Brookings Institution event Web site at *http://www.brookings.edu//health/events.*

Transcripts: Please be advised that transcripts will not be available.

SUPPLEMENTARY INFORMATION: On July 9, 2012, the President signed into law the Food and Drug Administration Safety and Innovation Act (FDASIA) (Pub. L. 112–144). Title I of FDASIA reauthorizes PDUFA and provides FDA with the user fee resources necessary to maintain an efficient review process for human drug and biological products. The reauthorization of PDUFA includes performance goals and procedures for the Agency that represent FDA's commitments during fiscal years 2013–2017 (PDUFA V). These commitments are fully described in the document entitled ''PDUFA Reauthorization Performance Goals and Procedures Fiscal Years 2013 Through 2017'' (PDUFA Goals Letter), available on FDA's Web site at *http://www.fda.gov/downloads/ForIndustry/UserFees/PrescriptionDrugUserFee/UCM270412.pdf.* Section XI of the PDUFA Goals Letter, entitled ''Enhancement and Modernization of the FDA Drug Safety System,'' includes Sentinel as a tool for evaluating drug safety issues that may require regulatory action. As part of this enhancement, FDA committed to hold a public meeting to engage stakeholders in a discussion of current and emerging Sentinel projects and facilitate stakeholder feedback and input to determine the feasibility of using Sentinel to evaluate drug safety issues that may require regulatory action, e.g., labeling changes, PMRs, or PMCs. The public workshop announced by this notice will fulfill this commitment.

Dated: November 5, 2013.

Leslie Kux,

Assistant Commissioner for Policy.

[FR Doc. 2013–26855 Filed 11–7–13; 8:45 am]

BILLING CODE 4160–01–P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA–2013–N–1317]

Tentative Determination Regarding Partially Hydrogenated Oils; Request for Comments and for Scientific Data and Information

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice; request for comments and for scientific data and information.

SUMMARY: Based on new scientific evidence and the findings of expert scientific panels, the Food and Drug Administration (FDA) has tentatively determined that partially hydrogenated oils (PHOs), which are the primary dietary source of industrially-produced *trans* fatty acids, or *trans* fat, are not generally recognized as safe (GRAS) for any use in food based on current scientific evidence establishing the health risks associated with the consumption of *trans* fat, and therefore that PHOs are food additives. Although FDA has not listed the most commonly used PHOs, they have been used in food for many years based on self-determinations by industry that such use is GRAS. If finalized, this would mean that food manufacturers would no longer be permitted to sell PHOs, either directly or as ingredients in another food product, without prior FDA approval for use as a food additive.

DATES: Submit either electronic or written comments and scientific data and information by January 7, 2014.

ADDRESSES: Submit electronic comments and scientific data and information to *http://www.regulations.gov.* Submit written comments and scientific data and information to the Division of Dockets Management (HFA–305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852. All submissions must include the Agency name and the docket number found in brackets in the heading of this document.

FOR FURTHER INFORMATION CONTACT: Mical Honigfort, Center for Food Safety and Applied Nutrition (HFS–265), Food and Drug Administration, 5100 Paint Branch Pkwy., College Park, MD 20740, 240–402–1278, FAX: 301–436–2972, email: *mical.honigfort@fda.hhs.gov.*

SUPPLEMENTARY INFORMATION:

I. Introduction

In accordance with the process set out in § 170.38(b)(1) (21 CFR 170.38(b)(1)), we are issuing this document announcing our tentative determination that PHOs are no longer GRAS under any condition of use in food and therefore are food additives subject to section 409 of the Federal Food, Drug, and Cosmetic Act (FD&C Act) (21 U.S.C. 348). If finalized, this would mean that food manufacturers would no longer be permitted to sell PHOs, either directly or as ingredients in another food product, without prior FDA approval for use as a food additive.

FDA's evaluation of the GRAS status of PHOs is centered on the *trans* fatty acid (also referred to as ''*trans* fat'') component of these oils. This document addresses PHOs because they are the primary dietary source of industrially-produced *trans* fat (Ref. 1). Although all refined edible oils contain some *trans* fat as an unintentional byproduct of their manufacturing process, *trans* fats are an integral component of PHOs and are purposely produced in these oils to affect the properties of the oil and the characteristics of the food to which they are added.

