	<0.01	<0.01
Chlorphyrifos methyl (mg/kg)	max. 0.05 mg/kg	<0.01	<0.01	<0.01
Diazinon (mg/kg)	max. 0.02 mg/kg	<0.01	<0.01	<0.01
Dichlorvos (mg/kg)	max. 0.01 mg/kg	<0.01	<0.01	<0.01
Dimethoate (mg/kg)	max. 0.05 mg/kg	<0.01	<0.01	<0.01
Disulfoton (mg/kg)	max. 0.02 mg/kg	<0.01	<0.01	<0.01
Ethion (mg/kg)	max. 0.02 mg/kg	<0.01	<0.01	<0.01
Fenitrothion (mg/kg)	max. 0.01 mg/kg	<0.01	<0.01	<0.01
Fenthion (mg/kg)	max. 0.02 mg/kg	<0.01	<0.01	<0.01
Malathion (mg/kg)	max. 0.02 mg/kg	<0.005	<0.005	<0.005
Methamidophos (mg/kg)	max. 0.01 mg/kg	<0.01	<0.01	<0.01
Methidathion (mg/kg)	max. 0.05 mg/kg	<0.01	<0.01	<0.01
Mevinphos (mg/kg)	max. 0.01 mg/kg	<0.01	<0.01	<0.01
Parathion methyl (mg/kg)	max. 0.05 mg/kg	<0.010	<0.010	<0.010
Phosphamidon (mg/kg)	max. 0.01 mg/kg	<0.01	<0.01	<0.01
Pirimiphos methyl (mg/kg)	max. 0.05 mg/kg	<0.01	<0.01	<0.01
Trichlorphon (mg/kg)	max. 0.10 mg/kg	<0.01	<0.01	<0.01
SOLVENTS				
Acetone (mg/kg)	max. not assigned	<0.1	<0.1	<0.1
Hexane (mg/kg)	max. 1mg/kg[1]	<0.1	<0.1	<0.1

[1]As per EU DIRECTIVE 2009/32/EC - https://eur-lex.europa.eu/legal content/EN/TXT/PDF/?uri=CELEX:32009L0032&from=en

Appendix 5 Chinese Approval Document For Sheanut Oil

一、乳木果油

中文名称	乳木果油	
英文名称	Shea butter (Sheanut oil, Shea oil)	
基本信息	来源：山榄科乳油木树（*Butyrospermum parkii*）果仁	
生产工艺简述	以乳油木树果仁为原料，经预处理压榨、浸提、脱乳木果胶和精炼等工艺而制成。	
质量要求	性状	白色至淡黄色半固体或固体
	脂肪酸组成（占总脂肪酸含量比）	
	硬脂酸（C18:0）	≥25%
	油酸 （C18:1）	≥25%
其他需要说明的情况	1. 使用范围：直接食用，巧克力、糖果、冰激淋、烘培产品及煎炸油，但不包括婴幼儿食品。 2. 卫生安全指标应当符合我国相关标准。	

乳木果油有关情况的说明

一、背景资料

乳木果油是从乳油木树果仁中提取的一种植物油，在非洲有着悠久而广泛的食用历史，是西非地区居民常用的烹调食用植物油之一。目前，乳木果油作为食品原料已在欧盟和美国等多个国家和地区批准使用，并广泛应用于食品加工。乳木果油与棕榈油和可可脂较为相似，是可可脂理想的替代物之一，主要用于巧克力、糖果、冰激淋、烘培产品及煎炸油，国际市场上已有 1000 多种含有乳木果油的食品。

二、安全性审查情况

根据《食品安全法》和《新食品原料安全性审查管理办法》，国家卫生计生委依照法定程序，对申请人提供的乳木果油来源、食用历史、生产工艺、质量标准、主要成分及含量、卫生学和毒理学试验以及国内外相关文献等安全性评估材料进行了审查，认为乳木果油作为食品原料在其他国家具有一定的食用历史，其卫生学和毒理学试验及相关安全性资料表明，按照公告内容生产和使用，符合食品安全要求。

