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ST. LOUIS, MISSOURI 63167  
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BY: -----

Chloe Pavely  
Regulatory Affairs Manager  
(314) 694-8553

February 25, 2009

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

RE: GRAS Notice for Stearidonic (SDA) Omega-3 Soybean Oil

Dear Dr. Martin:

Monsanto has developed and intends to market stearidonic (SDA) omega-3 soybean oil. As defined in the attached GRAS Notice, stearidonic (SDA) omega-3 soybean oil is GRAS on the basis of scientific procedures under specific conditions of use as a food ingredient. Information setting forth the basis for the GRAS determination, which includes a comprehensive summary of the data available and reviewed by an independent panel of experts in support of the safety of stearidonic (SDA) omega-3 soybean oil under the intended conditions of use, as well as *curricula vitae* evidencing the qualifications of the members of the panel of experts for evaluating the safety of food ingredients, are enclosed. Based on this GRAS determination and consistent with proposed 21 CFR §170.36 [Notice of a claim for exemption based on a Generally Recognized As Safe (GRAS) determination] published in the *Federal Register* (62 FR 18938) of the *Federal Food, Drug, and Cosmetic Act*, the use of stearidonic (SDA) omega-3 soybean oil in food as described in the notice is exempt from the requirement of premarket approval.

On February 6<sup>th</sup>, 2009 Monsanto met to inform the Center for Food Safety and Applied Nutrition (CFSAN) about stearidonic (SDA) omega-3 soybean oil and to discuss the rationale for stearidonic (SDA) omega-3 soybean oil being GRAS. As part of the FDA GRAS notification process, Monsanto is now submitting the enclosed GRAS Notice for stearidonic (SDA) omega-3 soybean oil.

Dr. Martin  
February 25, 2009

Should you have any questions concerning this GRAS Notice, please contact Dr. Russell Schneider, Regulatory Affairs Director, Washington DC, at 202-383-2866, or me at 314-694-8553.

Sincerely,

Chloe Pavely  
Regulatory Affairs Manager

cc: R. Schneider, Ph.D., Monsanto, Washington, DC  
Regulatory Files

enc.: Four paper copies of the GRAS Notice for stearidonic (SDA) omega-3 soybean oil  
One CD containing the GRAS Notice for stearidonic (SDA) omega-3 soybean oil and the  
*Curricula vitae* of the expert panel members

## **GRAS Notice for Stearidonic (SDA) Omega-3 Soybean Oil**

***Prepared for:***

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

***Prepared by:***

Monsanto Company  
800 North Lindbergh Blvd.  
St. Louis, MO 63167  
U.S.A.

February 25, 2009  
Monsanto 09-SY-195F

# STEARIDONIC (SDA) OMEGA-3 SOYBEAN OIL GRAS NOTICE

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## I GRAS EXEMPTION CLAIM

### A. Claim of Exemption From the Requirement for Premarket Approval Pursuant to Proposed 21 CFR §170.36(c)(1) [62 FR 18938 (17 April 1997)] (U.S. FDA, 1997)

As defined herein, stearidonic (SDA) omega-3 soybean oil has been determined by Monsanto Company (Monsanto) to be Generally Recognized as Safe (GRAS) for use in a variety of traditional food products. This determination is based on scientific procedures, as described in the following sections, under the conditions of intended use in food. Therefore, consistent with Section 201(s) of the *Federal Food, Drug, and Cosmetic Act*, the use of SDA soybean oil in food as described below is exempt from the requirement of premarket approval.

Signed,

---

Raymond C. Dobert, PhD  
Lead, US Biotech Regulatory Affairs  
Monsanto Company

---

Date

### B. Name and Address of Notifier

Raymond C. Dobert, PhD  
Lead, US Biotech Regulatory Affairs  
800 North Lindbergh Blvd.  
St. Louis, MO 63167  
U.S.A.

### C. Common Name of the Notified Substance

Stearidonic (SDA) omega-3 soybean oil

### D. Conditions of Intended Use in Food

Monsanto intends to market SDA soybean oil as a food ingredient in the United States in a variety of food products including baked goods and baking mixes, breakfast cereals and grains, cheeses, dairy product analogs, fats and oils, fish products, frozen dairy desserts and mixes, grain products and pastas, gravies and sauces, meat products, milk products, nuts and nut products, poultry products, processed fruit juices, processed vegetable products, puddings

## STEARIDONIC (SDA) OMEGA-3 SOYBEAN OIL GRAS NOTICE

and fillings, snack foods, soft candy, and soups and soup mixes. SDA soybean oil will be added to foods at levels that provide 375 mg SDA/serving.

### **E. Basis for the GRAS Determination**

Pursuant to 21 CFR § 170.30, SDA soybean oil has been determined by Monsanto to be GRAS on the basis of scientific procedures (U.S. FDA, 2008). This GRAS determination is based on data generally available in the public domain pertaining to the safety of SDA soybean oil, as discussed herein and in the accompanying documents, and on a consensus among a panel of experts<sup>1</sup> who are qualified by scientific training and experience to evaluate the safety of SDA soybean oil as a component of food [see Appendix A-1, entitled, “**EXPERT PANEL CONSENSUS STATEMENT REGARDING THE GENERALLY RECOGNIZED AS SAFE (GRAS) STATUS OF MONSANTO’S STEARIDONIC (SDA) OMEGA-3 SOYBEAN OIL FOR USE IN FOODS**” and Appendix A-2, entitled “**EXPERT PANEL REPORT CONCERNING THE NEW PROPOSED FOOD USES OF MONSANTO’S STEARIDONIC (SDA) OMEGA-3 SOYBEAN OIL IN FOODS**”].

### **F. Availability of Information**

The data and information that serve as the basis for this GRAS Notification will be sent to the U.S. Food and Drug Administration (FDA) upon request, or will be available for review and copying at reasonable times at the offices of:

Monsanto Company  
800 North Lindbergh Blvd.  
St. Louis, MO 63167  
U.S.A.

Should the FDA have any questions or additional information requests regarding this notification, Monsanto will supply these data and information.

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<sup>1</sup> The panel of experts consisted of Joseph F. Borzelleca, Ph.D. (Virginia Commonwealth University School of Medicine), Fergus M. Clydesdale, Ph.D. (University of Massachusetts Amherst), Ernst J. Schaefer, M.D. (Tufts University), and Ronald Walker, Ph.D. (University of Surrey).

## II. DETAILED INFORMATION ABOUT THE IDENTITY OF THE SUBSTANCE

### A. Identity

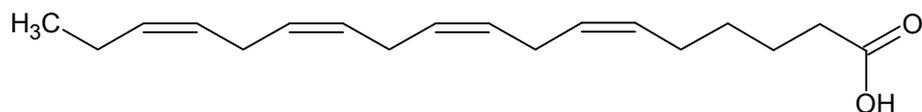
The fatty acid composition of stearidonic (SDA) omega-3 soybean oil (SDA soybean oil) produced from soybean variety MON 87769 (SDA soybean) is significantly different from conventional soybean oil. SDA soybean oil contains 15 to 30% SDA, which is not present in conventional soybean oil, 5 to 8% *gamma*-linolenic acid (GLA) (also not present in conventional soybean oil), and slightly higher levels of *alpha*-linolenic acid (ALA) and palmitic acid than in conventional soybean oil. It also contains lower levels of oleic acid and linoleic acid (LA) than those present in conventional soybean oil. The common or usual names for the fatty acids present at higher levels in SDA soybean oil compared to conventional soybean oil are presented in Table 1.

<b>Table 1 Common or Usual Name and Scientific Name for Fatty Acids Present at Higher Levels in SDA Soybean Oil Compared to Conventional Soybean Oil</b>	
<b>Common Name</b>	<b>Chemical Name</b>
Stearidonic Acid (SDA)	all cis-octadeca-3,6,9,12-tetraenoic acid
<i>Gamma</i> -linolenic acid (GLA)	all cis-6,9,12-Octadecatrienoic acid
<i>Alpha</i> -linolenic acid (ALA)	all-cis-3,6,9-Octadecatrienoic acid
Palmitic acid	Hexadecanoic acid

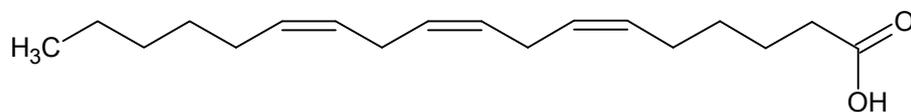
There is no Chemical Abstracts Services (CAS) number for SDA soybean oil. The CAS numbers, as well as the empirical formulae and molecular weights of the fatty acids present at higher levels in SDA soybean oil compared to conventional soybean oil are summarized in Table 2. Structural formulae of these fatty acids are presented in Figure 1.

<b>Table 2 CAS Numbers, Empirical Formulae, and Molecular Weights of Fatty Acids Present at Higher Levels in SDA Soybean Oil Compared to Conventional Soybean Oil</b>			
<b>Fatty Acid</b>	<b>CAS Number</b>	<b>Empirical Formula</b>	<b>Molecular Weight</b>
SDA	20290-75-9	C <sub>18</sub> H <sub>28</sub> O <sub>2</sub>	276.417
GLA	506-26-3	C <sub>18</sub> H <sub>30</sub> O <sub>2</sub>	278.433
ALA	463-40-1	C <sub>18</sub> H <sub>30</sub> O <sub>2</sub>	278.433
Palmitic acid	57-10-3	C <sub>16</sub> H <sub>32</sub> O <sub>2</sub>	256.427

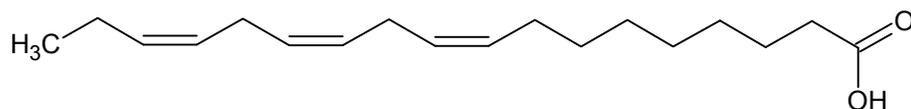
## STEARIDONIC (SDA) OMEGA-3 SOYBEAN OIL GRAS NOTICE



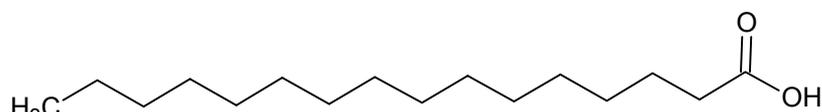
SDA (C18:4)



GLA (C18:3n-6)



ALA (C18:3n-3)



Palmitic Acid (C16:0)

**Figure 1 Structural Formulae of the Fatty Acids Present at Higher Levels in SDA Soybean Oil Compared to Conventional Soybean Oil**

### B. Method of Manufacture

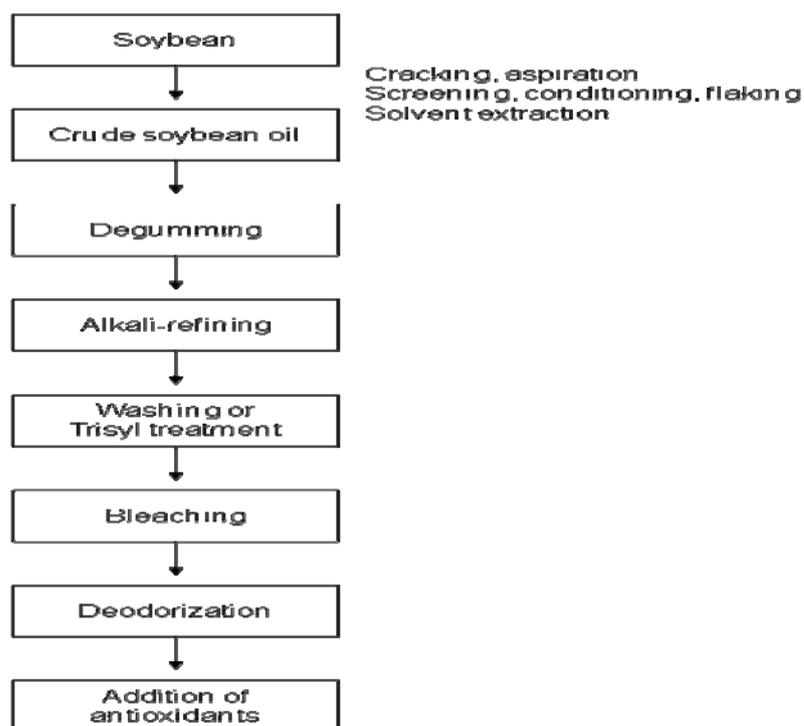
The production of SDA in soybean MON 87769 involves the introduction of two desaturase genes that encode for the proteins, *Primula juliae*  $\Delta 6$  desaturase and *Neurospora crassa*  $\Delta 15$  desaturase. Soybeans lack  $\Delta 6$  desaturase and the minimal requirement for production of SDA in soybeans would be the introduction of a gene encoding  $\Delta 6$  desaturase. However,  $\Delta 6$  desaturase also may convert LA to GLA. Addition of a  $\Delta 15$  desaturase with temporal expression similar to the  $\Delta 6$  desaturase increases the flux of ALA to SDA. The  $\Delta 15$  desaturase also lowers LA levels, thus lowering the substrate pool for GLA production. Compositional data on several lots of SDA soybean oil support the opinion that the phenotype is stable over several generations.

SDA soybean oil is processed using conventional industry standard processing methods, which include extrusion methods (Erickson *et al.*, 1980). Following cracking and aspiration of the soybeans to separate the hulls, the hulls are screened to recover the fines generated during cracking, and the cracked soybean meats are conditioned and flaked to rupture oil cells and prepare a thin flake with a large surface area for solvent extraction. The soybean flakes then undergo solvent extraction with iso-hexane/hexane to yield crude soybean oil and soybean meal. The crude oil is processed through a series of steps known as refining.

## STEARIDONIC (SDA) OMEGA-3 SOYBEAN OIL GRAS NOTICE

In the first step, phospholipids are removed through a process known as “degumming”. This involves mixing with water or an acid solution to form “gums”, followed by centrifugation. The fatty acids in the degummed oil are neutralized through the addition of a caustic solution (sodium hydroxide). The resulting soap solution is removed by centrifugation. Water washing and centrifugation or treatment with a suitable adsorbent followed by filtration removes soaps to levels compatible with bleaching. In the next step, the oil is “bleached” by mixing with a citric acid solution, followed by treatment with adsorbent clay to remove the peroxides, phosphatides, color bodies and traces of soap. Under vacuum to inhibit oxidation, the pigments are adsorbed and removed by filtration. In the final refining step, odoriferous components, flavor components and additional free fatty acids are removed by steam distillation. This process of deodorization is carried out at high temperatures (typically 225°C to 255°C) under vacuum. Permitted anti-oxidants (e.g., Tenox-20) are utilized to inhibit oxidation of the oil.

SDA soybean oil is produced using commercial food-grade soybean oil manufacturing practices with food-grade raw materials and processing agents. Because traditional soybean oil manufacturing processes are used to produce SDA soybean oil, which is well-characterized, the altered fatty acid profile of SDA soybean oil is a reflection of the SDA soybean variety and not due to or impacted by the manufacturing process. A schematic diagram of the manufacturing process for SDA soybean oil is presented in Figure 2. All processing aids used in the manufacture of SDA soybean oil are used in compliance with appropriate federal regulations (see Table 3).



**Figure 2 Schematic Overview of the Manufacturing Process for SDA Soybean Oil**

**STEARIDONIC (SDA) OMEGA-3 SOYBEAN OIL GRAS NOTICE**

<b>Table 3 List of Processing Aids Used In the Manufacture of SDA Soybean Oil</b>	
<b>Processing Aids Used in the Manufacture of SDA Soybean Oil</b>	<b>Reference to Appropriate Use in Food</b>
Iso Hexane/Hexane	21 CFR §172.340 Fish protein isolate (hexane is cleared as a solvent in the removal of lipids from fish protein isolate) 21 CFR §173.270 (hexane is cleared for use when present as a residue from the extraction of spices and in the production of hop extracts) No federal regulations pertaining to the use of hexane as a processing agent for use in the extraction of vegetable oils exist. However, hexane and similar paraffinic hydrocarbons have a long-history (pre-1958) of use in the manufacture of food oils in this regard; therefore these uses would be considered GRAS. The use of isohexane/hexane should be limited to current Good Manufacturing Practices (cGMP).
Anhydrous Citric Acid (diluted to 50% solution)	21 CFR §184.1033 Citric acid
Sodium Hydroxide	21 CFR §184.1763 Sodium hydroxide
Phosphoric Acid	21 CFR §182.1073 Phosphoric acid
Trisyl S165	21 CFR §177.2250 Filters, microporous polymeric
Tonsil 167 FF Bleaching Clay (Darco Carbon)	21 CFR §186.1256 Clay (kaolinin)
Antioxidants (Tenox™-20)	Tenox-20 consists of propylene glycol, citric acid, and tertiary butylhydroquinone (TBHQ). 21 CFR §184.1666 Propylene glycol 21 CFR §184.1033 Citric acid 21 CFR §172.185 TBHQ

CFR = Code of Federal Regulations

**C. Specifications for Food-Grade Material**

The product specifications and methods of analysis for SDA soybean oil are presented in Tables 4 and 5. Food Chemicals Codex (FCC) specifications for conventional soybean oil also are included for comparative purposes.

STEARIDONIC (SDA) OMEGA-3 SOYBEAN OIL GRAS NOTICE

<b>Table 4 Specifications and Analytical Methods for Soybean Oil (FCC) and SDA Soybean Oil (Monsanto)</b>			
<b>Parameter</b>	<b>FCC Soybean Oil Specification</b>	<b>SDA Soybean Oil Specification</b>	<b>Analysis Method</b>
Fatty acid composition	Please see Table 5	Please see Table 5	AOCS Ch 2a-94, Ce 1f-96
Cold test	Passes test	n/a <sup>1</sup>	n/a
Lovibond color (Yellow)	NMT 20	NMT 20	AOCS Cc 13j-97 (Lovibond)
Lovibond color (Red)	NMT 2.0	NMT 2.0	AOCS Cc 13j-97 (Lovibond)
Free fatty acids	NMT 0.1%	NMT 0.1%	AOCS Ca 5a-40
Iodine value	120 – 143	160 – 210	AOCS Tg 1a-64 (modified: POS Method IN-LS-26)
Lead	NMT 0.1 mg/kg	NMT 0.1 mg/kg	FCC Lead Limit Test, Atomic Absorption Spectrophotometric Graphite Furnace Method II
Peroxide value	NMT 10 meq/kg	NMT 10 meq/kg	AOCS Cd 8-53
Stability, Active oxygen method (AOM)	NLT 7 h	NLT 2 h	AOCS Cd 12-57
Unsaponifiable matter	NMT 1.5 %	NMT 1.5%	AOCS Ca 6a-40
Water	NMT 0.1%	NMT 0.1%	AOCS Ca 2c-25

n/a = not available; NLT = not less than; NMT = not more than

<sup>1</sup> Cold test was not included in the specifications for SDA soybean oil because SDA soybean oil will only be included as an ingredient in food and beverage products and will not be marketed itself as a retail product; thus, cloudiness of the oil (as measured by the cold test) is not relevant.

<b>Table 5 Specifications for Fatty Acid Composition of Soybean Oil (FCC) and SDA Soybean Oil</b>		
<b>Fatty acid</b>	<b>FCC Soybean Oil Specification (% weight)</b>	<b>SDA Soybean Oil Specification (% weight)</b>
<C14	<0.1	<0.1
C14:0 (myristic)	<0.5	<0.5
C16:0 (palmitic)	7.0 – 12	9 – 13
C16:1 (palmitoleic)	<0.5	<0.5
C18:0 (stearic)	2.0 – 5.5	2.0 – 5.5
C18:1 (oleic)	19 – 30	10 – 20
C18:2 (linoleic)	48 – 65	15 – 30
C18:3n-3 ( <i>alpha</i> -linolenic)	5 – 10	9 – 12
C18:3n-6 ( <i>gamma</i> -linolenic)	n/a	5 – 8
C18:4 (stearidonic)	n/a	15 – 30
C20:0 (arachidic)	<1.0	<1.0
C20:1 (eicosenoic)	<1.0	<1.0
C22:0 (behenic)	<0.5	<0.5
C22:1 (erucic)	<0.1	<0.1
C24:0 (lignoceric)	<0.3	<0.3

n/a = not available

## **STEARIDONIC (SDA) OMEGA-3 SOYBEAN OIL GRAS NOTICE**

For SDA soybean oil, the specifications for iodine value are higher compared to conventional soybean oil due to the increased levels of unsaturated fatty acids in SDA soybean oil. However, the specifications for iodine value of SDA soybean oil are similar to that of other oils rich in omega-3 fatty acids such as menhaden oil (AOCS, 2006).

### **Product Analysis**

Batch analyses data for several lots of SDA soybean oil produced from several generations of SDA soybeans and grown at various U.S. locations confirm that the manufacturing process produces a consistent product in terms of its chemical composition. Batch analyses results for 5 non-consecutive lots of SDA soybean oil are presented in Appendix B (Table B-1).

### **Stability of SDA soybean oil**

Results of stability testing demonstrate that SDA soybean oil is stable, with respect to peroxide value and fatty acid content, for at least 72 days when stored at room temperature, and for at least 4 to 5 days under accelerated conditions (55°C in air). More importantly, when stored under nitrogen at room temperature (typical storage conditions for commercial soybean oil) for as long as 9 months, SDA soybean oil still maintains a peroxide value similar to that of conventional soybean oil. See Appendix B-2 for details on product stability.

### **III. SELF-LIMITING LEVELS OF USE**

The use of SDA soybean oil is limited by the level of fat that can be added to the proposed foods.

## IV. BASIS FOR GRAS DETERMINATION

### A. Documentation to Support the Safety of SDA Soybean Oil

The determination that SDA soybean oil is GRAS is on the basis of scientific procedures, and the information supporting the general recognition of the safe use of SDA soybean oil includes:

- A long-standing history of safe consumption of SDA from several marine and plant sources as well as the fact that, in human fatty acid metabolism, SDA is an intermediate in the production of EPA and DHA from dietary ALA.
- Data pertaining to the identity, intended use, and estimated intake of SDA soybean oil. The exposure to SDA from the proposed food uses of SDA soybean oil is estimated to be no more than 2.2 g/day at the mean, and 4.2 g/day at the 90<sup>th</sup> percentile.
- Data pertaining to the manufacturing of SDA soybean oil [*i.e.*, it is manufactured in accordance with current Good Manufacturing Practice (cGMP) and meets appropriate food-grade specifications].
- Results of a published 90-day/one generation reproductive toxicity rat study in which a no-observed-adverse-effect level (NOAEL) of 1 g SDA/kg body weight/day (4 g Monsanto's SDA soybean oil/kg body weight/day) was determined.
- A published human study in which subjects consumed 3.66 g SDA (from a Monsanto SDA soybean oil)/day for 16 weeks and no adverse effects attributable to SDA soybean oil were reported.
- Additional published toxicological and nutritional studies on SDA and GLA from other sources.
- The regular dietary consumption of fats and oils containing ALA, LA, and palmitic acid, and by the permitted uses of LA and palmitic acid in food in the U.S.