The current scientific evidence, which is discussed in section IV of this document, identifies significant health risks caused by the consumption of *trans* fat. This evidence includes the opinions of expert panels and the 2005 recommendation of the Institute of Medicine (IOM) to limit *trans* fat consumption as much as possible while consuming a nutritionally adequate diet, recognizing that *trans* fat occurs naturally in meat and dairy products from ruminant animals and that naturally-occurring *trans* fat is unavoidable in ordinary, nonvegan diets without significant dietary adjustments that may introduce undesirable effects (Ref. 2). In addition, according to the Centers for Disease Control and Prevention (CDC), elimination of PHOs from the food supply could prevent 10,000 to 20,000 coronary events and 3,000 to 7,000 coronary deaths annually, if the marginal benefits of continuing to remove trans fats from food items remain constant (Ref. 3). (See accompanying economic analysis for more information on this estimate.) Given this evidence, we have tentatively determined that there is no longer a consensus among qualified scientific experts that PHOs, the primary dietary source of industrially-produced *trans* fatty acids, are safe for human consumption, either directly or as ingredients in other food products.

II. Background

A. Hydrogenation Process and Trans Fatty Acids

Chemical hydrogenation is the process by which hydrogen atoms are added to unsaturated sites on the carbon chains of fatty acids, in the presence of catalysts, thereby reducing the number of double bonds. ''Partial hydrogenation'' describes an incomplete saturation of the double bonds, in which some double bonds remain but may shift to a different position along the carbon chain and alter their configuration from *cis* to *trans.* The *trans* arrangement of hydrogen atoms results in a relatively straight configuration of the fatty acids and increases the melting point, shelf life,

and flavor stability of the hydrogenated oil. Because of these technical properties, PHOs have been used by the food industry in such products as margarine, shortening, and baked goods. The hydrogenation process can be controlled to meet the physical or chemical properties needed for a specific product application (Ref. 4). If an oil is allowed to hydrogenate completely, the carbon-carbon double bonds are mostly eliminated, resulting in a ''fully hydrogenated oil.'' The *trans* fatty acid content of PHOs can vary from approximately 10 to 60 percent of the oil, depending on how the oil is manufactured, with an average *trans* fatty acid content of 25 to 45 percent of the oil (Ref. 1). Changes in the pressure, temperature, amount of agitation in the reaction vessel, type and concentration of catalyst, reaction time, and fat source will affect the production of *trans* fatty acid isomers in PHOs.

As noted, *trans* fatty acids are also formed during the production of non-hydrogenated refined oils (i.e., soybean and cottonseed oils) as a result of the *cis* to *trans* isomerization induced by high temperatures used during processing, such as deodorization (Ref. 5). The concentration of *trans* fatty acids in non-hydrogenated refined oils is typically below 2 percent (Ref. 6). Low levels (below 2 percent) of *trans* fatty acids may also be found in fully hydrogenated oils due to incomplete hydrogenation (Ref. 7). Theoretically, a fully hydrogenated oil would be fully saturated and would not contain any *trans* fatty acids. However, no hydrogenation process is 100 percent efficient. In addition, the *trans* fatty isomer content of an edible oil can be controlled by blending different oils or through processing of mixed fatty acids (Ref. 4).[1]

B. The GRAS Standard

Section 409 of the FD&C Act provides that a food additive is unsafe unless it is used in accordance with certain conditions set forth in that section. ''Food additive'' is defined by section 201(s) of the FD&C Act (21 U.S.C. 321(s)) as any substance the intended use of which results or may reasonably be expected to result in its becoming a component or otherwise affecting the characteristics of any food, if such substance is not GRAS.[2] A substance is GRAS if it is generally recognized, among experts qualified by scientific training and experience to evaluate its safety, as having been adequately shown through scientific procedures (or, in the case of a substance used in food prior to January 1, 1958, through either scientific procedures or experience based on common use in food) to be safe under the conditions of its intended use. However, history of use prior to 1958 is not sufficient to support continued GRAS status if new evidence demonstrates that there is no longer a consensus that an ingredient is safe.