三、其他需要说明的情况

该原料作为一种新的食品原料，从风险预防原则使用范围不包括婴幼儿食品。根据检测结果，该原料的卫生安全指标（理化指标、污染物）符合 GB2762、GB29921 等相关基础标准要求。

Translation

Chinese name	Shea butter	
English name	Shea butter (Sheanut oil, Shea oil)	
Basic info	Source: Kernel of *Butyrospermum parkii*	
Processing description	Shea butter is made from shea nut kernel through pressing, solvent extraction, degumming, refining and other processes.	
Quality	State	White to pale yellow solid or semi-solid
	Fatty acid composition	
	Stearic (C18:0)	≥25%
	Oleic（C18:1）	≥25%
Other descriptions	1. Usage: direct consumption in chocolate, candy, ice cream, bakery, frying oil, not including infant food products. 2. Food hygiene and safety must comply with the Chinese regulations.	

Description of shea butter

1. Background

Shea butter is vegetable oil extracted from shea nut kernel. It has long been consumed in Africa, especially as a cooking vegetable oil in West Africa. Currently, the usage of shea butter as food source has been permitted in European Union, United States as well as other countries and regions, and it is widely used in processed food. Shea butter is very similar to palm oil and cocoa butter and is an ideal substitute for cocoa butter. It can be used in chocolate, candy, ice cream, baked goods, and frying oil. There are more than 1000 food products made with shea butter currently.

2. Food Safety Review

In accordance to the Food Safety Law and “Review and Approval Procedure for Safety of New Food Ingredient”, National Health and Family Planning Committee has evaluated shea butter based on its source, consumption history, production process, quality standard, main component and composition, toxicity tests, and other literatures-based safety assessments. Considering the long consumption history of shea butter in other countries and the toxicology and relevant test results, the committee deems that shea butter meets food safety requirements, when used based on processing and consumption guidelines.

3. Others

The application of shea butter as a new food ingredient does not include infant food product in accordance to risk prevention principles. Based on test results, the hygiene and safety standards of shea butter fulfill GB2762, GB29921, and other relevant standard requirements.

Appendix 6 Acute Oral Toxicity Studies for Oleic, Palmitic and Stearic Acids (CIR, 1987)