Moreover, these data were reviewed by a panel of experts, qualified by scientific training and experience to evaluate the safety of ingredients as components of food, who concluded that the proposed uses of SDA soybean oil are safe and suitable and are GRAS based on scientific procedures [see Appendix A-1, entitled, "**EXPERT PANEL CONSENSUS STATEMENT REGARDING THE GENERALLY RECOGNIZED AS SAFE (GRAS) STATUS OF MONSANTO'S STEARIDONIC (SDA) OMEGA-3 SOYBEAN OIL FOR USE IN FOODS**" and Appendix A-2, entitled "**EXPERT PANEL REPORT CONCERNING THE NEW PROPOSED FOOD USES OF MONSANTO'S STEARIDONIC (SDA) OMEGA-3 SOYBEAN OIL IN FOODS**"]. A summary of the data is presented herein.

**B. Estimated Intake of SDA Soybean Oil**

SDA soybean oil is intended for use in a variety of food products including baked goods and baking mixes, breakfast cereals and grains, cheeses, dairy product analogs, fats and oils, fish products, frozen dairy desserts and mixes, grain products and pastas, gravies and sauces, meat products, milk products, nuts and nut products, poultry products, processed fruit juices, processed vegetable products, puddings and fillings, snack foods, soft candy, and soups and soup mixes at levels that will provide 375 mg SDA per serving. James *et al.* (2003), using a dose of 1.5 g SDA/day, reported an increase in erythrocyte eicosapentaenoic acid (EPA) levels, which in combination with docosahexaenoic acid (DHA) levels has been reported to correlate with reduced risk of cardiovascular disease (Harris and von Schacky, 2004). On the basis of this study, Monsanto recommends that the daily minimum intake be 1.5 g SDA/day. The individual proposed food uses and use levels are presented in Table 6. Monsanto does not intend to sell SDA soybean oil as a pure supplement.

<b>Table 6 Proposed Food Uses for SDA Soybean Oil</b>	
<b>FDA Food Classifications (21 CFR §170.3(n))<sup>1</sup></b>	<b>Relevant Examples</b>
Baked goods and baking mixes	Biscuits, bagels, tortillas, English muffins <sup>2</sup>
	Breads
	Cookies
	Cakes
	Crackers
	Bars
Breakfast Cereals & Grains	Breakfast Cereals
Cheeses	Cottage Cheese
	Cheese
Dairy Product Analogs	Cream substitutes
	Soy milk
Fats & Oils	Margarine/Spreads <sup>3</sup>
	Mayonnaise
	Dressings for Salads
Fish Products	Entrees with Sauce
Frozen Dairy Desserts and Mixes	Milk desserts and frozen yogurt
	Novelties <sup>4</sup>
Grain Products and Pastas	Pasta
Gravies and Sauces	Main entrée sauces (spaghetti sauces)
Meat Products	Entrees with sauce, hot dogs, luncheon meat
Milk Products	Milk Based Drinks
	Milk Shakes
	Yogurt
Nuts and Nut Products	Peanut Butter
Poultry Products	Entrees with sauce, luncheon meat
Processed Fruit Juices	Fruit Drinks, Fruit Smoothies

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Processed Vegetable Products	Vegetable Juices
Puddings and fillings	Pudding
Snack Foods	All varieties
Soft Candy	Candy bars
Soups and soup mixes	Processed soups (not home made)

<sup>1</sup> Categories as defined in Food and Drug Administration's Reference amounts customarily consumed per eating occasion (21 CFR §101.12).

<sup>2</sup> Only select food categories listed under 21 CFR §101.12. e.g., bagels, tortillas, and wraps.

<sup>3</sup> Excludes margarines whose name indicated >80% fat content.

<sup>4</sup> Defined a "novelty" as any food sold as a single serve item (e.g. milk dessert bar, or stick).

The consumption of SDA soybean oil from all proposed food uses was estimated using the proposed food uses and use levels in conjunction with food consumption data included in the National Health and Nutrition Examination Surveys (NHANES 1999-2002) (CDC, 2007).

The current intake of fat, *trans* fat, and fatty acids in the diet as well as intake following the addition of 20 or 30% SDA soybean oil to the proposed food uses was calculated. SDA soybean oil was either added to foods or replaced an unhydrogenated oil (including soybean oil, oil 'not further specified', corn oil, cottonseed oil, peanut oil, sunflower oil, coconut oil, olive oil, canola oil, or palm oil). In order to achieve 375 mg SDA per serving of food, every target food needs to have 1.8 g of 20% SDA soybean oil or 1.3 g of 30% SDA soybean oil per serving of food. Recipes were used to determine the amount and type of oil in each food, and either added in or replaced soybean oil or non-soybean liquid oil with SDA soybean oil to ensure this measured oil quantity. When the main oil variety for a food was a hydrogenated oil, it was assumed that this hydrogenated oil contained a blend of 60% solid fat and 40% liquid oil [Proprietary formulation, Stuart Clegg (Leatherhead Food International) to Richard Wilkes (Monsanto), Aug. 9, 2006]. Only the liquid 40% portion of the hydrogenated oil blend was then made available for substitution of SDA soybean oil in order to maintain functionality of the oil blend.

Following the introduction of 20% SDA soybean oil to the proposed foods, the per capita mean and 90<sup>th</sup> percentile intakes of SDA soybean oil are estimated to be 10.1 and 19.6 g/day, respectively (0.18 and 0.38 g/kg body weight/day, respectively) (see Table 7). Fat intake increased from 78.8 and 136.5 g/day at the mean and 90<sup>th</sup> percentile, respectively, to 84.0 and 143.6 g/day, respectively (see Table 8). This increase is attributable to the addition of SDA soybean oil to foods that do not contain fat. Intake of SDA from all dietary sources increased from 0.004 g/day at the mean and 90<sup>th</sup> percentile to 2.1 g at the mean, and to 4.1 g/day at the 90<sup>th</sup> percentile. Mean and 90<sup>th</sup> percentile LA intakes also increased from 10.1 and 19.5 g/day, respectively, to 11.8 and 21.9 g/day, respectively, and mean and 90<sup>th</sup> percentile intakes of ALA increased from 0.9 and 1.8 g/day, respectively, to 1.9 and 3.6 g/day, respectively. Palmitic acid and GLA intakes increased marginally ( $\leq 1.2$  g/day), and changes in the remaining fatty acids were negligible.

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Population Group	20% SDA Soybean Oil Intake (g/day)		20% SDA Soybean Oil Intake (g/kg/day)	
	Per capita Mean	Per capita 90 <sup>th</sup> Percentile	Per capita Mean	Per capita 90 <sup>th</sup> Percentile
U.S. population	10.1	19.6	0.18	0.38
Males 1-8 years	8.8	14.8	0.45	0.80
Females 1-8 years	7.8	13.5	0.41	0.73
Males 9-19 years	11.0	20.8	0.21	0.42
Females 9-19 years	9.1	16.7	0.18	0.35
Males 20-49 years	11.9	23.1	0.14	0.28
Females 20-49 years	9.9	19.0	0.14	0.28
Males 50+ years	11.1	20.6	0.13	0.25
Females 50+ years	9.6	17.9	0.14	0.26

<sup>1</sup> The amount of SDA soybean oil consumed was calculated for each NHANES participant by subtracting the amount of SDA consumed at baseline from the POST SDA inclusion intake of SDA and dividing by 20.7% (SDA content of 20% SDA) (g/day) and divided by each individual's bodyweight (g/kg/day).

<sup>2</sup> Soybean oil was either added to foods or replaced an unhydrogenated oil (including soybean oil, oil 'not further specified', corn oil, cottonseed oil, peanut oil, sunflower oil, coconut oil, olive oil, canola oil, or palm oil) so that the amount of SDA soybean oil in each food was equivalent to 1.8 grams of oil per serving. Serving sizes based upon FDA's reference amounts customarily consumed located in 21CFR §101.12 (U.S. FDA, 2008).

Fatty Acid	Current Intake of Fatty Acids in Total Diet		Post 20% <sup>1</sup> SDA Soybean Oil Introduction in Total Diet	
	Mean	90 <sup>th</sup> Percentile	Mean	90 <sup>th</sup> Percentile
<i>U.S. Population</i>				
Total Fat	78.8	136.5	84.0	143.6
Palmitic 16:0	13.9	24.7	14.6	25.7
Stearic 18:0	7	12.6	7.1	12.7
Oleic 18:1	23.4	41.8	23.7	41.9
Linoleic 18:2	10.1	19.5	11.8	21.9
Alpha-linolenic 18:3	0.9	1.8	1.9	3.6
Gamma-linolenic 18:3n-6 <sup>2</sup>	0.03	0.1	0.7	1.3
SDA 18:4	0.004	0.004	2.1	4.1
Trans fat	5.9	11.6	4.9	9.8
EPA (20:5)	0.02	0.06	0.02	0.06
DHA (22:6)	0.02	0.06	0.02	0.06

<sup>1</sup> SDA soybean oil was either added to foods or replaced an unhydrogenated oil (including soybean oil, oil 'not further specified', corn oil, cottonseed oil, peanut oil, sunflower oil, coconut oil, olive oil, canola oil, or palm oil) so that the amount of SDA soybean oil in each food was equivalent to 1.8 grams of oil per serving. Serving sizes based upon FDA's reference amounts customarily consumed located in 21CFR §101.12 (U.S. FDA, 2008).

<sup>2</sup> Gamma-linolenic acid (18:3n-6) is only quantified in the Post 20% SDA soybean oil analyses. The other analyses present 18:3 not n-3 that includes gamma-linolenic acid.

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The estimated per capita mean and 90<sup>th</sup> percentile intakes of SDA soybean oil following the introduction of 30% SDA soybean oil to the proposed foods were determined to be 7.6 and 14.8 g/day, respectively (0.10 and 0.30 g/kg body weight/day) (see Table 9). Estimated intakes of individual fatty acids were similar to those reported for 20% SDA soybean oil due to the constant use level of SDA per serving (see Table 10).

<b>Table 9 Per capita Intake of SDA Soybean Oil Post 30% SDA Soybean Oil Introduction<sup>1,2</sup></b>				
<b>Population Group</b>	<b>30% SDA Soybean Oil Intake (g/day)</b>		<b>30% SDA Soybean Oil Intake (g/kg/day)</b>	
	<b>Per capita Mean</b>	<b>Per capita 90<sup>th</sup> Percentile</b>	<b>Per capita Mean</b>	<b>Per capita 90<sup>th</sup> Percentile</b>
U.S. population	7.6	14.8	0.1	0.3
Males 1-8 years	6.5	11.0	0.3	0.6
Females 1-8 years	5.8	10.0	0.3	0.5
Males 9-19 years	8.2	15.4	0.2	0.3
Females 9-19 years	6.7	12.2	0.1	0.3
Males 20-49 years	9.0	17.9	0.1	0.2
Females 20-49 years	7.4	14.4	0.1	0.2
Males 50+ years	8.4	15.5	0.1	0.2
Females 50+ years	7.3	13.7	0.1	0.2

<sup>1</sup> The amount of SDA soybean oil consumed was calculated for each NHANES participant by subtracting the amount of SDA consumed at baseline from the POST SDA inclusion intake of SDA and dividing by 28.7% (SDA content of 30% SDA) (g/day) and divided by each individual's bodyweight (g/kg/day).

<sup>2</sup> SDA soybean oil was either added to foods or replaced an unhydrogenated oil (including soybean oil, oil 'not further specified', corn oil, cottonseed oil, peanut oil, sunflower oil, coconut oil, olive oil, canola oil, or palm oil) so that the amount of SDA soybean oil in each food was equivalent to 1.3 grams of oil per serving. Serving sizes based upon FDA's reference amounts customarily consumed located in 21CFR §101.12 (U.S. FDA, 2008).

<b>Table 10 U.S. Population <i>Per capita</i> Intake of Fat and Fatty Acids from the Total Diet - NHANES 1999-2002 (g/day)</b>				
Fatty Acid	Current Intake of Fatty Acids in Total Diet		Post 30% <sup>1</sup> SDA Soybean Oil Introduction in Total Diet	
	Mean	90 <sup>th</sup> Percentile	Mean	90 <sup>th</sup> Percentile
<i>U.S. Population</i>				
Total Fat	78.8	136.5	82.1	140.8
Palmitic 16:0	13.9	24.7	14.4	25.3
Stearic 18:0	7	12.6	7.0	12.5
Oleic 18:1	23.4	41.8	23.1	41.1
Linoleic 18:2	10.1	19.5	11.0	20.8
<i>Alpha</i> -linolenic 18:3	0.9	1.8	1.7	3.1
<i>Gamma</i> -linolenic 18:3n-6 <sup>2</sup>	0.03	0.1	0.6	1.1
SDA 18:4	0.004	0.004	2.2	4.2
<i>Trans</i> fat	5.9	11.6	5.0	9.9
EPA (20:5)	0.02	0.06	0.02	0.06
DHA (22:6)	0.02	0.06	0.02	0.06

<sup>1</sup> SDA soybean oil was either added to foods or replaced an unhydrogenated oil (including soybean oil, oil 'not further specified', corn oil, cottonseed oil, peanut oil, sunflower oil, coconut oil, olive oil, canola oil, or palm oil) so that the amount of SDA soybean oil in each food was equivalent to 1.3 grams of oil per serving. Serving sizes based upon FDA's reference amounts customarily consumed located in 21CFR §101.12 (U.S. FDA, 2008).

<sup>2</sup> *Gamma*-linolenic acid (18:3n-6) is only quantified in the Post 30% SDA soybean oil analyses. The other analyses present 18:3 not n-3 that includes *gamma*-linolenic acid.

Several factors affect the magnitude and direction of changes in individual fatty acid intakes. First, some foods to which SDA soybean oil is intended to be added do not contain fat; therefore the addition of SDA soybean oil to these foods results in an increase in total fat and individual fatty acid intake, as well as a modest increase in calories (29.7 to 46.8 kcal/day, mean values for 30 and 20% SDA soybean oil, respectively). However, it is expected that food manufacturers will adjust their formulations such that the increase in calories will be negated. Second, the relative content of a particular fatty acid in SDA soybean oil compared to soybean oil or non-soybean oil that it replaces in a recipe influences the amount and direction of change.

**Current Regulatory Status and Background Dietary Intakes**

There are currently no specific regulations in the U.S. governing the use of SDA, GLA, or ALA as food ingredients. Both LA and palmitic acid are permitted for use as ingredients in food in the U.S. (21 CFR 184.1065; 21 CFR 172.860; 21 CFR 184.1329; 21 CFR 184.1505).

Refined Echium oil, extracted from the seeds of *Echium plantagineum* and containing not less than 10% (w/w) SDA (as a % of total fatty acids) is authorized in the European Union as a novel food ingredient for use in milk-based products and drinkable yogurt products delivered in a single dose, cheese preparations, spreadable fat and dressings, breakfast cereals, food supplements, dietary foods for special medical purposes, and foods intended

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for use in energy-restricted diets for weight reduction (2008/558/EC - Commission of the European Communities, 2008).

There are many natural sources of SDA in the food supply. Fish oils contain levels of SDA ranging from 0.9 to 3% (salmon, mackerel, cod, menhaden, herring, boal fish, and sardine) (Ghosh *et al.*, 1976; USDA, 2007). SDA also is present in certain edible algae species including *Undaria pinnatifida* and *Ulva pertusa* (16.3 to 26.3%) and several plant seed oils, notably black currant (*Ribes nigrum*) (2 to 4%) and Echium (*Echium plantagineum*) (8 to 15%) (Johansson *et al.*, 1997; Ishihara *et al.*, 2000; PDRNS, 2001; Stuchlík and Žák, 2002; Kapoor and Nair, 2005). Many dietary supplements made with fish oil, algae, or plant species such as black currant are rich in SDA and are consumed as a source of omega-3 fatty acids. Black currant seed oil is available as 500 and 1,000 mg capsules to be taken 3 to 6 times a day, providing 60 to 240 mg SDA per day (PDRNS, 2001).

Plant seed oils extracted from borage (*Borago officinalis*), black currant (*Ribes nigrum*), and evening primrose (*Oenothera biennis*) are utilized in dietary supplements as sources of fatty acids including GLA (Clough, 2001; PDRNS, 2001; Kapoor and Nair, 2005). For example, borage and evening primrose seed oils, which contain 20 to 27% and 7 to 14% GLA, respectively, are available in capsule form with recommended intakes that would provide 360 mg to 2 g GLA/day for the management of various conditions including rheumatoid arthritis, atopic dermatitis, and hypertriglyceridemia (PDRNS, 2001). Black currant seed oil has a GLA content of 15 to 20% (PDRNS, 2001).

GLA is an intermediate fatty acid in human metabolism, present in human breast milk at levels of 100 to 400 mg GLA/L (Horrobin, 1992), and breast feeding infants appear to have the highest dietary intake among age groups. GLA is an omega-6 fatty acid derived from the essential fatty acid, LA, and the estimated endogenous rate of formation of GLA from LA in adult humans ranges from 100 to 1,000 mg/day (Horrobin, 1992). Breast fed infants will consume on the order of 10 mg/kg body weight/day of GLA, equivalent to an intake of 0.7 g GLA in a 70 kg adult (Stoney *et al.*, 2004). Traditional food sources of GLA include barley (Qureshi *et al.*, 1984), beef, beef liver, beef kidney, pork, chicken, and egg yolk, although, these sources contains less than 1% GLA (Horrobin, 1990, 1992).

ALA is a normal component of soybean oil occurring at levels ranging from 5 to 10% in conventional soybean oil. It is the parent compound of the omega-3 polyunsaturated fatty acid (PUFA) family of essential fatty acids, and therefore, an important component in the diet (Beare-Rogers *et al.*, 2001). ALA is present at high levels in linseed and flaxseed oil and present in lower levels in many different seed oils (Ratnayake *et al.*, 1992; Innis and Elias, 2003). Additional rich sources of ALA include currant oil from the seeds of Ribes, perilla oil (*Perilla frutescens*), and dragonhead oil (*Dracocephalum moldavica*) (Stuchlík and Žák, 2002; Vecera *et al.*, 2003). DeFilippis and Sperling (2006) reported the ALA content of flaxseeds, butternuts, canola oil, walnuts, fish (catfish, mackerel, salmon, tuna) and flaxseed oil to be 18.1, 8.7, 9.3, 9.1, 0.2, and 53.3 g per 100 g food item, respectively.

LA is the parent compound of the omega-6 PUFA family of essential fatty acids and found in high amounts in vegetable oils (Stuchlík and Žák, 2002). According to the 1987–1988 USDA Nationwide Food Consumption Survey, yeast breads, rolls, cakes, cookies and pastries were the main contributors of LA intake, which was the principal PUFA for all age sex groups, contributing 87–92% of PUFA intake (Jonnalagadda *et al.*, 1995). Safflower oil represents the richest source of LA with a seed oil content of 60 g/100g and an LA content of 75% (Stuchlík and Žák, 2002). Sunflower seed oil and corn seed oil also are significant sources of the fatty acid, with LA concentrations of 65 and 59%, respectively (Stuchlík and Žák, 2002). LA also is present in currant oil from the seeds of *Ribes nigrum*, and seed oil from the Moroccan Boraginaceae (borage oil belongs to this family) (Vecera *et al.*, 2003).

Palmitic acid is a constituent of coconut oil, butter and other edible oils (JECFA, 1998). It also is used in foods as a plasticizing, lubricating, binding, and defoaming agent and as a reagent in the manufacture of other food grade additives (CIR, 1987). Palmitic acid is present in human and bovine milk at 22.6% and 26.3% of milk fat, respectively (German and Dillard, 2004).

### C. Absorption, Distribution, Metabolism, and Excretion (ADME)

#### Metabolic Fate

The fatty acids present in Monsanto's SDA soybean oil are metabolized primarily *via* mitochondrial *beta*-oxidation. SDA, for example, can undergo *beta*-oxidation to yield 9 units of acetyl-CoA. SDA also can undergo elongation to form long-chain omega-3 fatty acids such as EPA. Results from pre-clinical and human studies demonstrate that supplementation with SDA can enrich tissue lipid fractions with EPA, and more readily so than ALA. The relative efficacy of SDA:ALA at increasing tissue concentrations of EPA in animal studies range from 1:0.43 to 1:0.66, which may be reflective of the variation in rates of metabolism and incorporation of omega-3 PUFAs in different tissues. In humans, SDA:ALA efficacy is 1:0.25 and 1:0.26 in plasma and erythrocyte phospholipids, respectively (James *et al.*, 2003). The relative superior efficiency of SDA to ALA is attributed to the rate-limiting activity of the  $\Delta 6$  desaturase enzyme that converts ALA to SDA.

It also is possible to determine the relative efficacy of EPA to SDA at increasing tissue levels of EPA in animals and humans. In preclinical studies, EPA:SDA efficacies ranging from 1:0.2 (in heart glycerophospholipids of dogs) to 1:0.54 (in splenocyte total lipids of mice) were calculated (Hansen Petrik *et al.*, 2000; Ishihara *et al.*, 2002; Harris *et al.*, 2007). In humans, the relative efficacy of SDA to EPA was determined to be approximately 3:1 using erythrocyte and plasma phospholipid EPA values in individuals who consumed an average of 1.125 g SDA/day in ethyl ester form for 6 weeks (James *et al.*, 2003), and 5:1 using erythrocyte values in subjects who were given approximately 3.66 g SDA in the form of SDA soybean oil for 16 weeks (Harris *et al.*, 2008). It should be noted that even using the highest bioconversion ratio of 3:1 SDA to EPA, the intake levels of SDA from the proposed food uses (2.2 and 4.2 g/day at the mean and 90<sup>th</sup> percentile, respectively) would not exceed the

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maximum established level of 3 g/day per person combined EPA and DHA intake (as per FDA's limitation for menhaden oil; 21 CFR 184.1472(a)(3)). That is, the mean and 90<sup>th</sup> percentile intakes from proposed foods uses would be equivalent to 0.73 and 1.4 g/day, respectively, of EPA when the relative enrichment ratio is applied to SDA intakes.