FDA has defined safe as ''a reasonable certainty in the minds of competent scientists that the substance is not harmful under the intended conditions of use'' (21 CFR 170.3(i)), and general recognition of safety must be based only on the views of qualified experts (21 CFR 170.30(a)). To establish such recognition, there must be a consensus of expert opinion regarding the safety of the use of the substance. (See, e.g., *United States* v. *Western Serum Co., Inc.,* 666 F.2d 335, 338 (9th Cir. 1982) (citing *Weinberger* v. *Hynson, Westcott & Dunning,* 412 U.S. 609, 629–32 (1973)). Unanimity among experts regarding safety of a substance is not required. (See, e.g., *United States* v. *Articles of Drug * * * 5,906 boxes,* 745 F.2d 105, 119 n. 22 (1st Cir. 1984); *United States* v. *Articles of Food and Drug (Coli-Trol 80),* 518 F.2d 743, 746 (5th Cir. 1975) (''What is required is not unanimous recognition but general recognition.'')). However, the existence of a severe conflict among experts regarding the safety of the use of a substance precludes a finding of general recognition (See, e.g., *Premo Pharmaceutical Laboratories* v. *United States,* 629 F.2d 795, 803 (2d Cir. 1980)).

Importantly, the GRAS status of a specific use of a particular substance in food is time-dependent. That is, as new scientific data and information develop about a substance or the understanding of the consequences of consumption of a substance evolves, expert opinion regarding the safety of a substance for a particular use may change such that there is no longer a consensus that the specific use is safe. The fact that the status of a substance under section 201(s) of the FD&C Act may evolve over time is the underlying basis for FDA's regulation at § 170.38, which provides in part that FDA may, on its own initiative, propose to determine that a substance is not GRAS. (See generally 36 FR 12093 (June 25, 1971) (issuance of 21 CFR 121.3, the predecessor of § 170.38)). Further, as stated previously, history of the safe use of a substance in food prior to 1958 is not sufficient to support continued GRAS status if new evidence demonstrates that there is no longer expert consensus that an ingredient is safe.

As noted previously, under section 201(s) of the FD&C Act, a substance that is GRAS for a particular use in food is not a food additive, and may lawfully be utilized for that use without Agency review and approval. Currently, a GRAS determination is made when the manufacturer or user of a food substance evaluates the safety of the substance and the views of qualified experts and concludes that the use of the substance is GRAS. This approach is commonly referred to as ''GRAS self-determination.'' Substances that have been self-determined as GRAS are not comprehensively listed or otherwise publicly identified.

Other substances that are GRAS may be identified in FDA regulations in one of two ways. Following the passage of the 1958 Food Additives Amendment, FDA established in its regulations a list of food substances that, when used as indicated, are considered GRAS. This list (commonly referred to as the ''GRAS list'') now appears at 21 CFR part 182. Thereafter, in 1972, we established the GRAS affirmation process through which we affirmed, through notice and comment rulemaking, the GRAS status of particular uses of certain substances in food.[3] Regulations affirming the GRAS status of certain substances appear at 21 CFR parts 184 and 186.[4]

C. Status of PHOs

PHOs, which are the primary dietary source of industrially-produced *trans* fat (Ref. 1), have a long history of use as food ingredients. The partial hydrogenation process was developed in the 1930s and has been in widespread commercial use since the 1940s. Two common PHOs currently used by the food industry are partially

[1] Hydrogenation also occurs in the digestive tract of ruminant animals and results in the formation of some *trans* isomers in the fat components of dairy and meat products from these animals. These isomers usually make up only a small percent (typically around 3 percent) of the total fatty acids of such products (Ref. 5). This document is limited to PHOs and does not address the *trans* fat component of meat and dairy products from ruminant animals.

[2] Certain other substances that may become components of food are also excluded from the statutory definition of food additive, including pesticide chemicals and their residues, new animal drugs, color additives, and dietary ingredients in dietary supplements (21 U.S.C. 321(s)(1) through (s)(6)).

[3] As a general matter, FDA no longer lists GRAS substances in its regulations because, in April 1997, we proposed to establish a voluntary notification program for GRAS, which does not involve rulemaking (62 FR 18938, April 17, 1997). At the time of the proposal, FDA initiated a pilot of the GRAS notification program, which continues to function. A firm may voluntarily submit information on a GRAS self-determination to FDA for review through the GRAS notification program, but is not required to do so.

[4] For a more detailed discussion of the history of GRAS, see 62 FR 18938 at 18939 and 18940.

hydrogenated soybean oil and partially hydrogenated cottonseed oil, neither of which is listed as GRAS in FDA's regulations. However, these and other commonly used PHOs (e.g., partially hydrogenated coconut oil and palm oil) have been considered GRAS (through a GRAS self-determination) by the food industry for use in food at levels consistent with good manufacturing practice based on a history of use prior to 1958. We are not aware that either FDA or the United States Department of Agriculture (USDA) granted any explicit prior sanction or approval for any use of PHOs in food prior to the 1958 Food Additives Amendment to the FD&C Act.