Fatty acid tested	*Dose*	*Species (No. per group)*	*Results*
Oleic Acid[a]	5.0 g/kg	5 albino rats (bodyweight 193–217 g)	Range of BW after 7 days—235–273 g. No deaths. Signs of toxicity not reported. Oleic Acid classified "slightly toxic by ingestion"
Oleic Acid[b]	0.464, 1.00, 2.15, 4.64, 10.0, 21.5 ml/kg	5 male albino rats (BW 214–220 g)	LD_{50} > 21.5 ml/kg. Range in avg. BW gains 65–99. No deaths in any group
Oleic Acid—5.0% in cream formulation	5 ml/kg of cream	10 Fischer 344 rats (BW 135–175 g)	No deaths. Transient leg weakness, colored urine and feces
Palmitic Acid[a]	0.464, 1.00, 2.15, 4.64, 10.0 g/kg	5 male albino rats (BW 209–254 g)	Range, avg. BW gain—65–92 g. No deaths
Palmitic Acid—2.2% in shave cream formulation	5 g/kg of cream	≥ 10 albino rats (BW 200–300 g)	Formulation classified "non-toxic." No data or procedures (other than administration by gavage) reported; reference for test method - 16 CFR 1500.3(b)(6)(i)(A)
Stearic Acid (eutectic)[a]	0.464, 1.00, 2.15, 4.64, 10.0 g/kg	5 male albino rats (BW 213–223 g)	Range, avg. BW gain—71–101 g. One death in 4.64 g/kg dose group on day of dosage; one death in 4.64 g/kg dose group on final day of study
Stearic Acid—25% (w/v) in corn oil	0.464, 1.00, 2.15, 4.64, 10.0 g/kg	5 male albino rats (BW 216–225 g)	Range, avg. BW gain—90–104 g at lower doses, 77 g at 10.0 g/kg dose. One death in 10.0 g/kg on Day 7 of study
Stearic Acid—65% in ethylene oxide, diluted 1 : 3 in water	5 and 10 g/kg	10 male young adult ARS/Sprague-Dawley albino rats (BW 215–239 g)	Final avg. BW 5 g/kg group—317 g; 10 g/kg group—258 g. One death in 10 g/kg dose group on Day 5 following dosage. No pharmacotoxical signs noted. No remarkable alterations at necropsy
Stearic Acid—13% in face cream formulation	5 g/kg face cream	≥ 10 albino rats (BW 200–300 g)	Formulation classified "non-toxic." No procedures (other than administration by gavage) or data reported. Reference for test method - 21 CFR 1500.3(b)(6)(i)(A)
Stearic Acid—2.8% in skin lotion formulation	15 g/kg skin lotion	10(5M, 5F)albino rats (BW 206–258 g)	Final BW range—228–378 g. One death on Day 2
Stearic Acid—2.8% in skin lotion formulation	15 g/kg skin lotion	10(5M, 5F)albino rats (BW 218–254 g)	Final BW range—198–414 g. No deaths
Stearic Acid—2.8% in skin lotion formulation	5 g/kg skin lotion	10(5M, 5F)albino rats (BW 184–238 g)	Final BW range—174–386 g. Two deaths on Days 9 and 10
Stearic Acid—2.8% in skin lotion formulation	5 g/kg skin lotion	10(5M, 5F)albino rats (BW 202–264 g)	Final BW range—210–430 g. One female rat died on Day 7 postdosage. All rats appeared normal throughout study. At necropsy, fibrous tissue was observed encasing heart and lungs of rat that died and no gross changes were observed in other rats
Stearic Acid—2.8% in skin lotion formulation	5.0 ml/kg skin lotion	10 Sprague-Dawley rats (BW 200–254 g)	Range in BW gain—75–127 g. No deaths. All rats appeared normal throughout study. At necropsy, thoracic and abdominal organs appeared normal.
Stearic Acid—2.8% in skin lotion formulation	5.0 ml/kg skin lotion	10 Sprague-Dawley rats (BW 174–200 g)	Range in BW gain—85–118 g. No deaths. All rats appeared normal throughout study. At necropsy, thoracic and abdominal organs appeared normal
Stearic Acid—2.8% in skin lotion formulation	5.0 ml/kg skin lotion	10 Sprague-Dawley rats (BW 175–189 g)	Range in BW gain—42–118 g. No deaths. All rats appeared normal throughout study. At necropsy, thoracic and abdominal organs appeared normal
Stearic Acid—2.8% in skin lotion formulation	5.0 ml/kg skin lotion	6 Sprague-Dawley rats (BW 205–214 g)	Range in BW gain—102–129 g. No deaths. All rats appeared normal throughout study. At necropsy, thoracic and abdominal organs appeared normal
Stearic Acid	5 g/kg	rat	No deaths

[a] Fatty acid commercially supplied

[b] These studies were cited in reviews for the safety assessment of particular fatty acids as they are used in foods

Appendix 7 GRAS Associates Expert Panel Report

The Generally Recognized as Safe (GRAS) Status of the Proposed Uses of Shea Olein

January, 30 2019

BUNGE Loders Croklaan (hereinafter, "BUNGE") has concluded that shea olein is Generally Recognized As Safe (GRAS) for the proposed uses and use levels described in part 3 of their GRAS dossier on the basis of scientific procedures in accordance with Section 201(s) of the Federal Food, Drug, and Cosmetic Act. History of safe use provided corroborative evidence of safety. At the request of BUNGE, GRAS Associates, LLC, convened an independent panel of experts comprising Kara Lewis, Ph.D., Richard Kraska, Ph.D., DABT, and Richard Lane, Ph.D., DABT, to evaluate BUNGE's GRAS conclusion for the proposed uses and use levels. The GRAS Panel† has the requisite scientific training and experience in the safety of food and food ingredients to conduct this evaluation.