Human studies support the conclusion that ingested SDA does not generally accumulate to a significant degree in tissue lipid pools. In the human study reported by James *et al.* (2003), the administration of an average of 1.125 g SDA/day<sup>2</sup> over the course of 6 weeks failed to increase concentrations of SDA and its immediate elongation product, eicosatetraenoic acid (ETA), in phospholipid fractions of erythrocytes, platelets, and mononuclear cells as well as plasma cholesteryl ester and triacylglycerol (TAG) fractions. Furthermore, neither SDA nor ETA was detected in erythrocyte or heart glycerophospholipids obtained from dogs administered human equivalent doses of up to 13.5 g/day of SDA in ethyl ester form for a 12-week period (Harris *et al.*, 2007). Although Harris *et al.* (2008) reported that consumption of SDA soybean oil, providing 3.66 g SDA/day, for 16 weeks significantly increased erythrocyte SDA levels, the authors noted that final SDA levels remained low (less than 0.05% of total fatty acids).

### D. Preclinical Studies

The safety of SDA soybean oil under the intended conditions of use is supported by the results of pre-clinical toxicity studies conducted on the SDA soybean oil, including a 28-day study and a combined 90-day/one generation reproductive toxicity study. Additional published studies on SDA and GLA from other sources corroborate the safety of SDA soybean oil.

#### Subchronic and Chronic Studies

##### *Studies Conducted with Monsanto's SDA Soybean Oil*

The safety of Monsanto's SDA soybean oil was assessed in Sprague-Dawley rats in a 28-day toxicity study (Hammond *et al.*, 2008). Groups of 50 male and 50 female 6-week-old Sprague-Dawley rats were randomly assigned to receive 20% SDA soybean oil or conventional soybean oil (purchased from a commercial vendor) by gavage for a 28-day period. All animals survived until necropsy with no evidence of compound-related adverse effects on clinical observations, body weight, food consumption, hematology, serum chemistry or urinalysis. Macroscopic examination of organs did not reveal any compound-related changes and there were no significant differences in organ weights among the groups. No histological findings of toxicological significance and no test substance-related adverse events were observed in this study. The authors concluded that the absence of adverse effects in this study confirms the safety of Monsanto's SDA soybean oil for human consumption. The no-observed-effect level (NOEL) for oral administration was the highest

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<sup>2</sup> Dosing regimen: 0.75 g/day for the initial 3 weeks followed by 1.5 g/day for the subsequent 3 weeks. Calculation: [(0.75 g x 21 days) + (1.5 g x 21 days)]/42 days = 1.125 g/day

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dose tested at 3 g/kg body weight, and since the SDA soybean oil contained 20% SDA, the NOEL for SDA was 600 mg/kg/day (Hammond *et al.*, 2008).

In a combined 90-day/one generation reproductive toxicity study, rats were fed diets supplemented with 1.5 or 4.0 g SDA soybean oil/kg body weight/day (Hammond *et al.*, 2008). Diets containing control soybean oil derived from isogenic soybeans or menhaden oil (4.0 g/kg body weight/day) were provided to control groups. No statistically significant dose-dependent test article-related adverse effects were reported in any of the parameters evaluated, including clinical signs, behavior, mortality, body weight, organ weights, macroscopic appearance of tissues, and histopathology. Statistically significant differences observed between the control and SDA-treated groups included: increased food consumption at Weeks 1 and 2 (low-dose SDA, females); increased basophils (%) (high-dose SDA, females); decreased alanine transferase levels (low-dose SDA, females); decreased cholesterol levels (high-dose SDA, females); increased phosphorus levels (low-dose SDA, males); increased blood urea nitrogen levels (high-dose SDA, males); decreased triglycerides (high-dose SDA, males); and urine urobilinogen (low-dose SDA, males). Given that these changes were slight, within historical limits of the testing laboratory, not dose-dependent, and/or also were observed in the menhaden oil-treated group (*i.e.*, considered typical responses for rats fed high doses of long-chain polyunsaturated fatty acids), they were not considered to be of toxicological significance. Therefore, the NOAEL was determined to be 4 g SDA soybean oil/kg body weight/day (providing 1,051 and 1,073 mg SDA/kg body weight/day in male and female rats, respectively), the highest dose tested.

### *Studies Conducted on SDA from Other Sources*

Measurements of body weight gain, food consumption, and relative liver weight were not statistically significant among groups of 3-week-old male Balb/c mice (7/group) fed diets containing 1% of ALA, SDA, or EPA (supplied as TAG) *ad libitum* for a period of 3 weeks (Ishihara *et al.*, 2002). The animals in the SDA group ingested approximately 2,108 mg/kg body weight of SDA daily.

Groups of 4-week-old male Wistar rats were fed a lipid-free diet supplemented with 10% lard (control) or 9% lard plus 1% of ALA or SDA ethyl esters [providing approximately 1,000 mg/kg body weight/day (U.S. FDA, 1993)] for a period of 1 or 3 weeks (6/group/duration) (Yamazaki *et al.*, 1992). No significant difference in body weight among the 3 groups was observed and concentrations of serum lipids were comparable between the SDA and control groups. Although safety parameters were specifically assessed, no compound-related adverse effects reported in any group of male and female Sprague-Dawley rats (fed normal diets containing corn oil (as control), sunflower oil, or black currant oil at a level of 5 or 10% [providing approximately 200 or 400 mg SDA/kg body weight/day,

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respectively<sup>3</sup> (U.S. FDA, 1993)] for 36 or 96 days (Traitler and Winter, 1986). In a 3-month rat study conducted by Barzanti *et al.* (1995), all animals “appeared healthy” following dietary supplementation with 10% of olive oil (OO), black currant seed oil (BCO), or 1:1 mixture of OO and BCO. The OO, BCO, and OO/BCO diets comprised 0, 2.64, and 1.27% SDA, respectively, [providing approximately 0, 132, and 63.5 mg/kg body weight/day of SDA, respectively (U.S. FDA, 1993)]. No significant effects on body, liver, brain, and heart weights attributable to the experimental diets were observed.

Male Dunkin-Hartley guinea pigs (7/group) were fed diets containing 10% BCO, walnut oil, or lard *ad libitum* for a period of 40 days (Crozier *et al.*, 1989). BCO contained 2.6% SDA and 17.1% GLA and thus, the diet containing this oil provided approximately 104 and 684 mg/kg body weight of SDA and GLA, respectively (U.S. FDA, 1993). Animals were euthanized following an overnight fast and had their livers removed. There were no differences in final body weights and liver weights observed among the study groups.

Groups of 15 adult male Beagle dogs were provided test meals daily that provided 21.4, 64.2, or 192.9 mg SDA ethyl esters/kg body weight/day for a period of up to 12 weeks (Harris *et al.*, 2007). This study was not designed to specifically assess toxicology-relevant parameters although, the study authors indicated that all animals survived until scheduled necropsies and that no compound-related “clinical findings” (liver, kidney and heart appeared normal upon histologic examination) or effects on body weight or food consumption were observed.

Several repeated dose studies have been conducted on oils containing GLA. In the study of the longest duration (53 weeks) that included multiple endpoints related to safety, no GLA-related adverse effects were reported in rats administered evening primrose oil that provided 0, 27, 90, or 230 mg GLA/kg body weight/day (Everett *et al.*, 1988a).

### Reproductive and Developmental Studies

No adverse effects attributable to SDA soybean oil consumption with respect to body weight changes, food consumption, reproductive performance, and progeny survival and development were reported in the reproductive phase of the 90-day/one generation reproductive toxicity study described above (Hammond *et al.*, 2008). Therefore, the NOAEL for reproductive and developmental toxicity was determined to be 4 g SDA soybean oil/kg body weight/day (providing 1,041, 997, and 2,495 mg SDA/kg body weight/day during mating, gestation, and lactation, respectively). Safety is corroborated by results from pre-clinical studies conducted with SDA from other sources, *e.g.*, TAGs, ethyl esters, or plant oils (Yamazaki *et al.*, 1992; Traitler and Winter, 1986; Barzanti *et al.*, 1995; Crozier *et al.*, 1989; Harris *et al.*, 2007).

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<sup>3</sup> Calculation based on black currant oil containing 4% SDA (Traitler and Winter, 1986). [5% fed in the diet X 1,000 mg/kg body weight/day for a young rat = 5,000 mg black currant oil/kg body weight/day. 4% SDA content in black currant oil X 5,000 mg/kg body weight/day = 200 mg SDA/kg body weight/day].

The effects of dietary GLA from different sources and different concentrations on reproduction, growth, brain and behavioral development were assessed in mice (Wainwright *et al.*, 2003). Twenty B6D2F<sub>1</sub> female mice (8 weeks old) per group were fed diets containing 0 (control), borage oil containing 23% GLA, high GLA canola oil (HGCO) containing 23% GLA or HGCO containing 36% GLA [providing approximately 0, 11.5, 11.5, an 18 g GLA/kg body weight/day, respectively (U.S. FDA, 1993)] for a 6-month period. There were no significant differences in the number of successful pregnancies, gestation length, or maternal weight gain during gestation and lactation among the groups. Although litter size was the same among groups at birth (Day 19) and Day 21, both HGCO groups lost significantly more pups when compared to control in the first 2 days post-parturition. This finding was not considered to be toxicologically significant due to the non-significant larger litter size of the HGCO groups and the lack of any other reproductive findings. Pups in the HGCO (36% GLA) group weighed significantly less than control pups from birth to weaning, which was expected by the authors due to results of previous studies wherein mice consumed a high level of GLA. At birth, body weights of the pups from HGCO (23% GLA), borage oil and control groups were the same, but by weaning HGCO exposed pups (23% GLA) weighed less when compared to borage oil and control pups. The authors stated that the specific factors related to decreased body weights of the HGCO (23% GLA) animals could not be determined because body composition was not measured. There were no significant differences in brain weights or results from behavioral tests among groups. The authors concluded that although there were some differences in effects of GLA at equivalent concentrations from different sources, HGCO is appropriate as an alternative source of GLA.

## **E. Studies in Humans**

In a human study conducted on a Monsanto SDA soybean oil, physiological endpoints (heart rate, blood pressure, and body weight), lipid endpoints (cholesterol and triglycerides), and platelet function were not significantly different among subjects (33 healthy males and females, 21 to 70 years old with a Body Mass Index of 25 to 40) who consumed 3.66 g SDA/day (from SDA soybean oil), 0.98 g EPA (in ethyl ester form), or soybean oil (placebo) for 16 weeks (Harris *et al.*, 2008). Additionally, there were no clinically significant differences in serum chemistry parameters. No adverse events of clinical significance were reported.

Findings from additional human studies corroborate the safety of SDA soybean oil. No significant changes in inflammatory mediators or blood lipids were noted in subjects who consumed up to 1.5 g SDA ethyl esters/day for 6 weeks (James *et al.*, 2003). Similarly, no adverse effects on immune response or serum lipids were reported in studies involving subjects who ingested echium oil providing 1 or 1.875 g of SDA/day for a period of 12 and 4 weeks, respectively (Miles *et al.*, 2004a,b, 2006; Surette *et al.*, 2004). Comparatively, studies that utilized BCO instead of echium oil provided much lower doses of SDA (67.7 to 131 mg/day for up to 2 months) (Wu *et al.*, 1999; Tahvonen *et al.*, 2005). No compound-related adverse effects were reported in any of the studies that examined the effects of supplementation with plant oils containing SDA. Additional human studies indicate that the supplementation with GLA derived from fish or plant oils at intakes ranging from 320 mg to

4 g/day for periods of 1 to 6 months was generally well tolerated and without reports of serious adverse effects.

## F. Other Data Pertaining to the Safety of SDA Soybean Oil

### Safety of EPA Formed from SDA Following the Consumption of SDA Soybean Oil

Based on the results of metabolism studies, consumption of 4.2 g SDA from SDA soybean oil (the predicted 90<sup>th</sup> percentile intake of SDA from the proposed food uses of SDA soybean oil) will result in the formation of approximately 1.4 g EPA (using the highest bioconversion ratio of 3:1 SDA to EPA). This amount of EPA would not be expected to adversely affect bleeding time, glycemic control, and low-density lipoprotein (LDL) cholesterol level and would not exceed the maximum established level of 3 g/day per person combined EPA and DHA intake (as per FDA's limitation for menhaden oil; 21 CFR 184.1472(a)(3)).

### Potential Allergenicity

*Neurospora crassa*  $\Delta 15$  desaturase and *Primula juliae*  $\Delta 6$  desaturase are the only proteins of non-soybean origin that are expressed in MON 87769. SDA soybean oil is not expected to present an allergenic risk, based on the following:

- Several studies have evaluated the allergenicity of refined soybean and peanut oil in allergic individuals, and based on the results of these studies it is generally accepted that refined vegetable oils do not represent allergy risks (Hourihane *et al.*, 1997; Taylor *et al.*, 2004).
- Residual total protein levels in the SDA soybean oil are below the limit of detection (<0.15%).
- The  $\Delta 15$  and  $\Delta 6$  desaturase proteins comprise a trivial portion of the total protein fraction found in SDA soybeans and because total protein in SDA soybean oil is below the limit of detection, the amount of  $\Delta 15$  and  $\Delta 6$  desaturase proteins present in the refined SDA soybean oil will be negligible.
- The  $\Delta 15$  and  $\Delta 6$  desaturase proteins present in MON 87769 do not share common physio-chemical characteristics of known allergens. They comprise a trivial portion of the total protein in SDA soybeans and the full-length proteins are unstable in *in vitro* digestive fate assays (SGF/SIF). They do not share relevant sequence similarity with known allergens.

### Safety of Desaturases and Source Organisms

Fatty acid desaturases are ubiquitous and are widely present in plants and animals. The amino acid sequences of *Neurospora crassa*  $\Delta 15$  desaturase and *Primula juliae*  $\Delta 6$  desaturase are similar to other desaturases present in food.

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The fungus *Neurospora crassa*, the source of  $\Delta 15$  desaturase gene, is considered a non-pathogenic and non-allergenic organism (Perkins and Davis, 2000), and is found in food sources worldwide.

*Primula juliae*, the source of  $\Delta 6$  desaturase gene, is from a large genus of plants commonly known as Primrose and some plants from the *Primula* genus are used as herbal medicines and also for producing GLA-containing oils for human use.

### **G. Summary and Basis for GRAS Conclusion**

SDA soybean oil is manufactured in accordance with current Good Manufacturing Practice and meets appropriate food-grade specifications. SDA has a long-standing history of safe consumption in human foods from several marine and plant sources. In human fatty acid metabolism, SDA is an intermediate in the production of EPA and DHA from dietary ALA. The exposure to SDA from the proposed food uses of SDA soybean oil is estimated to be no more than 2.2 g/day at the mean, and 4.2 g/day at the 90<sup>th</sup> percentile. The safety of SDA soybean oil is supported by the results of a published 90-day/one generation reproductive toxicity rat study in which a NOAEL of 1 g SDA/kg body weight/day (4 g Monsanto's SDA soybean oil/kg body weight/day) was determined. No adverse effects attributable to SDA soybean oil were reported in a published human study in which subjects consumed 3.66 g SDA (from a Monsanto SDA soybean oil)/day for 16 weeks. Additional published studies on SDA and GLA from other sources corroborate the safety of SDA soybean oil. The safety of SDA soybean oil is further supported by the regular dietary consumption of fats and oils containing ALA, LA, and palmitic acid, and by the permitted uses of LA and palmitic acid in food in the U.S.

When viewed in its entirety, the scientific evidence presented above has been determined by Monsanto to not indicate any potential for adverse effects in humans following the consumption of SDA soybean oil under the conditions of intended use in foods. Following a critical evaluation of the scientific data generally available in the public domain that pertain to the safety of SDA soybean oil, a panel of experts, qualified by scientific training and experience to evaluate the safety of SDA soybean oil as a component of food, unanimously concluded that the proposed uses of SDA soybean oil are safe and suitable and are GRAS based on scientific procedures. Therefore, Monsanto has concluded that SDA soybean oil is GRAS under the intended conditions of use on the basis of scientific procedures.

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<b>Table of CFR Sections Referenced (Title 21—Food and Drugs)</b>		
<b>Part</b>	<b>Section §</b>	<b>Section Title</b>
101—Food labelling	101.12	Reference amounts customarily consumed per eating occasion
170—Food additives	170.3	Definitions
	170.30	Eligibility for classification as generally recognized as safe (GRAS)
172—Food additives permitted for direct addition to food for human consumption	172.185	TPHQ
	172.340	Fish protein isolate
	172.860	Fatty acids
173—Secondary direct food additives permitted in food for human consumption	173.270	Hexane
177—Indirect food additives: Polymers	177.2250	Filters, microporous polymeric
182—Substances generally recognized as safe	182.1073	Phosphoric acid
184—Direct food substances affirmed as generally recognized as safe	184.1033	Citric acid
	184.1065	Linoleic acid
	184.1329	Glyceryl palmitostearate
	184.1472	Menhaden oil
	184.1505	Mono- and diglycerides
	184.1666	Propylene glycol
184.1763	Sodium hydroxide	
186—Indirect food substances affirmed as generally recognized as safe	186.1256	Clay (kaolin)

**APPENDIX A**

**EXPERT PANEL REPORTS REGARDING THE GENERALLY  
RECOGNIZED AS SAFE (GRAS) STATUS OF MONSANTO'S  
STEARIDONIC (SDA) OMEGA-3 SOYBEAN OIL IN FOODS**

**APPENDIX A-1**

**EXPERT PANEL CONSENSUS STATEMENT REGARDING THE GENERALLY  
RECOGNIZED AS SAFE (GRAS) STATUS OF MONSANTO'S STEARIDONIC  
(SDA) OMEGA-3 SOYBEAN OIL FOR USE IN FOODS**

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# **EXPERT PANEL CONSENSUS STATEMENT REGARDING THE GENERALLY RECOGNIZED AS SAFE (GRAS) STATUS OF MONSANTO'S STEARIDONIC ACID (SDA) SOYBEAN OIL FOR USE IN FOODS**

**September 29, 2008**

## **INTRODUCTION**

At the request of Monsanto Company (Monsanto), an Expert Panel (the "Panel") of independent scientists, qualified by their relevant national and international experience and scientific training to evaluate the safety of food ingredients, was specially convened to conduct a critical and comprehensive evaluation of the available pertinent data and information, and determine whether the intended uses as a food ingredient, stearidonic acid (SDA) soybean oil are safe and suitable and would be Generally Recognized as Safe (GRAS) based on scientific procedures. The Panel consisted of: Dr. Joseph F. Borzelleca, (Virginia Commonwealth University School of Medicine), Dr. Fergus M. Clydesdale (University of Massachusetts Amherst), Dr. Ernst J. Schaefer (Tufts University), and Dr. Ronald Walker (University of Surrey). Curricula vitae evidencing the Panel members' qualifications for evaluating the safety of food ingredients are provided in Attachment 1.

The Panel, independently and collectively, critically examined a comprehensive package of scientific information and data on SDA soybean oil compiled from the literature and other published sources through August 2008 by Cantox Health Sciences International (Cantox). In addition, the Panel evaluated other information deemed appropriate or necessary, including data and information provided by Monsanto. The information evaluated by the Panel included details pertaining to the method of manufacture and product specifications, supporting analytical data, intended use-levels in specified food products, consumption estimates for all intended uses, and a comprehensive assessment of the available scientific literature pertaining to the safety of SDA soybean oil.

Following independent, critical evaluation of such data and information, the Panel convened on 29 September 2008 and unanimously concluded that the intended uses in traditional foods described herein for Monsanto's SDA soybean oil, meeting appropriate food-grade specifications as described in the supporting dossier [Documentation Supporting the Evaluation of Monsanto's Stearidonic Acid Soybean Oil as Generally Recognized as Safe] and manufactured according to current Good Manufacturing Practice (cGMP), are safe and suitable

and GRAS based on scientific procedures. A summary of the basis for the Panel's conclusion is provided below.

## DESCRIPTION OF SDA SOYBEAN OIL

### Background Information

Monsanto proposes to market soybeans genetically modified to produce SDA, an 18:4 omega-3 fatty acid. The SDA soybeans (MON 87769) will be processed to produce SDA soybean oil for use as an ingredient in traditional foods.

SDA is metabolically formed by the desaturation of *alpha*-linolenic acid (ALA). Because SDA bypasses the rate-limiting step in the conversion of ALA to the omega-3 fatty acids eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), it forms more EPA and possibly DHA in the body when consumed. Results of animal and human studies demonstrate that SDA can increase red blood cell (RBC) concentrations of EPA with a greater efficiency than ALA (James *et al.*, 2003; Harris *et al.*, 2007). The enrichment of RBCs with EPA and DHA has been shown to reflect cardiac membrane omega-3 fatty acid content (Harris *et al.*, 2004). Expressed as a percentage of total fatty acids, this 'Omega-3 Index' has been found to correlate with reduced risk of cardiovascular disease, particularly sudden cardiac death (Harris and Von Schacky, 2004).

SDA soybean oil contains 15 to 30% SDA, which is not present in conventional soybean oil, 5 to 8% *gamma*-linolenic acid (GLA) (also not present in conventional soybean oil), and slightly higher levels of ALA and palmitic acid than in conventional soybean oil. It also contains lower levels of oleic acid and linoleic acid (LA) than those present in conventional soybean oil.

### Manufacturing Process

The production of MON 87769 soybeans involves the introduction of 2 desaturase genes that encode for the proteins, *Primula juliae*  $\Delta 6$  desaturase and *Neurospora crassa*  $\Delta 15$  desaturase. Soybeans lack  $\Delta 6$  desaturase and the minimal requirement for production of SDA in soybeans would be the introduction of a gene encoding  $\Delta 6$  desaturase. However,  $\Delta 6$  desaturase also may convert LA to GLA. Addition of a  $\Delta 15$  desaturase with temporal expression similar to the  $\Delta 6$  desaturase increases ALA levels, allowing greater flux to SDA. The  $\Delta 15$  desaturase also lowers LA levels, thus lowering the substrate pool for GLA production. Compositional data on several lots of SDA soybean oil support the opinion that the phenotype is stable over several generations.

SDA soybean oil is produced using commercial food-grade soybean oil manufacturing practices with food-grade raw materials and processing agents. Because traditional soybean oil

manufacturing processes are used to produce SDA soy oil, which is well-characterized, the altered fatty acid profile of SDA soybean oil is a reflection of the SDA soybean variety and not due to or impacted by the manufacturing process. All reagents and processing aids used in the manufacture of SDA soybean oil are permitted for use in the U.S. in food production.

## Product Specifications

The product specifications and methods of analysis for SDA soybean oil are presented in Tables 1 and 2. Food Chemical Codex (FCC) specifications for conventional soybean oil also are included for comparative purposes.

Parameter	FCC Soybean Oil Specification	SDA Soybean Oil Specification	Analysis Method
Fatty acid composition	See Table 2	See Table 2	AOCS Ch 2a-94, Ce 1f-96
Cold test	Passes test	n/a <sup>1</sup>	n/a
Lovibond color (Yellow)	NMT 20	NMT 20	AOCS Cc 13j-97 (Lovibond)
Lovibond color (Red)	NMT 2.0	NMT 2.0	AOCS Cc 13j-97 (Lovibond)
Free fatty acids	NMT 0.1%	NMT 0.1%	AOCS Ca 5a-40
Iodine value	120 - 143	160 - 210	AOCS Tg 1a-64 (modified: POS Method IN-LS-26)
Lead	NMT 0.1 mg/kg	NMT 0.1 mg/kg	FCC Lead Limit Test, Atomic Absorption Spectrophotometric Graphite Furnace Method II
Peroxide value	NMT 10 meq/kg	NMT 10 meq/kg	AOCS Cd 8-53
Stability, Active oxygen method (AOM)	NLT 7 h	NLT 2 h	AOCS Cd 12-57
Unsaponifiable matter	NMT 1.5 %	NMT 1.5%	AOCS Ca 6a-40
Water	NMT 0.1%	NMT 0.1%	AOCS Ca 2c-25

n/a = not applicable; NLT = not less than; NMT = not more than

<sup>1</sup> Cold test was not included in the specifications for SDA soybean oil because SDA soybean oil will only be included as an ingredient in food and beverage products and will not be marketed itself as a retail product; thus, cloudiness of the oil (as measured by the cold test) is not relevant.

For SDA soybean oil, the specifications for iodine value are higher compared to conventional soybean oil due to the increased levels of unsaturated fatty acids in SDA soybean oil. Additionally, stability of SDA soybean oil is lower than that of conventional soybean oil because oils with higher polyunsaturated fatty acid content are less stable to oxidation.

<b>Table 2 Specifications for Fatty Acid Composition of Soy Oil (FCC) and SDA Soybean Oil</b>		
<b>Fatty acid</b>	<b>FCC Soybean Oil Specification (% weight)</b>	<b>SDA Soybean Oil Specification (% weight)</b>
<14	<0.1	<0.1
14:0 (myristic)	<0.5	<0.5
16:0 (palmitic)	7.0 – 12	9 – 13
16:1 (palmitoleic)	<0.5	<0.5
18:0 (stearic)	2.0 – 5.5	2.0 – 5.5
18:1 (oleic)	19 – 30	10 – 20
18:2 (linoleic)	48 – 65	15 – 30
18:3 ( $\alpha$ -linolenic)	5 – 10	9 – 12
18:3 ( $\gamma$ -linolenic)	n/a	5 – 8
18:4 (stearidonic)	n/a	15 – 30
20:0 (arachidic)	<1.0	<1.0
20:1 (eicosenoic)	<1.0	<1.0
22:0 (behenic)	<0.5	<0.5
22:1 (erucic)	<0.1	<0.1
24:0 (lignoceric)	<0.3	<0.3

n/a = not applicable

Monsanto provided batch analyses data for several lots of SDA soybean oil produced from several generations of soybeans and grown at various U.S. locations. These data demonstrate that the manufacturing process produces a consistent product in terms of its chemical composition.

### **Stability**

Results of stability testing demonstrate that SDA soybean oil is stable, with respect to peroxide value and fatty acid content, for at least 72 days when stored at room temperature, and for at least 4 to 5 days under accelerated conditions (55°C in air). More importantly, when stored under nitrogen at room temperature (typical storage conditions for commercial SDA soybean oil) for as long as 9 months, SDA soybean oil still maintains a peroxide value similar to that of conventional soybean oil.

## INTENDED USES AND EXPOSURE ESTIMATES

### Current Regulatory Status and Background Dietary Intakes

There are currently no specific regulations in the U.S. governing the use of SDA, GLA, or ALA as food ingredients.

Both LA and palmitic acid are permitted for use as ingredients in food in the U.S. (21 CFR 184.1065; 21 CFR 172.860; 21 CFR 184.1329; 21 CFR 184.1505).

Refined Echium oil, extracted from the seeds of *Echium plantagineum* and containing not less than 10% (w/w) SDA (as a % of total fatty acids) is authorized in the European Union as a novel food ingredient for use in milk-based products and drinkable yogurt products delivered in a single dose, cheese preparations, spreadable fat and dressings, breakfast cereals, food supplements, dietary foods for special medical purposes, and foods intended for use in energy-restricted diets for weight reduction (2008/558/EC - Commission of the European Communities, 2008).

There are many natural sources of SDA in the food supply. Fish oils contain levels of SDA ranging from 0.9 to 3% (salmon, mackerel, cod, menhaden, herring, boal fish, and sardine) (Ghosh *et al.*, 1976; USDA, 2007). SDA also is present in certain edible algae species including *Undaria pinnatifida* and *Ulva pertusa* (16.3 to 26.3%) and several plant seed oils, notably black currant (*Ribes nigrum*) (2 to 4%) and Echium (*Echium plantagineum*) (8 to 15%) (Johansson *et al.*, 1997; Ishihara *et al.*, 2000; PDRNS, 2001; Stuchlík and Žák, 2002; Kapoor and Nair, 2005). Many dietary supplements made with fish oil, algae, or plant species such as black currant are rich in SDA and are consumed as a source of omega-3 fatty acids. Black currant seed oil is available as 500 and 1,000 mg capsules to be taken 3 to 6 times a day (PDRNS, 2001).

Plant seed oils extracted from borage (*Borago officinalis*), black currant (*Ribes nigrum*), and evening primrose (*Oenothera biennis*) are utilized in dietary supplements as sources of fatty acids including GLA (Clough, 2001; PDRNS, 2001; Kapoor and Nair, 2005). For example, borage and evening primrose seed oils, which contain 20 to 27% and 7 to 14% GLA, respectively, are available in capsule form with recommended intakes that would provide 360 mg to 2 g GLA/day for the management of various conditions including rheumatoid arthritis, atopic dermatitis, and hypertriglyceridemia (PDRNS, 2001). Black currant seed oil has a GLA content of 15 to 20% (PDRNS, 2001).

GLA is an intermediate fatty acid in human metabolism, present in human breast milk at levels of 100 to 400 mg GLA/L (Horrobin, 1992), and breast feeding infants appear to have the highest dietary intake among age groups. GLA is an omega-6 fatty acid derived from the essential fatty acid, LA, and the estimated endogenous rate of formation of GLA from LA in an adult human ranges from 100 to 1,000 mg/day (Horrobin, 1992). Breast fed infants will consume on the

order of 10 mg/kg body weight/day of GLA, equivalent to an intake of 0.7 grams GLA in a 70 kg adult (Stoney *et al.*, 2004). Traditional food sources of GLA include barley (Qureshi *et al.*, 1984), beef, beef liver, beef kidney, pork, chicken, and egg yolk, although, these sources contains less than 1% GLA (Horrobin, 1990, 1992).

ALA is a normal component of soybean oil occurring at levels ranging from 5 to 10% in conventional soybean oil. It is the parent compound of the n-3 polyunsaturated fatty acid (PUFA) family of essential fatty acids, and therefore, an important component in the diet (Beare-Rogers *et al.*, 2001). ALA is present at high levels in vegetable fats and oils, especially, linseed and flaxseed oil, and present in lower levels in many different seed oils (Ratnayake *et al.*, 1992; Innis and Elias, 2003). Additional rich sources of ALA include currant oil from the seeds of *Ribes*, perilla oil (*Perilla frutescens*), and dragonhead oil (*Dracocephalum moldavica*) (Stuchlík and Žák, 2002; Vecera *et al.*, 2003). DeFilippis and Sperling (2006) reported the ALA content of flaxseeds, butternuts, canola oil, walnuts, fish (catfish, mackerel, salmon, tuna) and flaxseed oil to be 18.1, 8.7, 9.3, 9.1, 0.2, and 53.3 g per 100 g food item, respectively.

LA is the parent compound of the n-6 PUFA family of essential fatty acids and found in high amounts in vegetable oils (Stuchlík and Žák, 2002). According to the 1987–1988 USDA Nationwide Food Consumption Survey, yeast breads, rolls, cakes, cookies and pastries were the main contributors of LA intake, which was the principal PUFA for all age sex groups, contributing 87 to 92% of PUFA intake (Jonnalagadda *et al.*, 1995). Safflower oil represents the richest source of LA with a seed oil content of 60 g/100g and an LA content of 75% (Stuchlík and Žák, 2002). Sunflower seed oil and corn seed oil also are significant sources of the fatty acid, with LA concentrations of 65 and 59%, respectively (Stuchlík and Žák, 2002). LA also is present in currant oil from the seeds of *Ribes nigrum*, and seed oil from the Moroccan Boraginaceae (borage oil belongs to this family) (Vecera *et al.*, 2003).

Palmitic acid is a constituent of coconut oil, butter and other edible oils (JECFA, 1998). It also is used in foods as a plasticizing, lubricating, binding, and defoaming agent and as a reagent in the manufacture of other food grade additives (CIR, 1987). Palmitic acid is present in human and bovine milk at 22.6% and 26.3% of milk fat, respectively (German and Dillard, 2004).

### **Intended Uses**

SDA soybean oil is intended for use as an ingredient in various foods, including baked goods and baking mixes, breakfast cereals and grains, cheeses, dairy product analogs, fats and oils, frozen dairy desserts and mixes, puddings and fillings, grain products and pastas, milk products, nuts and nut products, processed fruit juices, processed vegetable products, and snack foods at levels that will provide 375 mg SDA per serving.

James *et al.* (2003), using a dose of 1.5 g SDA/day, reported an increase in erythrocyte EPA levels, which in combination with DHA levels has been reported to correlate with reduced risk of

cardiovascular disease (Harris and von Schacky, 2004). On the basis of this study, Monsanto recommends that the daily minimum intake be 1.5 g SDA/day.

### **Estimated Consumption**

The consumption of SDA soybean oil from all proposed food uses was estimated by Exponent using the proposed food uses and use levels in conjunction with food consumption data included in the National Health and Nutrition Examination Surveys (NHANES 1999-2002) (CDC, 2007).

The current intake of fat, *trans* fat, and fatty acids in the diet as well as intake following the addition of 20 or 30% SDA soybean oil to the proposed food uses was calculated. SDA soybean oil was either added to foods or replaced an unhydrogenated oil (including soybean oil, oil 'not further specified', corn oil, cottonseed oil, peanut oil, sunflower oil, coconut oil, olive oil, canola oil, or palm oil). In order to achieve 375 mg SDA per serving of food, every target food needs to have 1.8 g of 20% SDA soybean oil or 1.3 g of 30% SDA soybean oil per serving of food. Exponent used their proprietary recipes to determine the amount and type of oil in each food, and either added in or replaced soybean oil or non-soybean liquid oil with SDA soybean oil to ensure this measured oil quantity. When the main oil variety for a food was a hydrogenated oil, it was assumed that this hydrogenated oil contained a blend of 60% solid fat and 40% liquid oil [Proprietary formulation, Stuart Clegg (Leatherhead Food International) to Richard Wilkes (Monsanto), Aug. 9, 2006]. Only the liquid 40% portion of the hydrogenated oil blend was then made available for substitution of SDA soybean oil in order to maintain functionality of solid fat.

Following the introduction of 20% SDA soybean oil to the proposed foods, the per capita mean and 90<sup>th</sup> percentile intakes of SDA soybean oil are estimated to be 7.3 and 14.4 g/day, respectively (0.13 and 0.28 g/kg body weight/day, respectively). Fat intake increased from 78.8 and 136.5 g/day at the mean and 90<sup>th</sup> percentile, respectively, to 82.7 and 141.8 g/day, respectively. This increase is attributable to the addition of SDA soybean oil to foods that do not contain fat. Intake of SDA from all dietary sources increased from 0.004 g/day at the mean and 90<sup>th</sup> percentile to 1.5 g at the mean, and to 3.0 g/day at the 90<sup>th</sup> percentile. Mean and 90<sup>th</sup> percentile LA intakes also increased from 10.1 and 19.5 g/day, respectively, to 11.4 and 21.5 g/day, respectively, and mean and 90<sup>th</sup> percentile intakes of ALA increased from 0.9 and 1.8 g/day, respectively, to 1.7 and 3.1 g/day, respectively. Palmitic acid and GLA intakes increased marginally (less than 1 g/day), and changes in the remaining fatty acids were negligible.

The estimated per capita mean and 90<sup>th</sup> percentile intakes of SDA soybean oil following the introduction of 30% SDA soybean oil to the proposed foods were determined to be 5.2 and 10.5 g/day, respectively (0.09 and 0.20 g/kg body weight/day). Estimated intakes of individual

fatty acids were similar to those reported for 20% SDA soybean oil due to the constant use level of SDA per serving.

Several factors affect the magnitude and direction of changes in individual fatty acid intakes. First, some foods to which SDA soybean oil is intended to be added do not contain fat; therefore the addition of SDA soybean oil to these foods results in an increase in total fat and individual fatty acid intake, as well as a modest increase in calories (22 to 35 kcal/day, mean values for 30 and 20% SDA soybean oil, respectively). However, it is expected that food manufacturers will adjust their formulations such that the increase in calories will be negated. Second, the relative content of a particular fatty acid in SDA soybean oil compared to liquid soybean or non-soybean oil that it replaces in a recipe influences the amount and direction of change.

## **SAFETY OF SDA SOYBEAN OIL**

### **Absorption, Distribution, Metabolism, and Excretion**

#### **Metabolic Fate**

The fatty acids present in Monsanto's SDA soybean oil are metabolized primarily *via* mitochondrial *beta*-oxidation. SDA, for example, can undergo *beta*-oxidation to yield 9 units of acetyl-CoA. SDA also can undergo elongation to form long-chain n-3 fatty acids such as EPA. Results from pre-clinical and human studies demonstrate that supplementation with SDA can enrich tissue lipid fractions with EPA, and more readily so than ALA. The relative efficacy of SDA:ALA at increasing tissue concentrations of EPA in animal studies range from 1:0.43 to 1:0.66, which may be reflective of the variation in rates of metabolism and incorporation of n-3 PUFAs in different tissues. In humans, SDA:ALA efficacy is 1:0.25 and 1:0.26 in plasma and erythrocyte phospholipids, respectively (James *et al.*, 2003). The relative superior efficiency of SDA to ALA is attributed to the rate-limiting activity of the  $\Delta 6$  desaturase enzyme that converts ALA to SDA.

It also is possible to determine the relative efficacy of EPA to SDA at increasing tissue levels of EPA in animals and humans. In preclinical studies, EPA:SDA efficacies ranging from 1:0.2 (in heart glycerophospholipids of dogs) to 1:0.54 (in splenocyte total lipids of mice) were calculated (Hansen Petrik *et al.*, 2000; Ishihara *et al.*, 2002; Harris *et al.*, 2007). In humans, the relative efficacy of SDA to EPA was determined to be approximately 3:1 using erythrocyte and plasma phospholipid EPA values in individuals who consumed an average of 1.125 g SDA/day in ethyl ester form for 6 weeks (James *et al.*, 2003), and 5:1 using erythrocyte values in subjects who were given approximately 3.66 g SDA in the form of SDA soybean oil for 16 weeks (Harris *et al.*, 2008).

Human studies support the conclusion that ingested SDA does not generally accumulate to a significant degree in tissue lipid pools. In the human study reported by James *et al.* (2003), the

administration of an average of 1.125 g SDA/day<sup>1</sup> over the course of 6 weeks failed to increase concentrations of SDA and its immediate elongation product, eicosatetraenoic acid (ETA), in phospholipid fractions of erythrocytes, platelets, and mononuclear cells as well as plasma cholesteryl ester and triacylglycerol (TAG) fractions. Furthermore, neither SDA nor ETA was detected in erythrocyte or heart glycerophospholipids obtained from dogs administered human equivalent doses of up to 13.5 g/day of SDA in ethyl ester form for a 12-week period (Harris *et al.*, 2007). Although Harris *et al.* (2008) reported that consumption of SDA soybean oil, providing 3.66 g SDA/day, for 16 weeks significantly increased erythrocyte SDA levels, the authors noted that final SDA levels remained low (less than 0.05% of total fatty acids).

### **Toxicological Studies**

The safety of the intended uses of SDA soybean oil is supported by the results of pre-clinical toxicity studies conducted on the oil, including a combined 90 day/1-generation reproductive toxicity study, in which rats were fed diets supplemented with 1.5 or 4.0 g SDA soybean oil/kg body weight/day (Hammond *et al.*, 2008). Diets containing control soybean oil derived from isogenic soybeans or menhaden oil (4.0 g/kg body weight/day) were provided to control groups. No statistically significant dose-dependent test article-related adverse effects were reported in any of the parameters evaluated, including clinical signs, behavior, mortality, body weight, organ weights, macroscopic appearance or tissues, and histopathology. Statistically significant differences observed between the control and SDA-treated groups included: increased food consumption at Weeks 1 and 2 (low-dose SDA, females); increased basophils (%) (high-dose SDA, females); decreased alanine transferase levels (low-dose SDA, females), decreased cholesterol levels (high-dose SDA, females); increased phosphorus levels (low-dose SDA, males); increased blood urea nitrogen levels (high-dose SDA, males); decreased triglycerides (high-dose SDA, males); and urine urobilinogen (low-dose SDA, males). Given that these changes were slight, within historical limits of the testing laboratory, not dose-dependent, and/or also were observed in the menhaden oil-treated group (*i.e.*, considered typical responses for rats fed high doses of long-chain polyunsaturated fatty acids), they were not considered to be of toxicological significance. Therefore, the no-observed-adverse-effect level (NOAEL) was determined to be 4 g SDA soybean oil/kg body weight/day (providing 1,051 and 1,073 mg SDA/kg body weight/day in male and female rats, respectively), the highest dose tested.

Similarly, no adverse effects attributable to SDA soybean oil consumption with respect to body weight changes, food consumption, reproductive performance, and progeny survival and development were reported in the reproductive phase of the study. Therefore, the NOAEL for reproductive and developmental toxicity was determined to be 4 g SDA soybean oil/kg body weight/day (providing 1,041, 997, and 2,495 mg SDA/kg body weight/day during mating,

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<sup>1</sup> Dosing regimen: 0.75 g/day for the initial 3 weeks followed by 1.5 g/day for the subsequent 3 weeks. Calculation: [(0.75 g x 21 days) + (1.5 g x 21 days)]/42 days = 1.125 g/day

gestation, and lactation, respectively). Safety is corroborated by results from pre-clinical studies conducted with SDA from other sources, e.g., TAGs, ethyl esters, or plant oils.

Several repeated dose studies have been conducted on oils containing GLA. In the study of the longest duration (53 weeks) that included multiple endpoints related to safety, no GLA-related adverse effects were reported in rats administered evening primrose oil that provided 0, 27, 90, or 230 mg GLA/kg body weight/day (Everett *et al.*, 1988). Furthermore, there were no significant differences in tumor incidence between rats and mice administered evening primrose oil (providing 230 mg GLA/kg body weight/day) and those administered the control oil (corn oil) in a 2-year carcinogenicity study.

### **Human Studies**

In a human study conducted on SDA soybean oil, physiological endpoints (heart rate, blood pressure, and body weight), lipid endpoints (cholesterol and triglycerides), and platelet function were not significantly different among subjects (33 healthy males and females, 21 to 70 years old with a Body Mass Index of 25 to 40) who consumed 3.66 g SDA/day (from SDA soybean oil), 0.98 g EPA (in ethyl ester form), or soybean oil (placebo) for 16 weeks (Harris *et al.*, 2008). Additionally, there were no clinically significant differences in serum chemistry parameters. No adverse events of clinical significance were reported.

Findings from additional human studies corroborate the safety of SDA soybean oil. No significant changes in inflammatory mediators or blood lipids were noted in subjects who consumed up to 1.5 g SDA ethyl esters/day for 6 weeks (James *et al.*, 2003). Similarly, no adverse effects on immune response or serum lipids were reported in studies involving subjects who ingested echium oil providing 1 or 1.875 g of SDA/day for a period of 12 and 4 weeks, respectively (Miles *et al.*, 2004, 2006; Surette *et al.*, 2004). Comparatively, studies that utilized BCO instead of echium oil provided much lower doses of SDA (67.7 to 131 mg/day for up to 2 months) (Wu *et al.*, 1999; Tahvonon *et al.*, 2005). No compound-related adverse effects were reported in any of the studies that examined the effects of supplementation with plant oils containing SDA. Additional human studies indicate that the supplementation with GLA derived from fish or plant oils at intakes ranging from 320 mg to 4 g/day for periods of 1 to 6 months was generally well tolerated and without reports of serious adverse effects.

### **Safety of EPA Formed from SDA Following the Consumption of SDA Soybean Oil**

Based on the results of metabolism studies, consumption of 3 g SDA from SDA soybean oil (the predicted 90<sup>th</sup> percentile intake of SDA from the proposed food uses of SDA soybean oil) will result in the formation of approximately 0.6 to 1 g EPA. This amount of EPA would not be expected to adversely affect bleeding time, glycemic control, and low-density lipoprotein (LDL) cholesterol levels.

## Allergenicity

*Neurospora crassa*  $\Delta 15$  desaturase and *Primula juliae*  $\Delta 6$  desaturase are the only proteins of non-soybean origin that are expressed in MON 87769. SDA soybean oil is not expected to present an allergenic risk, based on the following:

- Residual total protein levels in the SDA soybean oil are below the limit of detection (<0.15%).
- The  $\Delta 15$  and  $\Delta 6$  desaturase proteins are expected to comprise a trivial portion of the total protein fraction found in SDA soybeans and because very little total protein is present in vegetable oils, the amount of  $\Delta 15$  and  $\Delta 6$  desaturase proteins present in the refined SDA soybean oil will be negligible.
- Several studies have evaluated the allergenicity of refined soybean and peanut oil in allergic individuals, and based on the results of these studies it is generally accepted that refined vegetable oils do not represent allergy risks (Hourihane *et al.*, 1997; Taylor *et al.*, 2004).
- The  $\Delta 15$  and  $\Delta 6$  desaturase proteins present in MON 87769 share no sequence homology to any proven allergens.