The GRAS Panel independently and critically reviewed information about the chemical composition, manufacturing process, specifications for, and stability of shea olein; the regulatory history of related substances; the estimated exposure resulting from the proposed use and use levels; and studies on the safety and toxicity of shea olein and other related substances.

Shea olein is a product of the fractionation and refinement of shea butter. Shea butter has a long history of use for cooking in Africa and Europe well prior to 1958. It is one of the six vegetable fats (other than cocoa butter) that is permitted to be added to chocolate products in the European Union (EU Directive 2000/36/EC). In addition, FDA established that sheanut oil, the stearine fraction of shea butter, is generally recognized as safe (21 CFR§184.1702).

BUNGE has shown that their shea olein is manufactured using a process that is equivalent to the process commonly used for the fractionation and refining of other commonly consumed vegetable oils and fats. The processing aids and

† Dr. Lewis, Chair of the Expert Panel, is a biologist with more than 10 years of experience preparing GRAS dossiers. Dr. Kraska is a toxicologist who worked on GRAS and food additive safety issues within FDA's GRAS Review Branch earlier in his career, and subsequently continued working within this area in the private sector. Dr. Lane is a board certified toxicologist who has worked on food safety issues, GRAS evaluations and food additive petitions for over 25 years. All three panelists have extensive technical backgrounds in the evaluation of food ingredient safety and in participating in deliberations of GRAS Expert Panels.

chemicals used in the manufacturing of shea olein are of food grade quality. The production of shea olein is carried out in accordance with Current Good Manufacturing Practice (CGMP) regulations. Shea olein is composed of approximately 92% w/w triglycerides and 8% unsaponifiable matter. The triglycerides and fatty acids present in shea olein are identical to those found in common edible vegetable oils and fats. Phytosterols account for almost all the unsaponifiable matter in shea olein, as is the case with other vegetable oils. Food grade specifications for shea olein have been established by BUNGE and three lots of shea olein have been shown to meet these specifications. Shea olein satisfies the criteria for edible fats and oils not covered by individual standards as described in the Codex Alimentarius (Codex Alimentarius, 1981b). Shea olein also satisfies standards for unrefined shea butter that can be used for direct food consumption (Codex Alimentarius, 2017). BUNGE has shown that shea olein is stable following nine months of storage at ambient temperature.

BUNGE proposes a maximum level of sterols of 9%, which is a higher level than the 1.5% limit for unsaponifiable matter currently specified for shea butter.

The GRAS Panel reviewed the published scientific literature addressing the safety and toxicity of shea olein as well as unpublished studies. No evidence of reproductive toxicity or carcinogenicity was observed for oral doses of shea olein at levels equivalent to 7.5 g/kg bw/day. A published subchronic toxicity study revealed that the addition of BUNGE's shea olein at 20% of the diet (10 to 15 g/kg bw/day) was well tolerated by rats and appeared to have no adverse effects. Unpublished studies showed that shea olein was not genotoxic as evidenced from a bacterial reverse mutation test or an in vitro micronucleus test. In an unpublished, but publicly available study, a new dietary ingredient containing shea that had a high level of unsaponifiable matter did not show genotoxicity or acute toxicity. In addition, a study in which daily intragastric doses of a supplement containing 50-70% of shea unsaponifiable matter was administered for 12 weeks did not report gross evidence of toxicity.

Published human studies in which doses of 1.5±3.3 g/day of a spread enriched with shea sterol extract, 3.3 g/day sheanut oil sterols, and 2.6 g/day 4,4-dimethylsterols (4,4-DMS) did not report adverse effects, with the exception of a small reduction in beta carotene absorption in the study with 3.3 g/day sheanut oil sterols. In addition, studies on Shea Flex products, which include 70 to 75% shea derived 4,4-DMS did not mention adverse effects when administered at a dose of 2.25 g (1.575 g sterols) or 2.16 g/day (1.62 g sterols). The human studies reviewed show that doses of up to 3.3 g/day of shea-derived sterols are safe.