## Safety of Desaturases and Source Organisms

Fatty acid desaturases are ubiquitous and are widely present in plants and animals. The amino acid sequences of *Neurospora crassa*  $\Delta 15$  desaturase and *Primula juliae*  $\Delta 6$  desaturase are similar to other desaturases present in food.

The fungus *Neurospora crassa*, the source of  $\Delta 15D$  gene, is considered a non-pathogenic and non-allergenic organism (Perkins and Davis, 2000), and is found in food sources worldwide.

*Primula juliae*, the source of  $\Delta 6$  desaturase gene, is a large genus of plants commonly known as Primrose and is not generally consumed as food. However, some plants from the *Primula* genus are used as herbal medicines and also for producing GLA-containing oils for human use.

## SUMMARY

SDA soybean oil is manufactured in accordance with current Good Manufacturing Practice and meets appropriate food-grade specifications. The exposure to SDA from the proposed food uses of SDA soybean oil is estimated to be no more than 1.5 g/day at the mean, and 3.0 g/day at the 90<sup>th</sup> percentile. The safety of SDA soybean oil is supported by the results of a published 90-day/1 generation reproductive toxicity rat study in which a NOAEL of 1 g SDA (4 g Monsanto's SDA soybean oil)/kg body weight/day was determined. No adverse effects attributable to SDA soybean oil were reported in a published human study in which subjects

consumed 3.66 g SDA (from Monsanto's soybean oil)/day for 16 weeks. Additional published studies on SDA and GLA from other sources corroborate the safety of SDA soybean oil. The safety of SDA soybean oil is further supported by the regular dietary consumption of fats and oils containing ALA, LA, and palmitic acid, and by the permitted uses of LA and palmitic acid in food in the U.S.

## CONCLUSION

We, the Expert Panel, have, independently and collectively, critically evaluated the data and information summarized above and conclude that the intended uses of Monsanto's stearidonic acid (SDA) soybean oil, meeting appropriate food-grade specifications presented in the supporting dossier [Documentation Supporting the Evaluation of Stearidonic Acid Soybean Oil as Generally Recognized as Safe] and produced consistent with current Good Manufacturing Practices (GMP), are safe and suitable.

We further conclude that the intended uses of Monsanto's SDA soybean oil, meeting appropriate food-grade specifications presented in the supporting dossier and produced consistent with current GMP, are Generally Recognized as Safe (GRAS) based on scientific procedures.

It is our opinion that other qualified experts would concur with these conclusions.

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30 September 2008  
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<b>Table of CFR Sections Referenced (Title 21—Food and Drugs)</b>		
Part	Section §	Section Title
172—Food additives permitted for direct addition to food for human consumption	172.860	Fatty acids
184—Direct food substances affirmed as generally recognized as safe	184.1065	Linoleic acid
	184.1329	Glyceryl palmitostearate
	184.1505	Mono- and diglycerides

**APPENDIX A-2**

**EXPERT PANEL REPORT CONCERNING THE NEW PROPOSED FOOD USES  
OF MONSANTO'S STEARIDONIC (SDA) OMEGA-3 SOYBEAN OIL IN FOODS**

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# EXPERT PANEL REPORT CONCERNING THE NEW PROPOSED FOOD USES OF MONSANTO'S STEARIDONIC ACID (SDA) OMEGA-3 SOYBEAN OIL IN FOODS

## INTRODUCTION

As independent experts qualified by relevant national and international experience and scientific training to evaluate the safety of food ingredients, we, the undersigned, Dr. Joseph F. Borzelleca, (Virginia Commonwealth University School of Medicine), Dr. Fergus M. Clydesdale (University of Massachusetts Amherst), Dr. Ernst J. Schaefer (Tufts University), and Dr. Ronald Walker (University of Surrey), were requested by the manufacturer, Monsanto Company (Monsanto), as an Expert Panel (hereinafter referred to as the Panel) to evaluate the impact of the new proposed food uses on the Generally Recognized as Safe (GRAS) status of stearidonic acid (SDA) omega-3 soybean oil (SDA soybean oil), under the conditions of intended use as a food ingredient.

Previously, the safety of SDA soybean oil as an ingredient in a number of foods was critically evaluated by the Expert Panel (See Attachment 1). The Panel concluded that the use of SDA soybean oil under the intended conditions of use was GRAS based on scientific procedures.

SDA soybean oil is intended for use as an ingredient in foods at levels that will provide 375 mg SDA per serving. Following the introduction of SDA soybean oil containing 20% SDA into the proposed foods in the previous GRAS determination, the *per capita* mean and 90<sup>th</sup> percentile intakes of SDA soybean oil were estimated to be 7.3 and 14.4 g/day, respectively (0.13 and 0.28 g/kg body weight/day, respectively). Fat intake increased from 78.8 g/day to 82.7 g/day at the mean, and from 136.5 g/day to 141.8 g/day at the 90<sup>th</sup> percentile. This increase is attributable to the addition of SDA soybean oil to foods that do not contain fat. Intake of SDA from all dietary sources increased from 0.004 g/day at the mean and 90<sup>th</sup> percentile to 1.5 g at the mean, and to 3.0 g/day at the 90<sup>th</sup> percentile. Mean linoleic acid (LA) intakes also increased from 10.1 g/day to 11.4 g/day at the mean, and from 19.5 g/day to 21.5 g/day at the 90<sup>th</sup> percentile. Mean intakes of *alpha*-linolenic acid (ALA) increased from 0.9 to 1.7 g/day, and 90<sup>th</sup> percentile intakes of ALA increased from 1.8 g/day to 3.1 g/day. Palmitic acid and *gamma*-linolenic acid (GLA) intakes increased marginally (less than 1 g/day), and changes in the remaining fatty acids were negligible.

The estimated *per capita* mean and 90<sup>th</sup> percentile intakes of SDA soybean oil containing 30% SDA to the proposed foods in the previous GRAS determination resulted in soybean oil intakes

of 5.2 and 10.5 g/day, respectively (0.09 and 0.20 g/kg body weight/day). Estimated intakes of individual fatty acids were similar to those reported for 20% SDA soybean oil due to the constant use level of SDA per serving.

In the course of reviewing the impact of expanding the uses of SDA soybean oil, the Expert Panel reviewed intake estimates for the previous GRAS uses and the increased exposures from the new proposed uses, information present in the original GRAS dossier, and any additional relevant information.

Following independent, critical evaluation of such data and information, the Expert Panel concluded that under the conditions of expanded uses in foods, SDA soybean oil, meeting appropriate food grade specifications and manufactured in accordance with current good manufacturing practices, is “Generally Recognized as Safe” based on scientific procedures. A summary of the basis for the Panel’s conclusion is provided below.

## DIETARY EXPOSURE

The previous and proposed new uses of SDA soybean oil are shown in the attached Table 1. There are several new proposed food categories and foods within existing categories, which are underlined. The new categories (and relevant examples) include: fish products (entrees with sauce), gravies and sauces (main entree sauces [spaghetti sauces]), meat products (entrees with sauce, hot dogs, luncheon meat), poultry products (entrees with sauce, luncheon meat), soft candy (candy bars), and soups and soup mixes (processed soups [not home made]). Cakes have been added to the existing category of baked goods and baking mixes. The use levels have not changed from the previous GRAS determination.

The consumption of SDA soybean oil from all previous and proposed new food uses was estimated by Exponent using the proposed food uses and use levels in conjunction with food consumption data included in the National Health and Nutrition Examination Surveys (NHANES 1999-2002) (CDC, 2007).

Following the introduction of 20% SDA soybean oil to the new proposed foods, the *per capita* mean and 90<sup>th</sup> percentile intakes of SDA soybean oil are estimated to be 10.1 and 19.6 g/day, respectively (0.18 and 0.38 g/kg body weight/day, respectively). Fat intake increased from 82.7 and 141.8 g/day at the mean and 90<sup>th</sup> percentile, respectively, to 84 and 143.6 g/day, respectively. Although fat intakes, and thus, caloric intakes, increased with the addition of the new food uses, food manufacturers will likely adjust their formulations such that the increase in calories will be negated. Intake of SDA from all dietary sources increased from 1.5 and 3.0 g/day at the mean and 90<sup>th</sup> percentile, respectively, to 2.1 g at the mean, and to 4.1 g/day at the 90<sup>th</sup> percentile. Palmitic acid, LA, ALA, and GLA intakes increased by  $\leq 0.5$  g/day, and changes in the remaining fatty acids were negligible.

The estimated *per capita* mean and 90<sup>th</sup> percentile intakes of SDA soybean oil following the introduction of 30% SDA soybean oil to the previous and new proposed foods were determined to be 7.6 and 14.8 g/day, respectively (0.1 and 0.3 g/kg body weight/day). The mean and 90<sup>th</sup> percentile U.S. *per capita* fat intake from the targeted foods increased from 81.3 and 140.0 g/day, respectively, to 82.1 and 140.8 g/day, respectively. SDA intakes increased to 2.2 g/day at the mean and 4.2 g/day at the 90<sup>th</sup> percentile. Palmitic acid, LA, ALA, and GLA intakes increased by 0.4 g/day or less. Changes in the remaining fatty acids were negligible.

## **SAFETY INFORMATION**

The safety of SDA soybean oil under the intended conditions of use is supported by the results of a published 90-day/1 generation reproductive toxicity rat study in which a NOAEL of 1 g SDA/kg body weight/day (4 g Monsanto's SDA soybean oil/kg body weight/day), the highest dose tested, was determined. No adverse effects attributable to SDA soybean oil were reported in a published human study in which subjects consumed 3.66 g SDA (from Monsanto's soybean oil)/day for 16 weeks. Additional published studies on SDA and GLA from other sources corroborate the safety of SDA soybean oil. The safety of SDA soybean oil is further supported by the regular dietary consumption of fats and oils containing ALA, LA, and palmitic acid, and by the permitted uses of LA and palmitic acid in food in the U.S.

The addition of the new proposed food uses increased the *per capita* estimated intakes of SDA by 0.7 g/day at the mean and 1.2 g/day at the 90<sup>th</sup> percentile. The estimated intakes of 20% SDA soybean oil increased by 2.8 and 5.2 g/day at the mean and 90<sup>th</sup> percentile, respectively, and the estimated intakes of 30% SDA soybean oil increased by 2.4 and 4.3 g/day at the mean and 90<sup>th</sup> percentile, respectively. The information used to support the uses of SDA soybean oil in the previous GRAS determination may therefore also be used in the current assessment. Based on the information reviewed previously and the lack of any recent new information that raises any safety concerns, the expanded food uses resulting in increased consumption levels do not impact the safety of SDA soybean oil.

## CONCLUSION

We, the Expert Panel, have, independently and collectively, critically evaluated the data and information summarized above and conclude that the intended new proposed uses of Monsanto's stearidonic acid (SDA) soybean oil, meeting appropriate food-grade specifications and produced consistent with current Good Manufacturing Practices (GMP), are safe and suitable.

We further conclude that the intended new proposed uses of Monsanto's SDA soybean oil, meeting appropriate food-grade specifications presented in the supporting dossier and produced consistent with current GMP, are Generally Recognized as Safe (GRAS) based on scientific procedures.

It is our opinion that other qualified experts would concur with these conclusions.

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Medicine

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Date

21 January 2009

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2/4/09 Feb. 4, 2009

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Ronald Walker, Ph.D., CChem, FIFST  
University of Surrey

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Date

18<sup>th</sup> February 2009

<b>Table 1 Proposed Food Uses for SDA Soybean Oil (New Proposed Uses Underlined)</b>	
<b>FDA Food Classifications (21 CFR §170.3(n))<sup>1</sup></b>	<b>Relevant Examples</b>
Baked goods and baking mixes	Biscuits, bagels, tortillas, English muffins <sup>2</sup>
	Breads
	Cookies
	<u>Cakes</u>
	Crackers
	Bars
Breakfast Cereals & Grains	Breakfast Cereals
Cheeses	Cottage Cheese
	Cheese
Dairy Product Analogs	Cream substitutes
	Soy milk
Fats & Oils	Margarine/Spreads <sup>3</sup>
	Mayonnaise
	Dressings for Salads
<u>Fish Products</u>	<u>Entrees with Sauce</u>
Frozen Dairy Desserts and Mixes	Milk desserts and frozen yogurt
	Novelties <sup>4</sup>
Grain Products and Pastas	Pasta
<u>Gravies and Sauces</u>	<u>Main entree sauces (spaghetti sauces)</u>
<u>Meat Products</u>	<u>Entrees with sauce, hot dogs, luncheon meat</u>
Milk Products	Milk Based Drinks
	Milk Shakes
	Yogurt
Nuts and Nut Products	Peanut Butter
<u>Poultry Products</u>	<u>Entrees with sauce, luncheon meat</u>
Processed Fruit Juices	Fruit Drinks, Fruit Smoothies
Processed Vegetable Products	Vegetable Juices
Puddings and fillings	Pudding
Snack Foods	All varieties
<u>Soft Candy</u>	<u>Candy bars</u>
<u>Soups and soup mixes</u>	<u>Processed soups (not home made)</u>

<sup>1</sup> Categories as defined in Food and Drug Administrations Reference amounts customarily consumed per eating occasion (21 CFR §101.12).

<sup>2</sup> Only select food categories listed under 21 CFR §101.12. e.g., bagels, tortillas, and wraps.

<sup>3</sup> Excludes margarines whose name indicated >80% fat content.

<sup>4</sup> Defined a "novelty" as any food sold as a single serve item (e.g. milk dessert bar, or stick).

**APPENDIX B**

**SUMMARY OF ANALYTICAL DATA, OTHER COMPOSITIONAL INFORMATION,  
AND STABILITY DATA**

**APPENDIX B-1**

**BATCH ANALYSES OF SDA SOYBEAN OIL**

## BATCH ANALYSES OF SDA SOYBEAN OIL

Five non-consecutive manufactured lots of SDA soybean oil (from several generations of soybeans) were analyzed to indicate that the manufacturing process produces a consistent product in terms of its chemical composition. The analytical data is presented in Tables B-1.1 and B-1.2. Additional characteristics are presented in Table B-1.3.

Variations between lots in fatty acid composition are a reflection in the natural variation of the resultant SDA soybean oil due to differences in temperature, humidity, soil composition or moisture, daylight *etc.* that occur when the SDA soybeans are grown in different years at different geographical locations.

Parameter	Specification	Lot Number				
		080319259S	070118018S	070418508S	070418543S	070618757S
Lovibond color (Yellow)	NMT 20	9.0	4.5	4.3	4.1	5.7
Lovibond color (Red)	NMT 2.0	0.3	0.2	0.2	0.2	0.2
Free fatty acids	NMT 0.1%	0.01	0.02	0.02	0.08	0.07
Iodine value	160-210	167	181	196	194	198
Lead	NMT 0.1 mg/kg	<0.10	<0.10	<0.10	<0.10	<0.10
Peroxide value	NMT 10 meg/kg	0.00	0.00	0.00	0.00	0.00
Stability, Active oxygen method (AOM)	NLT 2 h	5.5	4.6	5.0	5.3	16.5 <sup>1</sup>
Unsaponifiable matter	NMT 1.5 %	0.56	0.41	0.62	0.82	0.51
Water	NMT 0.1%	0.01	0.05	0.08	0.02	0.04

NLT = not less than; NMT = not more than  
<sup>1</sup>This lot contained stabilizer.

Fatty acid	Specification (% weight)	Lot Number				
		080319259S	070118018S	070418508S	070418543S	070618757S
< C14	<0.1	<0.1	< 0.1	< 0.1	< 0.1	< 0.1
C14:0 (myristic)	<0.5	0.1	0.1	0.1	0.1	0.1
C16:0 (palmitic)	9 - 13	12.0	11.6	11.6	11.5	11.7
C16:1 (palmitoleic)	<0.5	0.1	0.1	0.1	0.1	0.1
C18:0 (stearic)	2.0 - 5.5	4.6	4.3	3.9	4.0	3.8
C18:1 (oleic)	10 - 20	19.6	16.0	13.6	13.4	12.3
C18:2 (linoleic)	15 - 30	27.1	22.2	17.2	19.2	18.3

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Fatty acid	Specification (% weight)	Lot Number				
		080319259S	070118018S	070418508S	070418543S	070618757S
C18:3n-3 ( <i>alpha</i> -linolenic)	9 – 12	9.8	10.3	9.8	9.9	10.0
C18:3n-6 ( <i>gamma</i> -linolenic)	5 -8	6.2	6.1	6.8	6.5	7.2
C18:4 (stearidonic)	15 -30	16.9	20.2	26.9	24.2	25.9
C20:0 (arachidic)	<1.0	0.4	0.4	0.4	0.4	0.3
C20:1 (eicosenoic)	<1.0	0.3	0.2	0.2	0.3	0.3
C22:0 (behenic)	<0.5	0.4	0.3	0.3	0.3	0.3
C22:1 (erucic)	<0.1	<0.1	< 0.1	< 0.1	< 0.1	< 0.1
C24:0 (lignoceric)	<0.3	0.1	0.1	0.1	0.1	0.1

Analysis	Codex Soybean Oil Specification	Lot Number				
		080319259S	070118018S	070418508S	070418543S	070618757S
<b>Tocopherols (mg/100 gm)</b>						
alpha	0.9 – 35.2	7.5	7.6	5.0	5.7	5.0
gamma	8.9 – 98.3	62.1	76.1	64.7	76.9	76.3
delta	15.4 – 93.2	23.5	22.5	26.3	27.6	30.0
Total	60 – 337	93.1	106.0	96.0	110.0	111.3
<b>Sterols (mg/100 gm)</b>						
Campesterol	28.44 – 108.9	59.8	45.8	59.8	68.3	51.0
Stigmasterol	26.82 – 85.95	50.6	33.5	35.2	46.4	35.4
beta-Sitosterol	84.6 – 270	197.0	132.0	191.0	206.0	190.0
Others	10.26 – 68.85	77.8	54.4	76.9	91.5	76.2
Total	180 – 450	385.2	266.0	362.0	412.0	352.6

**APPENDIX B-2**

**DATA PERTAINING TO THE STABILITY OF SDA SOYBEAN OIL**

## STABILITY OF SDA SOYBEAN OIL

The stability of SDA soy oil, with respect to peroxide value (PV) and fatty acid content, has been investigated in accelerated aging and shelf-life studies using oils of 21% to 29% (w/w) SDA (as a % of total fatty acids) content.

In one study, oils were aged under stress conditions with air exposure at 55°C. Oils were aged in the presence of the chelating agent citric acid at 60 ppm. The terminal point of aging was chosen to be the oil transition point at approximately 8 to 9 days, as measured by peroxide value. However, data are reported for the period bounded by a more practical target point of aging, which was the point when PV reached 10, in accordance with FCC vegetable oil specifications for fresh oil. Because oil lots were sampled at predetermined time points, samples could not be obtained at precisely the PV of 10. A PV of 10 was reached between the 4 to 5 and 5 to 6 days sampling times. Only slight degradation of SDA soybean oil was observed by fatty acid composition through the aging period (Table B-2.1).

In another study representing conditions more typical of expected storage conditions, samples from the same lots were aged at 25°C in air for a period through PV = 10, which fell between the 72 and 89 day sampling time points. Only slight degradation of SDA soybean oil was observed by analysis of fatty acid composition through the aging period (Table B-2.2).

In another example, a 26% (w/w) SDA (as a % of total fatty acids) soybean oil lot and a soybean oil control lot that was processed in the same oil processing campaign, were aged at 25°C under nitrogen for 9 months (Table B-2.3). Only slight degradation of SDA soybean oil and soy oil was observed by fatty acid composition through the aging period. The PV of SDA soybean oil was slightly lower than that of conventional soybean oil after 9 months of storage.

The results described above demonstrate that SDA soybean oil maintains a PV <10 for at least 72 days when stored at room temperature (25°C in air) and for at least 4 to 5 days under accelerated aging conditions (55°C in air). The PV transition times for SDA soybean oil under these accelerated aging conditions are within the ranges observed for other omega-3 oils: unstabilized soy oils (some with citric acid) range from 4 to 19 days and stabilized fish and algal oils range from 4 to 11 days. Typically, oils with higher polyunsaturated fatty acid content such as fish, algal, and SDA soybean oils are less stable to oxidation than conventional soybean oil. However, when stored under nitrogen at room temperature for as long as 9 months, aged SDA soybean oil still maintains a PV similar to that of conventional soybean oil. The stability profile of SDA soybean oil meets the conditions for its intended use as an ingredient in a range of food applications.

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**Table B-2.1 Fatty Acid Composition (C18 series) and Peroxide Values for SDA Soybean Oils Aged at 55°C in Air**

*Fatty acid content in % total fatty acids*

Soybean Oil Description	Aging Day	Peroxide Value	C18:4n-3		C18:3n-3		C18:3n-6		C18:2		C18:1		C18:0	
			Value	% intact from T=0	Value	% intact from T=0	Value	% intact from T=0	Value	% intact from T=0	Value	% intact from T=0	Value	% intact from T=0
29% SDA soybean oil	0.0	0.56	28.79		10.88		7.44		18.66		16.12		4.37	
with 60 ppm Citric Acid	5.0	2.49	28.65	99.51	10.72	98.53	7.39	99.33	18.53	99.30	15.98	99.13	4.24	97.03
Lot 070418508S	6.0	36.24	27.78	96.49	10.56	97.06	7.28	97.85	18.59	99.62	16.47	102.17	4.40	100.69
21% SDA soybean oil	0.0	0.22	21.50		11.28		6.55		23.76		18.73		4.70	
with 60 ppm Citric Acid	5.0	2.15	20.84	96.93	10.94	96.99	6.40	97.71	23.56	99.16	18.93	101.07	4.71	100.21
Lot 070118018S	6.0	18.38	20.75	96.51	10.92	96.81	6.40	97.71	23.60	99.33	19.00	101.44	4.73	100.64
21% SDA soybean oil	0.0	0.14	20.72		11.35		6.51		24.31		18.95		4.78	
with 60 ppm Citric Acid	4.2	1.98	20.76	100.19	11.24	99.03	6.50	99.85	24.21	99.59	18.75	98.94	4.66	97.49
Lot 070118033S	5.0	14.2	20.48	98.84	11.16	98.33	6.45	99.08	24.23	99.67	18.91	99.79	4.72	98.74

**Table B-2.2 Fatty Acid Composition (C18 series) and Peroxide Values for SDA Soybean Oils Aged at 25°C in Air**

*Fatty acid content in % total fatty acids*

Soybean Oil Description	Aging Day	Peroxide Value	C18:4n-3		C18:3n-3		C18:3n-6		C18:2		C18:1		C18:0	
			Value	% intact from T=0	Value	% intact from T=0	Value	% intact from T=0	Value	% intact from T=0	Value	% intact from T=0	Value	% intact from T=0
29% SDA soybean oil	0	0.56	28.79		10.88		7.44		18.66		16.12		4.37	
with 60 ppm Citric Acid	72	2.53	28.98	100.66	10.74	98.71	7.41	99.60	18.53	99.30	15.88	98.51	4.18	95.65
Lot 070418508S	89	62.56	28.57	99.24	10.72	98.53	7.38	99.19	18.59	99.62	16.06	99.63	4.23	96.80
21% SDA soybean oil	0	0.22	21.50		11.28		6.55		23.76		18.73		4.70	
with 60 ppm Citric Acid	72	1.80	21.51	100.05	11.16	98.94	6.52	99.54	23.65	99.54	18.54	98.99	4.61	98.09
Lot 070118018S	89	12.08	21.23	98.74	11.10	98.40	6.48	98.93	23.71	99.79	18.73	100.00	4.64	98.72
21% SDA soybean oil	0	0.14	20.72		11.35		6.51		24.31		18.95		4.78	
with 60 ppm Citric Acid	72	2.31	20.20	97.49	11.04	97.27	6.39	98.16	24.13	99.26	19.12	100.90	4.81	100.63
Lot 070118033S	89	52.32	20.36	98.26	11.14	98.15	6.44	98.92	24.26	99.79	18.98	100.16	4.74	99.16

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**Table B-2.3 Fatty Acid Composition (C18 series) and Peroxide Values for SDA Soybean Oils Aged at 25°C under Nitrogen for 9 Months**

*Fatty acid content in % total fatty acids*

Soybean Oil Description	Aging Month	Peroxide Value	C18:4n-3		C18:3n-3		C18:3n-6		C18:2		C18:1		C18:0	
			% intact from T=0											
26% SDA soybean oil with 60 ppm Citric Acid Lot 070418543S	0	0.06	26.55		11.14		7.25		21.19		16.30		4.44	
	3	1.30	26.13	98.42	11.00	98.74	7.22	99.59	21.05	99.34	16.29	99.94	4.48	100.90
	6	2.43	26.21	98.72	11.08	99.46	7.23	99.72	21.12	99.68	16.50	101.23	4.62	104.05
	9	2.98	26.38	99.36	11.01	98.83	7.21	99.45	21.01	99.15	16.22	99.51	4.47	100.68
Control soybean oil* with 60 ppm Citric Acid Lot 070418542S	0	0.13	n.d.		8.98		n.d.		54.71		19.80		4.29	
	3	2.32	n.d.	n/a	8.91	99.22	n.d.	n/a	54.36	99.36	19.76	99.80	4.32	100.70
	6	3.35	n.d.	n/a	8.91	99.22	n.d.	n/a	54.36	99.36	20.13	101.67	4.44	103.50
	9	3.66	n.d.	n/a	8.86	98.66	n.d.	n/a	54.42	99.47	19.96	100.81	4.33	100.93

\* Control soybean oil comes from conventional soybean that has a genetic background similar to that of SDA soybeans with the exception of the introduced trait.



**Professional Certification**

Fellow, Academy of Toxicological Sciences

**Professional Affiliations**Societies

Academy of Toxicological Sciences\* \*\*  
American Association for the Advancement of Science  
American Chemical Society  
American College of Toxicology\*  
American Society of Pharmacology and Experimental Therapeutics\*\*  
(Environmental Pharmacology Committee; Liaison Committee, SOT;  
Toxicology Committee)  
Institute of Food Technologists (Professional Member)  
International Society of Regulatory Toxicology and Pharmacology\*  
(Member of Council)  
Sigma XI  
Society of Experimental Biology and Medicine\*  
(Councilor; Program Chairman of Southeastern Section)  
Society for Risk Analysis  
Society of Toxicology\* \*\*  
(Member and/or Chairman: Awards, Education, Legislative Affairs, Membership,  
Nominating Committees; Secretary of the Society, Councilor, and President;  
President,  
Food Safety Specialty Section)  
Virginia Academy of Science\*  
(Chairman, Medical Sciences Division)

\* Held elected office

\*\* Held appointed office or position

Board of Directors

ILSI (until 2002)

Board of Scientific and Policy Advisors

American Council on Science and Health (until 2000)

**Journals**

Editor, Food Chemical Toxicology, 1992-

Editorial Board

Environmental Carcinogenesis Reviews, 1981-2000  
Journal of Environmental Pathology, Toxicology and Oncology 1977- 2000  
Journal of Environmental Science and Health, 1979-2004  
Journal of the American College of Toxicology, 1982-  
Journal of Toxicology: Cutaneous and Ocular Toxicology, 1982- 1992  
Journal of Applied Toxicology, 1989-  
Pharmacology, 1978-  
Pharmacology and Drug Development, 1980-  
Toxicology and Applied Pharmacology, 1975-1978

**Consultantships (Past, Present)**Governmental

Food and Drug Administration  
National Institute of Mental Health  
National Cancer Institute  
Environmental Protection Agency  
Department of Labor - OSHA (Chairman, Carcinogens Standards Committee)  
U.S. Army - Research and Development Command

Non-Governmental

National Academy of Sciences - NRC  
Committee on Toxicology (Member, Chairman)/Board on Toxicology and  
Environmental Health Hazards  
Safe Drinking Water Committee  
Evaluation of Household Substances Committee (1138 Committee)  
Food Protection Committee  
Food Additives Survey Committee  
Committee on Risk-Based Criteria for Non-RCRA Hazardous Wastes  
Committee on Risk Assessment of Flame-Retardant Chemicals  
Food Chemicals Codex Committee

Federation of American Societies of Experimental Biology  
Select Committee on GRAS Substances  
Flavors and Extracts  
Biotechnology Product Safety  
Caprenin GRAS Committee

World Health Organization  
Joint Meeting on Pesticide Residues (JMPPR) (Member, Chairman)

NATO/CCMS Drinking Water Committee

Industrial

Chemical Companies; Trade Associations

## University Activities

### Related to Instruction

Prepared a laboratory manual in pharmacology (animal and human studies) (1960)  
Introduced the use of closed circuit TV and TV tapes in pharmacology (1960)  
Introduced clinical pharmacological experiments into the medical and dental programs (1960)  
Planning and participation in continuing education program (Schools of Dentistry, Medicine and Pharmacy)  
Planning and administration: each of the three major efforts in pharmacology (dental, medical, pharmacy) since 1960.  
Graduate Program - assisted in developing graduate training program in toxicology

### Current Teaching Activities

Present lectures on Toxicological Issues, Food Intake and Control

### Not Directly Related to Instruction

Elected senator from the graduate school, then vice-president of the University Senate  
Served on various committees (e.g. Curriculum, Search, Animal Care,) in each of the four major schools (Dentistry, Graduate, Medical, Pharmacy)

## Research

Research was continuously funded from 1956. Sources of support included governmental (U.S.P.H.S.; N.I.H; E.P.A.; N.I.D.A.) and non-governmental (industrial). (A list of publications is attached).

## Awards

DOD - US Army - Chemical Research Development and Engineering Center  
Distinguished Service Award, 1986

National Italian - American Foundation Award  
Excellence in Medicine and Community Service, 1987

Thomas Jefferson University  
Distinguished Alumnus Award, 1987

Virginia Commonwealth University - School of Basic Health Sciences  
Outstanding Faculty Award, 1987

Virginia Commonwealth University, Dept. of Pharmacology and Toxicology  
Professor of the Year- 1992

American College of Toxicology  
Distinguished Service Award - 1997

Virginia's Life Achievement in Science Award- April 2001

Bernard L. Oser Food Ingredient Safety Award by the Institute of Food Technologists-  
June 2001

International Society for Regulatory Toxicology and Pharmacology's International  
Achievement Award for 2001- December 2001

Society of Toxicology - Education Award- March 2002

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Borzelleca, J.F. and Manthei, R.W.: Factors influencing pentobarbital sleeping time in mice. Arch. Int. Pharmacodyn. Ther. 111: 296, 1957.

Borzelleca, J.F.: Studies of the contribution of bladder absorption to the physiological changes induced by pentobarbital. J. Pharm. Exp. Ther. 129: 305, 1960.

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Borzelleca, J.F., Bowman, E.R. and McKennis, H., Jr.: The cardiovascular and respiratory effects of (-)-cotinine. J. Pharmacol. Exp. Ther. 137: 313, 1962.

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Lowenthal, W. and Borzelleca, J.F.: Drug absorption from the rectum. I. J. Pharm. Sci. 54: 1790, 1965.

Ambrose, A.M., Borzelleca, J.F., Larson, P.S., Smith, R.B., Jr. and Hennigar, G.R.: Toxicologic studies on monochloroacetaldehyde: 2,4-dinitrophenylhydrazone, a foliar fungicide. Toxicol. Appl. Pharmacol. 8: 472, 1966.

Borzelleca, J.F. and Doyle, C.H.: Excretion of drugs in saliva. Salicylate, barbiturate, sulfanilamide. J. Oral. Ther. Pharmacol. 3: 104, 1966.

Borzelleca, J.F. and Lowenthal, W.: Drug absorption from the rectum. II. J. Pharm. Sci. 55: 151, 1966.

Wooles, W.R. and Borzelleca, J.F.: Prolongation of barbiturate sleeping time in mice by stimulation of the reticuloendothelial system. J. Reticuloendothel. Soc. 3: 41, 1966.

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- Borzelleca, J.F.: The excretion of glucose in saliva. *Dog. J. Oral Ther. Pharmacol.* 4: 338, 1968.
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- Larson, P.S., Egle, J.L., Jr., Hennigar, G.R., Lane, R.W. and Borzelleca, J.F.: Acute, subchronic and chronic toxicity of chlordecone. Toxicol. Appl. Pharmacol. 48: 29, 1979.
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**PUBLICATIONS**

Smith, L.W. and Borzelleca, J.F.: Movement of cadmium in rat submaxillary slices. *Toxicol. Appl. Pharmacol.* 55: 403, 1980.

Smith, L.W. and Borzelleca, J.F.: Movement of mercury in rat submaxillary slices. *Toxicology* 18: 169, 1980.

Borzelleca, J.F.: Report of the NATO/CCMS drinking water pilot study on health aspects of drinking water contaminants. *Sci. Tot. Environ.* 18: 205, 1981.

Carmines, E.L., Carchman, R.A. and Borzelleca, J.F.: Investigations into the mechanism of paraquat toxicity utilizing a cell culture system. *Toxicol. Appl. Pharmacol.* 58: 353, 1981.

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Tarka, S.M., Jr., Applebaum, R.S. and Borzelleca, J.F.: Evaluation of the perinatal, postnatal and teratogenic effects of coca powder and theobromine in Sprague-Dawley/CD rats. *Food Chem. Toxicol.* 24: 375, 1986.

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- Evaluation of the health aspects of certain zinc salts as food ingredients. 1973.
- Evaluation of the health aspect of pulps as they may migrate to food from packaging materials. 1973.
- Evaluation of the health aspects of propylene glycol and propylene glycol monostearate as food ingredients. 1973.
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- Evaluation of the health aspects of agar-agar as a food ingredient. 1973.
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- Evaluation of the health aspects of aconitic acid as a food ingredient. 1974.
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- Evaluation of the health aspects of sorbose as a food ingredient. 1974.
- Evaluation of the health aspects of sulfuric acid and sulfates as food ingredients. 1974.
- Evaluation of the health aspects of potassium iodide, potassium iodate, and calcium iodate as food ingredients. 1975.
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- Evaluation of the health aspects of glycerin and glycerides as food ingredients 1975
- Evaluation of the health aspects of dextrin and corn dextrin as food ingredients. 1975.
- Evaluation of the health aspects of sodium thiosulfate as a food ingredient. 1975.

**Contributing authorship on the following publications of the Life Sciences Research Office, Federation of American Societies of Experimental Biology (FASEB):**

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Evaluation of the health aspects of hydrochloric acid as a food ingredient. 1979.

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CAST Issue Paper Number 8, November 1997

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University of Toronto, Ontario, Canada	B.A. Food Chemistry
University of Toronto, Ontario, Canada	M.A. Food Chemistry
University of Massachusetts, Amherst, MA	Ph.D. Food Science & Technology
University of Massachusetts, Amherst, MA	Post-Doctoral Fellow - Food Science & Technology

**HONORS:**

- . Prince of Wales Gold Medal (1960) Awarded to the top graduating senior at Victoria College, University of Toronto.
- . National Research Council of Canada Scholarship (1961).
- . IFT - General Foods Fellowship (1964).
- . University of Massachusetts Distinguished Teacher Award (1972). (Three awards presented per year on a University-wide basis from among 1500 faculty).
- . William V. Cruess Award for Excellence in Teaching - presented by the Institute of Food Technologists, 1976.
- . Distinguished Food Scientist Award - co-recipient with F.J. Francis, presented by the New York Section of the IFT, 1978.
- . Elected to Fellow of the Institute of Food Technologists, 1979.
- . Recipient of the Third Annual Ethel Austin Martin Visiting Professorship in Human Nutrition at South Dakota State University, January 1983.
- . Recipient of the Lectureship Award from the Philadelphia Section of the IFT for "Dedicated Service and Outstanding Contributions to Food Science and Technology", 1983.
- . Recipient of the 1984 Babcock Hart Award, presented by the Institute of Food Technologists "to honor a person who has distinguished himself/herself by research contributions to food technology which have resulted in improved public health through some aspect of nutrition or more nutritious foods".
- . Named the F.W. Tanner Lecturer by the Chicago Section of the Institute of Food Technologists, 1985.
- . Donald K. Tressler Award for Outstanding Contributions to Food Science and Technology and their Communication to both Scientific Peers and the Public. Presented by the Institute of Food Technologists 1986.
- . Named the Ethel Austin Martin Distinguished Lecturer for 1986. South Dakota State University.
- . Elected to an Honorary Fellow of the Australian Institute of Food Science and Technology. 1987.
- . Recipient of the 1989 Nicholas Appert Award presented by the Institute of Food Technologists to honor a person for preeminence in and contributions to the field of food technology.
- . Elected to President of Phi Tau Sigma, the National Food Science Honors Society, 1992.
- . Recipient of the 1993 Charles A. Black Award for scientific accomplishment and communication presented by the Council for Agricultural Science and Technology (CAST).

- . Named the G. Malcolm Trout Visiting Scholar at Michigan State University, 1993.
- . Named the 1993 Centennial Visiting Professor by the Tokyo University of Fisheries.
- . Recipient of the Carl R. Fellers Award for bringing honor and recognition to the profession of Food Science. Presented by the Institute of Food Technologists, 1995.
- . Named a Fellow of the American College of Nutrition, 1996.
- . Named the Ernest Newberry Memorial Lecturer for the 14th International SAAFoST Congress in Pretoria, South Africa, 1997.
- . Named a member of the IFT Chief Research Officer's Food Council, 1997-present.
- . Inducted as an Honorary Member in "L'Association Internationale Nicolas Appert", 1999.
- . Elected Chair of the Board of Trustees of ILSINA (2001-present).
- . University of Massachusetts endowed the F.M. Clydesdale Professorship (2001) with funds raised by the Food Science Alumni and friends of the Department.
- . Reappointed for a third time as Chair of NAS, IOM, Food Forum through December 31, 2002.
- . Named a University of Massachusetts Distinguished Professor by the Board of Trustees, May, 2003.
- . Designated a National Associate of the National Academy of Sciences, December, 2003.
- . Named Chair of the IFT Expert Committee on Functional Foods (2004-05)
- . Appointed to the HHS/USDA 2005 Dietary Guidelines Committee
- . Appointed to an NIH Advisory Panel, 2005
- . Elected, as a Fellow, to the International Academy of Food Science and Technology, 2006
- . Awarded a University Leadership in Action Grant, 2006
- . Appointed to the Keystone Food and Nutrition Roundtable, 2007
- . Recipient of the Distinguished Faculty Award by the University of Massachusetts Alumni Association, 2007

#### **HONORARY SOCIETIES:**

Sigma Xi, Phi Kappa Phi, Phi Tau Sigma. (President, 1992)  
 President University of Massachusetts Chapter of Sigma X, 1986-1987.

#### **PROFESSIONAL SOCIETIES:**

American College of Nutrition (Fellow)  
 Institute of Food Technologists (Fellow)  
 American Society for Nutritional Sciences  
 American Chemical Society  
 American Association for the Advancement of Science  
 International Association for Food Protection

#### **ACADEMIC EXPERIENCE:**

***Distinguished University Professor and Head*** May 2003 - present.  
***Professor and Head*** July 1, 1989 - May 2003. Department of Food Science.  
***Director*** of the University of Massachusetts Amherst Food Science Strategic Research Alliance 1996 - present  
***Director*** of the University of Massachusetts Amherst Food Science Strategic Policy Alliance, 2004-present.

**Chair** Search Committee for Dean of the Isenberg School of Management, 2005-2007  
**Chair** Chancellor's Inaugural Academic Events Planning Committee 2002, 2003.  
**Chair** Provost's Committee on Revenue Development, 2001  
**Co-chair** of the University Life Sciences Steering Committee 1996 - 1998.  
**Acting Head** - Sept. 1988-June 30, 1989. Department of Food Science and Nutrition, University of Massachusetts.  
**Adjunct Professor** - Sept. 1, 1988 - 1993. Department of Human Nutrition, Universite Laval, Quebec, Canada.  
**Professor** - September 1976 to September, 1988, Department of Food Science and Nutrition, University of Massachusetts.  
**Visiting Food Scientist** - January 1976 to July 1976. Department of Food Science Technology, University of California, Davis, California.

**Associate Professor** - February 1972 to September 1976, Department of Food Science and Nutrition, University of Massachusetts.  
**Assistant Professor** - April 1967 to February 1972, Department of Food Science, University of Massachusetts.  
**Post Doctoral Appointment** - 1966-67, Department of Food Science, University of Massachusetts.  
**Research Associate** - 1962-66, Department of Food Science, University of Massachusetts.  
**Instructor** - 1961-62, Department of Food Chemistry, University of Toronto, Toronto, Canada.  
**Research Associate** - 1960-61, Department of Food Chemistry, University of Toronto, Toronto, Canada.

#### **INDUSTRIAL AND GOVERNMENT EXPERIENCE:**

Chemist, Canadian Industries Limited, Paint Research and Development Laboratories Carried out product development of automotive and retail paints. Followed this by conducting storage studies, stability tests and complete quality testing of products developed which were deemed to have a marketable value.  
Physiological Chemist, Defense Research Medical Laboratories, Canadian Department of National Defense. Investigated the effect of high pressure oxygen on the metabolic pathways of gamma-amino butyric acid in rats.

#### **SELECTED PROFESSIONAL EXPERIENCE IN ACADEMICS:**

- a. Research:  
Director of research grants in color and appearance of foods and the chemical changes involved in processing, with emphasis on minerals, pigments, and dietary fiber. Have graduated over 20 Ph.D. candidates and a similar number of M.S. candidates.
- b. Teaching:  
Food Science and Nutrition FS&N 850, Colorimetry and Appearance (graduate course).  
FS&N 860, Pigment Chemistry (graduate course).  
FS&N 101, The Struggle for Food (average enrollment is 250 students per semester). Total overall responsibility, teach 50%.  
FS&N 391A, Senior Seminar in Product Development.  
FS&N 385, Special Problems in Food Science.  
FS&N 872, Graduate seminar.  
Organized short courses in Food Color Measurement and Thermal Processing as well as Symposia.
- c. Administration and Counseling (Selected Responsibilities):

Director and Coordinator of the Undergraduate resident instruction program in the Department of Food Science during the 1970's.  
Past Chairman of the College of Food and Natural Resources Educational Policies Committee.  
Past Member of the College of Food and Natural Resources Educational Policies Committee.  
Have served as both a member and chairman of the Food Science Personnel Committee which makes recommendations on salary, promotion and tenure.  
Overall responsibility for counseling undergraduate majors in Food Science during the 1980's.  
Past Chairman of the Food Science Undergraduate-Faculty Liaison Committee.  
Past member of the Food Science Graduate-Faculty Liaison Committee.  
Actively involved with University summer student and parent counseling program.  
Past Chairman of the Food Science Undergraduate Curriculum Committee.  
Member of the University Standing Advisory Committee to the Center for Instructional Resources and Improvement.  
Chairman of the University Distinguished Teacher Award Committee (1974).  
Member of the Search Committee for a Director of the University Center for Instructional Resources and Improvement (1974).  
Member of the Search Committee for a Dean of the College of Food and Natural Resources (1976).  
Member of the Search Committee for a Department Head in the Department of Food Science and Nutrition (1978).  
Chairman of the Food Science and Nutrition Departmental Research Coordination Committee (1979).  
Past Member of the Food Science and Nutrition Graduate Policies Committee in Food Science and Nutrition.  
Invited participant in a University Workshop sponsored by the Provost and Vice Chancellor for Deans and Department Heads on Working with the Media, 1985 and on University Outreach in 1996.  
Member of the University Employee Assistance Program Board, 1982-1986.  
Member of the College of Food and Natural Resources Committee on Teaching Improvement 1989-1991.  
Member, University Life Sciences Steering Committee, 1995-present.  
Co-Chair, University Life Sciences Steering Committee, 1996-1998.  
Member, University Committee on Science and Technology Advancement, 1996-present.  
Chair, University Committee on Revenue Development, 2001.  
Member of the University Search Committee for a CFNR Development Officer, 2002.  
Chair of the University Affairs Inauguration Committee for Chancellor Lombardi, 2003  
University Homecoming Weekend Academic Planning Committee, 2004  
Search Committee for the Provost and Senior Vice Chancellor, 2004  
University Task Force on the Journalism/Communications Departments Merger, 2004  
Served as a faculty leader at Commencement, 2004  
Chaired the University Committee to evaluate Dean Thomas O'Brien of ISOM, 2005  
Member of the Provost's First Fall Convocation planning and selection group, 2005  
Faculty leader during Commencement, 2005  
Chaired the Search Committee for the Dean of ISOM, 2006, 2007

#### PROFESSIONAL SOCIETY OFFICES:

- . Past Chairman of the Education Committee of the North East Section of the Institute of Food Technologists.
- . Inter-Society Color Council Delegate to the National Institute of Food Technologists.
- . Chairman of the IFT Communications Committee on Food Safety and Nutrition from its inception in 1972 to 1978.
- . Member of the IFT Sub-committee on Nutrition Education (1973).
- . Member of the Graduate Jury Awards Committee of the IFT (1975-76).
- . Member of the IFT Committee on Graduate Education (1974).
- . Member of the North East Section IFT Professional Relations Committee (1974-76).
- . Nominated to the Board of Directors of the Inter-Society Color Council of America (1976).
- . Member of the William V. Cruess Awards Committee of the IFT (1976-79).
- . Member of the Program Committee of the IFT (1976-79).
- . Chairman of the Program Committee for the 1981 Annual Meeting of IFT.
- . Member of the IFT Communications Committee on Food Safety and Nutrition. 1972 to present.
- . Chairman of the Expert Panel on Scientific Affairs of the IFT, 1986 to 1994.
- . Elected to Membership on the IFT Executive Committee 1987-90.
- . Member of the IFT Policy Board of the Office of Scientific Public Affairs. 1986-1993.
- . Elected to the IFT Council (1989-92).
- . Elected as a member and Secretary of the Board of Trustees of the North American Division of the International Life Sciences Institute (1990-present). Elected to Chair of the Board, 2001-2003.
- . Elected as a member of the Board of Trustees of the International Life Sciences Institute (1990-present).
- . Scientific Advisor to the Food Nutrition and Safety Committee of the International Life Sciences Institute - Nutrition Foundation (1986-1990).
- . Chair of the Scientific Advisors of the Food Nutrition and Safety Committee of the International Life Sciences Institute (1990-present).
- . Member of the IFT Consumer Task Force, 2001-2002.
- . Member of the IFT Committee on Science, Communications and Government Relations, 2000-2003
- . Member of the American Dietetic Association Task Force on National Health, Food and Nutrition Policy, 2001-2002.