The estimated daily intakes of shea olein, using NHANES data and anticipated use levels, for the total population of consumers resulting from the proposed uses would be 0.26 and 0.56 g/kg bw/day and 15.24 g/day and 30.33 g/day for persons at the mean and 90th percentiles, respectively. Adult males would be the highest consumers with consumption levels of 34.27 g/day. The Institute of Medicine (IOM) stated that the acceptable distribution range for the percent of energy intake as fat for children ages 1 to 3 years, children ages 4 to 18 years, and adults were 30 to 40%, 25-35% and 20-35%, respectively (IOM, 2005). Based on a 2,000 calories per day diet, adults would consume 400 to 700 calories as fat per day. This is equivalent to 44 to 78 g of fat per day. Consumption of shea olein would be fall below the upper limit of the range .

Global shea nut supply is limited compared to other sources of vegetable oil. It is estimated that if the entire global shea supply was converted to shea olein and consumed entirely in the United States that the per capita consumption would be 0.74 g/person/day. Multiplying this by a factor of 3 to estimate 90th percentile consumption, yields an estimate of 2.2 g/person per day (31.7 mg/kg bw/day) for shea olein.

Sterols account for at most 8% of olein consumption or approximately 2.8 g sterols/day. This is a more reasonable estimate of maximum exposure to DMS.

The GRAS panel believes that this level of consumption is safe based on the results of the toxicology studies and history of safe use in Africa and Europe. The GRAS Panel notes the review by the Joint FAO/WHO GRAS Committee on Food Additives (JECFA) which set an acceptable daily intake (ADI) of 0–40 mg/kg bw for desmethyl phytosterols, phytostanols and their esters from various plant sources.

Based on the available evidence, including several published toxicology studies and a long history of safe consumption in Africa and Europe, the GRAS Panel considers it reasonable to conclude that the proposed uses of shea olein with the proposed food grade specifications are safe. All critical data on which the Panel's conclusion is based are publicly available. In addition, several unpublished studies add corroborative evidence that shea olein, with the proposed specifications, is safe. BUNGE Loders Croklaan has assured the GRAS Panel that all relevant unpublished information have been discussed.

Conclusion

Following an independent, critical evaluation, the GRAS Panel conferred and unanimously agreed that BUNGE's shea olein, when produced in accordance with Current Good Manufacturing principles and when used as proposed by BUNGE, is Generally Recognized As Safe.

Kara Lewis, Ph.D., Chair

Richard Lane, Ph.D., DABT

Richard Kraska, Ph.D., DABT

From:	Ginny Bank
To:	DiFranco, Stephen; William J. Rowe; Amy Mozingo
Subject:	Re: GRN 850 Clarification on Methods used
Date:	Wednesday, January 15, 2020 9:58:54 AM
Attachments:	image001.png

HI Steve
I have confirmed with the manufacturer that the methods are validated.
Do they need to provide a statement from the external lab or proof of internal validation?

Ginny

Ginny Bank
Senior Associate
GRAS Associates
(720) 304-7335
(303) 809-8082

From: "DiFranco, Stephen" <Stephen.DiFranco@fda.hhs.gov>
Date: Tuesday, January 14, 2020 at 10:04 AM
To: Will Rowe <wrowe@nutrasource.ca>, Amy Mozingo <amozingo@gras-associates.com>, Ginny Bank <gbank@gras-associates.com>
Subject: GRN 850 Clarification on Methods used

Good Afternoon,

In reviewing GRN 850 for shea olein we had a minor question for clarification; The notice lists specifications for their shea olein along with methods used to verify that produced shea olein meets these specifications. Our chemists would like conformation that these methods are validated for the use presented.

Please feel free to respond via email such that I may include it with the administrative record on this.

Best,

Steve

Stephen DiFranco, PhD
Regulatory Review Scientist/Chemist

Center for Food Safety and Applied Nutrition
Office of Food Additive Safety
Division of Food Ingredients
U.S. Food and Drug Administration
Tel: 240-402-2710

stephen.difranco@fda.hhs.gov

From:	Ginny Bank
To:	DiFranco, Stephen
Cc:	Amy Mozingo; William J. Rowe
Subject:	Re: GRN 000850 Update Request
Date:	Tuesday, March 03, 2020 12:50:35 PM
Attachments:	image001.png image007.png image013.png

Hi Stephen

Yes, both of these are typos. Thank you for correcting them.
We look forward to receiving the final response.