#### EDITORIAL BOARDS:

**Editor** of Critical Reviews in Food Science and Nutrition, CRC Press.

**Editor** of the CRC Book Series in Food Science and Nutrition.

**Member** of the Editorial Board of in Nutraceuticals World.

**Associate Editor** of the Encyclopedia of Food Science and Nutrition, John Wiley and Sons.

**Member** of the Editorial Board of Trends in Food Science and Technology, Elsevier Publishing Company.

**Member** of the Editorial Board of the Journal of Food Protection.

**Member** of the Editorial Board of Food Research International.

**Member** of the Editorial Board of Ciencia y Tecnologia Alimentaria.

**PUBLICATIONS:**

360 Technical Publications (see attached).  
20 Books and Monographs  
250 Invited Presentations to technical societies, industrial groups  
consumer groups, radio and TV (past 5 years).

**GRANTS AND DEVELOPMENT:**

Have been a co-principal investigator or principle investigator of grants from NIH, USDA, the Department of Defense, Industry, Trade Associations, Institutes and Foundations, as well as participating in regional Hatch projects over the past 35 years.

Over the last 5 years Grants have included [redacted] Cola Foundation, PI, Food Science/Policy Consumer Acceptan [redacted], [redacted]. USDA, CoPI with 5 others and a PI, Seafoo 99-02, [redacted]. [redacted] gic Research Alliance, Director 98-02, [redacted].

[redacted] 989, during my tenure as Departme [redacted] ave received over [redacted] in non [redacted] over [redacted] in endowment gift [redacted] r a f over [redacted].

Total gifts inc [redacted] 1990 to FY 2001. Endowment giving increased from [redacted] and non endowment gifts increased [redacted] times.

[redacted] ted our fifth endowment campaign. This campaign will be for [redacted] in support of graduate student scholarships.

**CONSULTANTSHIPS (selected)**

Have acted and am acting as a consultant to several major U.S. and international food companies.

Serve on or chair Scientific and Technical Advisory Boards and Committees for a number of major food companies, government agencies and the National Academies.

Served as a consultant to the University of Florida Agricultural Research and Education Center, Lake Alfred, Florida, in color chemistry to the National Science Foundation as a member of overview committees and to the National Academies and FOA.

Consulted for the Institute of Nutrition, University of North Carolina, Chapel Hill, North Carolina and Purdue University, Harvard University and Tufts in the area of curriculum design.

**APPOINTMENTS AND PRESENTATIONS (selected)**

Appointed to the Keystone Round Table on Food Nutrition and Health 2006

Appointed to an NIH Advisory Panel, 2005.

Appointed to the committee to review and establish the 2005 Dietary Guidelines for Americans by the Department of Health and Human Services.

Appointed to the National Academy, IOM Committee on the Use of Dietary Reference Intakes on Nutrition Labeling, 2002-2003.

Appointed as a special consultant to FDA 1998-2002.

Elected Chair of the Board of Trustees of ILSI-NA 2001-2003.

Appointed to Chair the Food Forum of the Food and Nutrition Board of the Institute of Medicine National Academy of Science, 1996-1999. Reappointed 1999-2001. Reappointed 2001-2002.

Elected to the Board of the IFIC Foundation 1996-present.

Chaired the FDA Working Panel to evaluate Olestra, November 14-17, 1995.

Appointment to the Food Advisory Committee of the Food and Drug Administration, 1994-1998. Reappointed as an ad hoc non voting member, 1999-present.

Appointed to the Food and Nutrition Board of the Institute of Medicine, National Academy of Sciences 1994-1997. Reappointed 1997-2000.

Appointed to the Keystone Committee on National Policy Dialogue on Food, Nutrition and Health 1993-1996.

Appointed to the National Academy of Sciences, Institute of Medicine Committee on Research Opportunities in Nutrition and Food Science 1990-1993.

Appointed to the Oversight Committee of the Designer Foods Program, in the National Cancer Institute, 1991.

Appointed to the Expert Panel on "Emerging Issues in Food Safety and Quality During the Next Decade". This was a panel of the Life Sciences Research Office of the Federation of American Societies for Experimental Biology to advise the Food and Drug Administration for the 1990's. (1989)

Appointed to the United States Senate Select Committee on Nutrition and Human Needs as a member of the panel on Nutrition and the Consumer. (1974).

Appointed to the National Academy of Sciences - National Research Council Board on Agriculture Committee "Scientific and Regulatory Issues Underlying Pesticide Use Patterns and Agricultural Innovations". 1985-87.

Appointed to the National Academy of Sciences - National Research Council General Committee on the DOD Food Program. 1974-77. 1978-81.

Appointed to the National Academy of Sciences - National Research Council Committee on Food Service Systems. 1974-77. Reappointed 1978-81.

Appointed to the Committee on General Nutrition Education of the Pennsylvania State University Nutrition Education Conference Workshop. 1974.

Elected to the Board of Governors of Food Update of the Food and Drug Law Institute, (1984-87).

Appointed to the Board of Advisors of Brigham Young University Ezra Taft

Benson Agricultural Institute, (1983-1991).

Invited to present a paper at the 4th International Congress of Food Science and Technology, Madrid, Spain. 1974.

Invited to present papers at the Gordon Research Conference on Food and Nutrition, in 1974 and 1975.

Invited to testify at the Federal Trade Commission Hearings on Food Advertising, in 1976 and 1977.

Invited to submit testimony to Subcommittees on both the House and Senate on several occasions.

Invited to present an address to the Royal Canadian Institute (Canada's oldest scientific society), 1979.

Invited to present the Annual Lecture to the British Nutrition Foundation, London, England. (1979).

Invited to present a paper at the 6th Annual Congress of the International Nutritional Anemia Consultative Group in Santiago, Chile, 1981, sponsored by AID.

Invited to present a paper to a joint meeting of the British Nutrition Foundation and the Soc. Chem. Ind. London, England, 1986.

Keynote speaker at the annual meeting of the Australian IFST, 1987. Albury, Australia.

Ellen Park, 14th Annual Memorial Lecture. Univ. of Toronto, 1987.

Invited to present one of four Plenary Papers at the Opening Session of the 50th Anniversary Annual Meeting of the Institute of Food Technologists, Chicago, IL, 1989.

Invited as the Foreign Speaker to present the main lecture at the 50th Anniversary of the Finnish Meat Research Institute in Hameenlinna, Finland. August, 1990.

Invited to present a Plenary Paper at the 8th World Congress of Food Science and Technology, Toronto, Canada, October 1991.

Invited to present a paper at the International Congress of Nutrition in Adelaide, Australia, October 1993.

Invited to present the Centennial Lecture at the Tokyo University of Fisheries, 1993.

Invited to present a paper at the Unilever Research Center, Celebratory Symposium at Colworth House, Bedford, England. 1995.

Invited to present a paper at the 16th International Congress of Nutrition in Montreal Canada, 1997.

Invited to present the Ernest Newbury Memorial Lecture at the 14th South

African Institute of Food Science and Technology International Congress, Pretoria, South Africa, 1997.

Invited to present the opening address at the Celebratory Scientific Symposium, of 25th Anniversary" Euro R&D Center, CPC Europe 35th Anniversary" Institute for Research and Development, CPC Germany, 1997.

Invited to present a paper on Research Priorities for Functional Foods to the USDA Advisory Committee, March 13, 2000.

Organized and Chaired a Symposium on Food Science and Health: Towards a National Rational Health Policy, Amherst, MA, November 7, 8, 2001.

Organized and Chaired a Symposium on Future Directions in Food Safety Research sponsored by the Food forum of the Institute of Medicine, National Academy of Science, Washington, DC, February 27, 2002.

Invited to moderate a session on Metabonomics in a Symposium on Food, Nutrition and Health sponsored by the Food Forum of the Institute of Medicine, National Academies of Science, Washington, DC, May 6, 2003.

**OUTREACH:**

Initiated, organized and serve as Director of the new University of Massachusetts Food Science Strategic Research Alliance which has 20 member Companies.

Formalized the utilization of our Pilot Plant by State Industries.

Began a series of seminars which led to an off campus MS program at Company Headquarters within the State.

Began a certification program for scientific personnel in a Connecticut Company.

Actively involved in teaching short courses to industry as a means of updating current techniques.

Informal counseling to several major food industries, on regulatory issues, health, nutrition and technology.

Work in close cooperation with the State Food Industry and with local groups and organizations.

Presented some 120 interviews to public interest groups and the press in the past five years.

## PERSONAL PUBLICATIONS

### Original Research:

Wood, J.D., W.J. Watson and F.M. Clydesdale. 1963. Gamma-Amino-butyric Acid and Oxygen Poisoning. *Journal of Neurochemistry*, 10:625-633.

Clydesdale, F.M. and C.H. Podlesney, Jr. 1968. A Computer Program for the Interconversion of Color Data. *Color Engineering*, 6(3):55-56.

Clydesdale, F.M. and F.J. Francis. 1968. A study of chlorophyll changes in thermally processed spinach as influenced by enzyme conversion and pH adjustment. *Food Technol.*, 22(6):135-138.

Clydesdale, F.M. and F.J. Francis. 1969. Color Measurement in Foods: Correlation of Raw, Transformed and Reduced Data with Visual Ratings for Spinach Puree. *Food Sci.*, 34:349-352.

Clydesdale, F.M. and C.H. Podlesny, Jr. 1968. Addition to a Computer Program for the Interconversion of Color Data. *Color Engineering*, (6),24.

Lin, Yi-Do, F.M. Clydesdale and F.J. Francis. 1970. Organic Acid Profiles of Thermally Processed Spinach. *J. Food Sci.*, 35:641-644.

Huang, I-Lo, F.J. Francis and F.M. Clydesdale. 1970. Colorimetry of Foods: Color measurement of squash using the Kubelka-Munk concept. *J. Food Sci.*, 35:315-317.

Huang, I-Lo, F.J. Francis and F.M. Clydesdale. 1970. Colorimetry of Foods: Carrot puree. *J. Food Sci.*, 35:771-773.

Fleischmann, D.L., F.M. Clydesdale and F.J. Francis. 1970. Effect of magnesium carbonate and sodium phosphate on the extraction of chlorophyll-like pigments after thermal processing of spinach puree. *J. Milk and Food Technol.*, 33:456-459.

Lin, Yi-Do, F.M. Clydesdale and F.J. Francis. 1971. Organic Acid Profiles of Thermally Processed, Stored Spinach Puree. *J. Food Sci.*, 36:240-242.

Clydesdale, F.M., D.L. Fleischmann and F.J. Francis. 1970. Maintenance of Color in Processed Green Vegetables. *Food Product Development*, 4(5):127-138.

Clydesdale, F.M., A.W. Goodman and F.J. Francis. 1971. The effect of a phosphate buffer and magnesium carbonate of quality attributes of cooked green vegetables. *J. Milk and Food Technol.*, 34:78-81.

Clydesdale, F.M., Y.D. Lin and F.J. Francis. 1972. Formation of 2-pyrrolidone-5-carboxylic acid from glutamine during processing and storage of spinach puree. *J. Food Sci.*, 37:45-47.

Lin, Y.D., F.M. Clydesdale and F.J. Francis. 1972. A simplified method for the analysis of glutamine. *J. Food Sci.*, 37:488-489.

Ehmann, E.P., R.A. Ageloff and F.M. Clydesdale. 1972. A multipurpose colorimetric computer program. *Food Product Development*, 6:111-112.

- Gullett, E.A., F.J. Francis and F.M. Clydesdale. 1972. Colorimetry of Foods: 5. An orange beverage - Tang. *Can. Inst. Fd. Sci. Tech. J.*, 5(1):32-36.
- Gullett, E.A., F.J. Francis and F.M. Clydesdale. 1972. Colorimetry of Foods: 4. Orange Juice. *J. Food Sci.*, 37:389-393.
- Driver, M., F.J. Francis and F.M. Clydesdale. 1976. Colorimetry of Dry Breakfast-Type Cereals. *J. Food Sci.*, 41:1353-1356.
- Bibeau, T.C., F.M. Clydesdale and F.M. Sawyer. 1974. Glutamine as a predictive measurement in the quality assessment of carrot puree. *J. Food Sci.*, 2:365-367.
- Johnson, L., F.M. Clydesdale and F.J. Francis. 1976. The use of colorimetric data to predict chemical and visual changes in solution. 4th International Congress of Food Science and Technology. Vol. II:150-159.
- Chu, N.T., F.M. Clydesdale and F.J. Francis. 1973. Isolation and identification of some fluorescent phenolic compounds in cranberries. *J. Food Sci.*, 38:1038-1042.
- Eagerman, B.A., F.M. Clydesdale and F.J. Francis. 1973. Comparison of color scales for dark colored beverages. *J. Food Sci.*, 38:1051-1055.
- Eagerman, B.A., F.M. Clydesdale and F.J. Francis. 1973. Development of new transmission color scales for dark colored beverages. *J. Food Sci.*, 38:1056-1059.
- Bibeau, T.C. and F.M. Clydesdale. 1975. Organic acid profiles of thermally processed carrot puree. *J. Milk and Food Technol.*, 38(9):518-520.
- Chu, N.T. and F.M. Clydesdale. 1976. Decomposition of organic acids during processing and storage. *J. Milk and Food Technol.*, 39:477-480.
- Chu, N. T. and F.M. Clydesdale. 1976. Reactions between amino acids and organic acids. Reaction of tryptophan and alpha-ketoglutaric acid. *J. Food Sci.*, 41:895-898.
- Chu, N.T. and F.M. Clydesdale. 1976. Reactions between amino acids and organic acids. Reaction of tryptophan and pyruvic acid. *J. Food Sci.*, 41:891-894.
- Chu, N. and F.M. Clydesdale. 1975. The effect of concentration, thermal processing, and storage temperature on the interaction between alpha-ketoglutaric acid and tryptophan. *J. Milk and Food Technol.* 38(10):573-580.
- Johnson, J., F.M. Clydesdale and F.J. Francis. 1975. Use of expanded color scales to predict chemical and visual changes in solutions. *J. Food Sci.*, 41:74-77.
- Bibeau, T.C. and F.M. Clydesdale, 1976. Variations in organic acid profiles of thermally processed green beans of different varieties *Phaseolus vulgaris* L. *J. Milk and Food Technol.*, 39:536-538.
- Bibeau, T.C. and F.M. Clydesdale. 1978. Thermal Stability of Subsidiary Dyes Associated with FD&C Yellow No. 6. *J. Food Sci.*, 43(2):521-523.

- Eagerman, B.A., F.M. Clydesdale and F.J. Francis. 1977. Determination of fresh meat color by objective methods. *J. Food Sci.*, 42:707-710.
- Anderson, N.E. and F.M. Clydesdale. 1978. Estimation of tryptophan content by spectrophotometric methods: Analysis of the interaction between alpha-ketoglutaric acid and tryptophan. *J. Food Protection*. 41(3):163-167.
- Anderson, N.E. and F.M. Clydesdale. 1978. Analysis of tryptophan utilizing its reaction with alpha-ketoglutaric acid. *J. Food Sci.*, 43:1595-1599.
- Eagerman, B.A., F.M. Clydesdale and F.J. Francis. 1978. A rapid method for following changes in myoglobin in beef muscle. *J. Food Sci.*, 43:468-469.
- Main, J.H., F.M. Clydesdale and F.J. Francis. 1978. Spray drying anthocyanin concentrates for use as food colorants. *J. Food Sci.*, 43:1693-1694.
- Bibeau, T.C. and F.M. Clydesdale. 1978. Thermal Stability of Subsidiary dyes in Red #2. *Can. J. Food Sci. and Technol.*, 11(4):173-176.
- Lee, K. and F.M. Clydesdale. 1979. Quantitative determination of the elemental, ferrous, ferric, soluble and complexed iron in foods. *J. Food Sci.*, 44:540-554.
- Kostyla, A.S. and F.M. Clydesdale. 1979. Psychophysical relationships between color, flavor, aroma, sourness and sweetness in a red cherry flavored beverage. Presented at IFT meeting, Dallas, 1978.
- Clydesdale, F.M., J.H. Main, F.J. Francis and R.H. Damon. 1978. Concord grape pigments as colorants for beverages and desserts. *J. Food Sci.*, 43:1687-1692, 1697.
- Clydesdale, F.M., J.H. Main and F.J. Francis. 1978. Cranberry pigments as colorants for beverages and gelatin desserts. *J. Food Prot.*, 42:196-201.
- Clydesdale, F.M., J.H. Main and F.J. Francis. 1978. Roselle, Hibiscus Sabdariffa L, anthocyanins as colorants for beverages and gelatin desserts. *J. Food Prot.*, 42:204-207.
- Clydesdale, F.M., J.H. Main and F.J. Francis. 1978. Effect of anthocyanin preparations as colorants on hygroscopicity of dry pack food products. *J. Food Prot.* 42:225-227.
- Camire, A. and F.M. Clydesdale. 1979. Analysis of anthocyanins by HPLC. *J. Food Sci.*, 44:926-927.
- Metivier, R.P., F.J. Francis, and F.M. Clydesdale. 1980. Solvent extraction of anthocyanins from wine pomace. *J. Food Sci.*, 45:1099-110.
- Camire, A.L., F.M. Clydesdale and F.J. Francis. 1980. Effect of Cinnamic Acid on Anthocyanin Stability in Cranberry Juice. *J. Food Prot.*, 43(1):36-37.
- Lee, K. and F.M. Clydesdale. 1980. Chemical changes of iron in food and drying processes. *J. Food Sci.*, 45:711-715.
- Anderson, N.E. and F.M. Clydesdale. 1980. An analysis of the dietary fiber content of a standard wheat bran. *J. Food Sci.*, 45:336-340.

- Anderson, N.E. and F.M. Clydesdale. 1980. Effects of processing on the dietary fiber content of wheat bran, pureed green beans, and carrots. *J. Food Sci.*, 45:1533-1537.
- Anderson, N.E. and F.M. Clydesdale. 1980. An analysis of the dietary fiber content of corn bran. *J. Food Prot.*, 43:760-762.
- Lee, K. and F.M. Clydesdale. 1980. Effect of baking on the forms of iron in iron-enriched flour. *J. Food Sci.*, 45:1500-1504.
- Lee, K. and F.M. Clydesdale. 1981. The effect of thermal processing on the endogenous and added iron in canned spinach. *J. Food Sci.*, 46:1064-1068, 1073.
- Camire, A.L. and F.M. Clydesdale. 1981. The effect of pH on the binding of Ca, Mg, Zn, and Fe to wheat bran and fractions of a dietary fiber. *J. Food Sci.*, 46:548-551.
- Nojeim, S.J. and F.M. Clydesdale, 1981. The effect of pH and ascorbic acid on iron valence in model systems and food. *J. Food Sci.*, 46:606-611, 616.
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- 23) Clydesdale, F.M. (Associate Editor). 2000. *Wiley Encyclopedia of Food Science and technology, 2<sup>nd</sup> Edition* (F.J. Francis, Editor). 4 Volumes, 2768 pp.
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## CURRICULUM VITAE

**Name:** Ernst J. Schaefer, M.D. 01/25/05

**Date of Birth:** November 18, 1945

**Citizenship:** United States

**Marital Status:** [REDACTED]

**Current Positions:** Distinguished University Professor  
Tufts University School of Medicine  
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Director & Senior Scientist, Lipid Metabolism Laboratory,  
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Director, Lipid and Heart Disease Prevention Clinic  
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**Education:** 1968 - B.A., Harvard University, Cambridge, MA, (cum laude, biology)  
1970 - B.M.S., Dartmouth Medical School, Hanover, NH.  
1972 - M.D., Mount Sinai School of Medicine, New York, NY.

**Board** American Board of Medicine

**Certification:** American Board of Internal Medicine

**Brief Summary:** Dr. Schaefer received his B.A. cum laude (biology) from Harvard University, his B.M.S. from Dartmouth Medical School, and his M.D. with honors from Mt. Sinai School of Medicine. He did his medical residency at Mt. Sinai Hospital, New York, and an endocrinology fellowship at the National Institutes of Health, where he also was a senior investigator and head of the clinical service of the Molecular Disease Branch of the National Heart, Lung, and Blood Institute. Since 1982 he has been at Tufts University where he is currently a Distinguished University Professor at Tufts University School of Medicine and the Friedman School of Nutrition Science and Policy at Tufts University, as well as Director of the Cardiovascular Research Laboratory and the Lipid and Heart Disease Prevention Clinic in Boston. He is also a Senior Scientist and Director of the Lipid Metabolism Laboratory at the Jean Mayer USDA Human Nutrition Research Center on Aging at Tufts University.

For his research at the NIH, Dr. Schaefer received the J.D. Lane Award of the U.S. Public Health Service (1981) and the Irvine H. Page Arteriosclerosis Research Award from the American Heart Association (1981) for defining the metabolic defect in Tangier disease and describing two new genetic disorders apoA-I/C-III/A-IV and apoE deficiency characterized by premature heart disease.

For his research, teaching, and clinical care at Tufts University and Tufts-New England Medical Center Dr. Schaefer has received the Saul Horowitz Research Award from Mt. Sinai School of Medicine (1989), the Oliver Smith Award of New England Medical Center for Patient Care (1999, 2001, 2003), the E.V. McCollum Research Award of the American Society for Clinical Nutrition (2000), and a Distinguished Faculty Award from Tufts University (2001).

Dr. Schaefer is an author or co-author of over 400 publications and served on the first and second adult treatment panels of the National Cholesterol Education Program of the National Institutes of Health, on the Nutrition and Metabolism Study Section of the NIH, and the Nutrition Committee of the American Heart Association. Since 1997 Dr. Schaefer has been the U.S. editor of the journal *Atherosclerosis*.

His research focuses on the nutritional and genetic regulation of plasma lipoproteins, and their relationship to coronary heart disease risk, and on the dietary and drug treatment of lipid disorders, as well as on optimal diets for the prevention of heart disease in the elderly. Areas of significant research at Tufts University in the past

two decades have been characterization of plasma lipoprotein metabolism in the fasting and post-prandial state, definition of genetic lipoprotein disorders associated with premature heart disease, effects of different diets restricted in saturated fat and cholesterol on heart disease risk, the role of HDL subspecies in reverse cholesterol transport, the effects of popular diets on weight loss and heart disease risk, genetic markers of heart disease, and the effects of statins, niacin, estrogens, and cholesterol transfer protein inhibitors on plasma lipoprotein metabolism.

<b>Employment:</b> 1971	Research Rotation on Lipoproteins, Albert Einstein College of Medicine, (Drs. Paul Roheim, Howard Eder).
1972-1975	The Mount Sinai Hospital, New York, New York, Medical Internship, First and Second Year Medical Residency (Dr. Solomon Berson, Dr. Fenton Schaffner, Dr. Richard Gorlin)
1974-1975	Guest Investigator, Rockefeller University, New York, New York; (on elective time from Mt. Sinai); (Dr. Paul Schreiber)
1975-1978	Staff Associate, Molecular Disease Branch, National Heart Lung and Blood Institutes of Health, Bethesda, MD; (Dr. Robert Levy, Dr. Bryan Brewer).
1978-1980	Endocrinology Fellow, National Institutes of Health, Bethesda, MD. (Dr. Bruce Weintraub).
1980-1982	Senior Investigator, Molecular Disease Branch, National Heart, Lung, and Blood Institute, National Institutes of Health, Bethesda, MD. (Dr. Bryan Brewer).
1982-present	Director, Lipid Metabolism Laboratory, Jean Mayer USDA Human Nutrition Research Center on Aging at Tufts University, Boston, MA. (Drs. Hamish Munro, Harold Sandstead, Irwin Rosenberg, Robert Russell).
1982-2004	Director, Lipid Clinic and Lipid Division, New England Medical Center, Boston, MA
1982-1989	Associate Professor of Medicine, Tufts University School of Medicine, Boston, MA
1982-1989	Associate Professor of Nutrition, School of Nutrition, Tufts University, Medford, MA
1989-2001	Professor of Medicine, Tufts University School of Medicine, Boston, MA
1989-2001	Professor of Nutrition, Friedman School of Nutrition Science & Policy, Boston, MA
2001-present	Distinguished University Professor
2004-	Director, Lipid and Heart Disease Prevention Clinic and Research Program, Cardiovascular Research Associates, Inc., Boston, MA

**Military Service:** 1975-82: Surgeon, Commissioned Corps, U.S. Public Health Service.

**Societies:** Fellow, American Heart Association, Council on Arteriosclerosis  
Fellow, American Federation of Clinical Research  
Fellow, American Society of Clinical Investigation  
Fellow, American Institute of Nutrition  
Fellow, American College of Physicians  
Member, American Association for the Advancement of Science

**Honors:** B.A., cum laude, Harvard University, 1968.  
Mosby Book Award for Excellence in Clinical Medicine, Mount Sinai School of Medicine, Class of 1972.  
J. D. Lane Investigator Award, U.S. Public Health Service Professional Association (shared with D.W. Anderson, Ph.D. and H. Bryan Brewer, Jr., M.D.), 1981.  
Irvine H. Page Arteriosclerosis Research Award for Young Investigators, American Heart Association Council on Arteriosclerosis, 1981.  
Saul Horowitz Jr. Memorial Research Award, Mt. Sinai School of Medicine, NY, 1989.  
Outstanding Publication of the Year, 1992, Jean Mayer USDA Human Nutrition Research Center on Aging at Tufts University (shared with J.S. Cohn).  
Oliver Smith Award for excellence, compassion, and service to patients at New England Medical Center, 1999, 2001. and 2003  
E.V. McCollum Award, American Society for Clinical Nutrition, 2000.  
Distinguished Faculty Award, Tufts University, 2001.

**Special Scientific Recognition, Professional Activities:**

USA-USSR First Lipoprotein Symposium and Scientific Exchange, Leningrad, 1981.  
David Rubinstein Lecture, Canadian Lipoprotein Club, Quebec, 1982.

Seminar in Medicine, Beth Israel Hospital, Boston, 1983.  
 Reviewer, NIH grants and Program Projects, 1982-present.  
 Member, American Heart Association, Council on Arteriosclerosis, Credentials Committee, 1984-1986.  
 Member, American Heart Association, Lipoprotein Metabolism Grant Review Committee, 1983-1987.  
 Member, American Heart Association, Council on Arteriosclerosis, Program Committee, 1985-1987.  
 Member, Parent Committee for Evaluation of Specialized Centers of Research on Arteriosclerosis, National Heart, Lung, and Blood Institute, 1985-1986.  
 Member, Parent Committee for Evaluation of National Demonstration and Education Programs in Arteriosclerosis, NHLBI, 1986.  
 Member, Editorial Board, *Circulation*, 1983-1986.  
 Member, Editorial Board, *Metabolism*, 1985-1992.  
 Member, Editorial Board, *Journal of Nutrition*, 1987-1992.  
 Member, National Cholesterol Education Program, Expert Panel on Adult Detection and Treatment (ATP I), National Heart, Lung and Blood Institute, National Institutes of Health, 1986-1987.  
 Member, Nutrition Study Section, National Institutes of Health, 1986-1990.  
 USA-USSR Second Lipoprotein Symposium and Scientific Exchange, Bethesda, MD, 1986. Member, Policy Board, Atherosclerosis Risk in Communities, National Heart, Lung and Blood Institute, 1986-present.  
 Member, Cholesterol Education Program, American Heart Association, Massachusetts Affiliate, 1988-1996; Chairman 1990-1991.  
 Member, American Heart Association Nutrition Committee, 1989-1992; and Chairman, Program Committee 1989-1991.  
 Member, National Cholesterol Education Program, Second Expert Panel on Adult Detection and Treatment (ATP II), National Heart Lung and Blood Institute, National Institutes of Health, 1991-1992.  
 Member, Metabolism Study Section, National Institutes of Health, 1995-2000; Chairman 1998-2000.  
 Editor, *Atherosclerosis*, 1997 - present.  
 Member, US-Italy Scientific Exchange, 2002, 2003.  
 Speaker, XIIIth International Symposium on Atherosclerosis, Kyoto, Japan, 2003  
 Plenary Speaker, Japan Atherosclerosis Society Meeting, Fukuoka, Japan, 2004  
 Keynote Speaker, Korean Society of Lipidology, Seoul, Korea, 2004  
 Speaker, Pharmacogenetics Symposium, Cold Spring Harbor Laboratories, NY 2004

#### Major Current Research Support:

1. Tufts University Contract with the U.S. Department of Agriculture at the Human Nutrition Research Center on Aging at Tufts University, "Lipoproteins, Nutrition, and Aging" Contract 53-3K06-5-10 (10/82-present; E.J. Schaefer, M.D., Principal Investigator) (70%).
2. National Institutes of Health, "Caloric Density, Obesity, and Cardiovascular Risk", Grant R01HL-57981; (8/1/99 - 7/30/04, E.J. Schaefer, M.D., Principal Investigator) (renewal pending).
3. National Institutes of Health, Human Metabolic and Genetic Core Laboratory, Tufts-New England Medical Center, Boston Obesity Nutrition Research Center, Center Grant with Boston University, Harvard School of Public Health, and Beth Israel Deaconess Medical Center, Harvard Medical School, (7/1/03 – 6/30/08; E.J. Schaefer, M.D., Core Laboratory Director, B. Corkey, Principal Investigator) (5%)
4. National Institutes of Health, "Pharmacogenetics of Statins", Grant R01 HL 074753 (3/1/04 – 2/29/08. E.J. Schaefer, MD, Principal Investigator) (25%).
5. Veterans Affairs Contract Central Laboratory for Diabetes Intervention Study, (9/1/01 – 8/30/07, E.J. Schaefer, Principal Investigator).
6. National Institutes of Health, "HDL Subspecies and Coronary Heart Disease," (4/1/00 – 4/30/05, B.F. Asztalos, Ph.D., Principal Investigator) (renewal pending).
7. National Institutes of Health, "Hormone Replacement, Inflammation, and Coronary Artery Disease," (11/1/03 – 10/30/06, S. Lamon-Fava, M.D., Ph.D., Principal Investigator).
8. National Institutes of Health, "Molecular Basis of HDL Deficiency", 1998-2008, Current Principal Investigator ME Brousseau, PhD
8. National Institutes of Health R01HL-54727, Dietary Fat, Plasma Lipids and other CHD Risk Factors (5/96- present, A.H. Lichtenstein, D.Sc., Principal Investigator).
9. National Institutes of Health, Markers of Cholesterol Metabolism and Heart Disease, (11/1/03 – 10/30/06, A.H. Lichtenstein, D.Sc., Principal Investigator).

Past NIH Grant Support to Dr. Schaefer:

1. "Apolipoprotein Gene Polymorphism and Atherosclerosis (with Dr. J. Ordovas) 1985-1988
2. "Effects of Dietary Fats on Lipoprotein Metabolism" (with Dr. A. Lichtenstein) 1988-1999
- 3.

**BIBLIOGRAPHY** \* invited reviews

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3. Gordon M, Schaefer EJ, Finkel M: Treatment of protein losing gastropathy with atropine. *Am J Gastroenterol*. 66:535-539, 1976.
4. Schaefer EJ, Jenkins LL, Brewer HB Jr: Human chylomicron apolipoprotein metabolism. *Biochem. Biophys. Res. Commun.* 80:405-412, 1978.
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7. Schaefer EJ, Levy RI, Anderson DW, Danner RN, Brewer HB Jr, Blackwelder WC: Plasma-triglycerides in regulation of HDL-cholesterol levels. *Lancet* 2:391-393, 1978.
8. Schaefer EJ, Foster DM, Jenkins LL, Lindgren FT, Berman M, Levy RI, Brewer HB Jr: The composition and metabolism of high density lipoprotein subfractions. *Lipids* 14:511-521, 1979.
9. Schaefer EJ, Levy RI: Composition and metabolism of high density lipoproteins. In *Lipoprotein Metabolism*, Eisenberg, S. (ed.), Prog. Biochem. Pharmacology. S. Karger, Basel. Vol. 15, pp. 186-201, 1979.\*
10. Chu FC, Kuwabara T, Cogan PG, Schaefer EJ, Brewer HB Jr: Ocular manifestations of familial high density lipoprotein deficiency (Tangier disease). *Arch. Ophthalmol.* 97:1926-1928, 1979.
11. Brewer HB Jr, Schaefer EJ, Osborne JC Jr, Zech, LA: High density lipoproteins: an overview. In *Report on the High Density Lipoprotein Workshop*, Lippel, K. (ed.), U.S. DHEW NIH Publ. 79-1661, pp. 29-41, 1979.\*
12. Brewer HB Jr, Schaefer EJ, Zech LA, Osborne JC JR: Human plasma lipoproteins: structure, function, and metabolism. In *Lipoproteins and Coronary Heart Disease*. (ed.) H. Greten, P.O. Lang, G. Schettler, Verlag G. Witzstrock, pp. 7-16, 1979.\*
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416. Li Z, Lamon-Fava S, Otvos J, Lichtenstein AH, Velez-Carrasco W, McNamara JR, Ordovas JM, Schaefer EJ. Fish consumption shifts lipoprotein subfractions to a less atherogenic pattern in humans. *J Nutr* 2004; 134:1724-1728.
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### **University Service**

1983-1992	Annual lectures in Tufts University School of Nutrition; Nutritional Biochemistry Course.
1984-1991	Annual lecture in Tufts University School of Dental Medicine; Nutrition and Prevention Course.
1984-present	Annual lectures in Tufts University School of Medicine; Pharmacology course.
1985-1986	Member, Search Committee for Chairman of Biochemistry.
1985-2004	Member, Promotions Committee, Jean Mayer USDA Human Nutrition Research Center on Aging at Tufts University.
1985-1989	Member, Clinical Appointments and Promotions Committee, Tufts University School of Medicine.
1992-2000	Course Director, Clinical Nutrition and Aging, student elective.
1993-present	Annual lecturer in Tufts University School of Medicine; Nutrition Course and Pharmacology Course.
2001-present	Chairman, Awards Committee, Jean Mayer USDA Human Nutrition Research Center on Aging at Tufts University

### **Post-Doctoral Fellows, Visiting Scientists and Current Positions**

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**Graduate Students** (Ph.D. Candidates, Subsequent or Current Positions).

**Endocrinology Fellows with Lipid Clinic Training Rotation**

**Medical Students on Research Rotations**

**Students on Research Rotations**

**Technicians and Subsequent Positions**

### Significant Original Research Accomplishments

1. Documentation of transfer of chylomicron apoA-I and apoA-II to plasma HDL and its recirculation in vivo and in vitro (references 4, 38, 322).
2. Documentation of metabolic and genetic defect studies in Tangier disease, a form of genetic HDL deficiency (references 6, 15, 19, 24, 36, 54, 66, 221, 348, 364, 381, 369).
3. Description of first kindred in which plasma apoA-I was lacking, associated with marked HDL deficiency and premature atherosclerosis and delineation of molecular defect (references 30, 66, 79, 137).
4. Description of first kindred in which plasma apoE was lacking, associated with marked accumulation of chylomicron remnants and atherosclerosis, delineation of molecular defect (references 28, 82, 90).
5. Documentation that apoA-I fractional catabolism is a major determinant of HDL cholesterol and apoA-I plasma levels, and that apoA-I catabolism is enhanced in the setting of hypertriglyceridemia (references 6, 33, 42, 86, 332).
6. Documentation that females produce more apoA-I than do males, and that estrogen administration increases apoA-I production (references 33, 52, 293).
7. Documentation that restriction fragment length polymorphisms within or adjacent to the apoA-I, C-III, A-IV, apoB and apoA-II genes are not useful markers for coronary heart disease risk (references 83, 119, 120, 152, 161, 179).
8. Documentation that an intestinal cell line (CaCo<sub>2</sub>) synthesizes apolipoproteins and lipoproteins and can be utilized for studies on nutritional effects of lipoprotein production in vitro (references 94, 109, 197).
9. Development of methodology to carry out population studies (with the Framingham Heart Study) to assess normal ranges and the utility of apolipoproteins, lipoproteins and their isoforms and genotypes, fatty acids, and lipoprotein subspecies as biochemical markers of premature coronary artery disease (references 95, 96, 101, 102, 195, 212, 213, 214, 216, 219, 220, 224, 227, 229, 233, 238, 240, 252, 259-265, 267, 268, 270, 272, 273, 274, 275, 281, 286, 287, 290, 297).
10. Precise studies documenting postprandial alterations in plasma lipoproteins and fat soluble vitamins in the young and the elderly (references 112, 115, 123, 131, 135, 144, 146, 149, 202, 394).
11. Documentation that cells can make HDL following apoA-I gene transfection (reference 97).
12. Research on the diagnosis and management of lipid disorders (references 10, 13, 15, 17-19, 24, 26, 27, 53, 58, 64, 65, 67, 69, 74, 77, 84, 85, 89, 91-93, 99, 106, 108, 124, 126, 140-143, 154, 156, 168, 169, 175, 189, 190, 194, 199, 204, 244, 250, 251, 252, 253, 255, 270, 271, 280, 304, 307).
13. Development and use of stable isotope methods to study the effects of diet and aging on cholesterol and apolipoprotein kinetics in the constantly fed state (references 144, 155, 180, 186, 217, 218, 249, 278, 279, 283, 284, 293, 295, 299, 302).
14. Delineation of lipoprotein abnormalities and familial lipoprotein disorders and other disorders associated with premature coronary artery disease (references 62, 63, 65, 66, 71, 75, 83, 91, 92, 113, 114, 117, 118, 154, 162, 163, 171, 173, 178, 184, 190, 198, 209, 213, 214, 219, 220, 224, 235, 237, 238, 244, 264, 307).
15. Effects of estrogen replacement on plasma lipoproteins in elderly women (references 116, 127, 139, 153, 175, 188).
16. Definitive studies on factors (mainly triglyceride levels) affecting LDL particle size and documentation that LDL size is not an independent risk factor for coronary heart disease (references 103, 110, 127, 138, 165, 178, 191, 192, 265).

17. Documentation of the effects of dietary fat saturation and dietary cholesterol as well as antioxidants and lovastatin on plasma lipoprotein metabolism and hepatic and intestinal apolipoprotein and LDL receptor mRNA levels and diet-induced aortic foam cell formation in monkeys and hamsters (references 147, 174, 182, 218, 222, 231, 241, 242, 243, 247, 256, 291, 298).
18. Documentation of the effects of dietary fats and cholesterol on plasma lipoprotein composition, metabolism, and immune status in humans (references 17, 26, 112, 115, 128, 144, 165, 181, 193, 196, 210, 211, 217, 218, 223, 228-230, 234, 256, 258, 259, 276, 282, 285, 288, 294, 301, 305, 306, 402).
19. Documentation that specific common mutations within the apoE gene and the apoA-IV gene affect the LDL cholesterol lowering response to dietary saturated fat and cholesterol restriction and HMG CoA reductase inhibitors. (references 223, 229, 244, 255, 276, 294, 389).
20. Documentation of the efficacy of various National Cholesterol Education Program Step 2 diets and variability in response in LDL cholesterol lowering (references 201, 247, 250, 251, 256, 257, 258, 276).
21. Documentation that ad libitum diets restricted in fat (15% of calories) promote weight loss and LDL cholesterol lowering (230, 252).
22. Development and evaluation of methods to directly measure serum Lp(a), LDL, and remnant lipoprotein cholesterol levels (216, 241, 297, 405).
23. Documentation of the effect of fat feeding on human intestinal apoB mRNA levels and editing (234).

## Curriculum Vitae

Professor Ronald WALKER PhD, FRSC, CChem, FIFST  
Emeritus Professor of Food Science,  
Food Safety Group,  
School of Biomedical & Life Sciences,  
University of Surrey,  
GUILDFORD GU2 5XH.  
United Kingdom

Professor Walker is a Food Toxicologist with research interests in mechanisms of toxicity of food additives and contaminants (including mycotoxins and intrinsic natural toxicants). He has more than 150 research publications.

### Membership of Scientific Societies:

Fellow of the Institute of Food Science and Technology  
Fellow of the Royal Society of Chemistry  
Member of: Biochemical Society  
British Toxicology Society

For 20 years has been involved in regulatory committees dealing with safety evaluation and risk assessment of food additives and contaminants and novel foods, both at national and international levels, viz:

### 1. INTERNATIONAL COMMITTEES:

#### Joint WHO/FAO Expert Committee on Food Additives (JECFA):

served as WHO Temporary Adviser from 1981 to 1992.  
Member and Chairman, 1993, 1996, 1998, 2000, 2001; Vice-Chairman 1995, 1997, 1999, 2001.

#### International Programme on Chemical Safety (WHO, International Labour Organisation and U.N. Environmental Programme):

Member and rapporteur of an *ad hoc* Working Group on Updating Methodology for Testing and Assessing Chemicals in Food, 1983 to 1987.  
Member of *ad hoc* Working Group drafting Environmental Health Criteria Monograph on General Principles and Methods for Chemical Safety (Human Health Protection), 1993 - 1996.

#### Joint WHO/FAO Meeting on Chemicals in Food, Food Standards and Food Trade 1991: Temporary Adviser to WHO Secretariat

#### European Commission; Scientific Committee for Food (SCF):

Member of *ad hoc* Working Group on Nitrates, Nitrites and *N*-nitrosamines, 1988-90.  
Member of Contaminants Working Group for Nitrates, Nitrites and *N*-nitroso compounds, 1993-1995  
Appointed member of the Plenary Committee, 1999; Member of Working Groups on Food Additives, Food Contaminants, Food Flavours and Upper Safe Levels of Nutrients. Member of Ad hoc working groups on Dioxins and Polycyclic aromatic hydrocarbons

2. **NATIONAL COMMITTEES:**

U.K. Ministry of Agriculture, Fisheries and Food:

**MAFF Advisory Committee on Food Safety Research**, Member 1984-1985.

U.K. Ministry of Agriculture, Fisheries & Food and AFRC:

**Food Safety and Applied Nutrition Research Consultative Committee**,  
Chairman, 1988-1989.

U.K. Department of Health/MAFF:

**Advisory Committee on Novel Foods and Processes**. Member, 1988 - 2000.

**Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment (COT)**. Member, 1989 - 1997.

**Novel Foods Panel, Committee on Medical Aspects of Food Policy (COMA)**  
Member, 1995 - 1999

U.K. House of Commons:

Expert Scientific Adviser to the **House of Commons Select Committee on Agriculture Inquiry into Food Safety** November 1997-March 1998

3. **Other**

**International Life Sciences Institute (Europe)** Chairman, Scientific Committee on Toxicology/Food Safety: 1992 - 1999

Editor of the Journal "Food Additives and Contaminants" 1983-2000

**SUBMISSION END**