Ginny

Ginny Bank
Senior Associate
GRAS Associates
(720) 304-7335
(303) 809-8082

From: "DiFranco, Stephen" <Stephen.DiFranco@fda.hhs.gov>
Date: Tuesday, March 3, 2020 at 8:41 AM
To: Ginny Bank <gbank@gras-associates.com>
Cc: Amy Mozingo <amozingo@gras-associates.com>, Will Rowe <wrowe@nutrasource.ca>
Subject: RE: GRN 000850 Update Request

Good Morning Ginny,

We hope to have our response letter to you soon.

In drafting the response there were a few items that came up I was hoping that you could comment on:

Page 7 of the notice lists the CAS Registry number for Shea Olein as 93348-6-9. This is not a valid CAS Reg. number. We note that the notified ingredient is identified by CAS Reg. No. 93348-**61**-9, and this was likely a typo. Please confirm this change for the administrative record.

Page 18 of the notice states that the shea tree is in the Saponaceae family. FDA notes that the shea tree actually belongs to the Sapotacae family. Again, we believe this was a simple typo but would like that confirmed for the administrative record.

Thanks,

Steve

Stephen DiFranco, PhD
Regulatory Review Scientist/Chemist

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

From: Ginny Bank <gbank@gras-associates.com>
Sent: Monday, March 02, 2020 4:43 PM
To: DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>; William J. Rowe <wrowe@nutrasource.ca>
Cc: Amy Mozingo <amozingo@gras-associates.com>
Subject: Re: GRN 000850 Update Request

Dear Dr. DiFranco

We are following up on GRN 850 as you had hoped to have a response by 2/23/20.

Thank you.

Ginny Bank

Ginny Bank
Senior Associate
GRAS Associates
(720) 304-7335
(303) 809-8082

From: "DiFranco, Stephen" <stephen.difranco@fda.hhs.gov>
Date: Friday, December 13, 2019 at 11:38 AM
To: Will Rowe <wrowe@nutrasource.ca>
Cc: Amy Mozingo <amozingo@gras-associates.com>, Ginny Bank <gbank@gras-associates.com>
Subject: RE: GRN 000850 Update Request

Good afternoon Mr. Rowe,

Unfortunately, review of GRN 850 is taking a little longer than I had hoped. In accordance with 21 CFR 170.265 (b)(2) we are extending the review time frame by an additional 90 days from the original 180-day date. Our records indicate that the notice was filed on May 29, 2019, which puts the 180-day date November 25, 2019. We hope to get you a response by February 23, 2020, although I do not anticipate it taking us that long. We thank you for your continued patience in this matter.

Best,

Steve

Stephen DiFranco, PhD
Chemist/Consumer Safety Officer

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

From: William J. Rowe <wrowe@nutrasource.ca>
Sent: Friday, December 13, 2019 1:20 PM
To: DiFranco, Stephen <Stephen.DiFranco@fda.hhs.gov>
Cc: Amy Mozingo <amozingo@gras-associates.com>; Ginny Bank <gbank@gras-associates.com>
Subject: GRN 000850 Update Request

Dear Mr. DiFranco,

On May 29, 2019 FDA filed a GRAS notice for shea olein (GRN 000850), which was submitted by GRAS Associates on behalf of BUNGE Loders Croklaand on March 13, 2019.

It has been more than 180 days since the notice was filed and more than 9 months since it was received by FDA. We would appreciate it if you could let us know the status of the notice.

I am copying my colleagues Amy Mozingo and Ginny Bank of GRAS Associates LLC and give permission for them to receive all further communications regarding this GRAS notice.

Thank you!

Will

William J. Rowe, BA

President, CEO and Co-Founder

O: 519-341-3360 | C: 519-827-8129

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