In contrast, the partially hydrogenated versions of low erucic acid rapeseed oil (LEAR oil; 21 CFR 184.1555(c)(2)) and menhaden oil (21 CFR 184.1472(b)) are affirmed by regulation as GRAS for use in food. Partially hydrogenated LEAR oil was affirmed as GRAS for use in food (50 FR 3745; January 28, 1985) through scientific procedures. Partially hydrogenated menhaden oil was affirmed as GRAS for use in food (54 FR 38219; September 15, 1989) on the basis that the oil is chemically and biologically comparable to commonly used partially hydrogenated vegetable oils such as corn and soybean oils. Partially hydrogenated LEAR and menhaden oils are not currently widely used by the food industry.[5]

Although none of the food standards of identity in FDA's regulations explicitly refers to PHOs, the nature of some of the products for which there are standards of identity is such that PHOs historically have been used in their manufacture in conformance with those standards (e.g., shortening in bread, rolls, and buns (21 CFR 136.110(c)(5)), French dressing (21 CFR 169.115), mayonnaise (21 CFR 169.140), and margarine (21 CFR 166.110)). However, no food standard of identity requires the use of PHOs and, therefore, industry's ability to comply with any standard would not be prevented by a change in the regulatory status of PHOs.

D. Labeling of Trans Fat

As an initial step to address the negative health effects of *trans* fat consumption in the United States, we issued a proposed rule in the **Federal Register** of November 17, 1999 (64 FR 62746) entitled ''Food Labeling: *Trans* Fatty Acids in Nutrition Labeling, Nutrient Content Claims, and Health Claims'' (the November 1999 proposal), in which we proposed that *trans* fat content be provided in nutrition labeling to help consumers determine how each food product contributes to their overall dietary intake of *trans* fat. Our proposal was supported by findings from intervention and observational studies that evaluated the evidence that dietary *trans* fatty acids influence blood lipid levels in humans and increase their risk of coronary heart disease (CHD) (64 FR 62746 at 62750). In the November 1999 proposal, we discussed research that showed that diets containing *trans* fatty acids resulted in increased serum low-density lipoprotein cholesterol (LDL–C), a major risk factor for CHD (64 FR at 62746 at 62749 through 62754). In the **Federal Register** of July 11, 2003 (68 FR 41434), we issued a final rule (the July 2003 final rule) amending our nutrition labeling regulations to require declaration of the *trans* fatty acid content of food in the nutrition label of conventional foods and dietary supplements (21 CFR 101.9(c)(2)(ii)). This requirement was effective January 1, 2006.[6] In the July 2003 final rule (68 FR 41434 at 41457), the Agency noted that the IOM/National Academy of Sciences (IOM/NAS) report about *trans* fat (Ref. 2) did not make quantitative recommendations for establishing a Daily Reference Value (DRV) for *trans* fat. The IOM/NAS report recommended that the intake of *trans* fat be as low as possible while maintaining a nutritionally balanced diet and did not provide a daily reference intake (DRI) for *trans* fat or information that the Agency needs to establish a DRV for nutrition labeling purposes. Therefore, in the absence of a scientific basis or recommendation for *trans* fat consumption by an authoritative body, FDA did not establish a DRV for *trans* fat, and therefore, the July 2003 final rule did not require listing of Percent of Daily Value (% DV) for *trans* fat on product labels.

III. Current Dietary Intake of *Trans* Fat From PHOs

In the July 2003 final rule, we estimated that mean adult (aged 20 years or more) intake of *trans* fat from products containing PHOs was 4.6 grams per day (g/d) (2.0 percent of energy based on a 2,000 calorie diet) (68 FR 41434 at 41470).[7] We also estimated that total *trans* fat intake from products containing PHOs and from animal products containing *trans* fat (1.2 g/d) was 5.8 g/d for adults (2.6 percent of caloric energy). Based on food composition data collected in 2009 and 2010, we updated our intake estimate of *trans* fat from products containing PHOs. Our analysis showed that many food products have been reformulated to eliminate or to substantially reduce the amount of industrially-produced *trans* fatty acids (Ref. 8). However, as discussed further in this section, certain population groups still consume high levels of *trans* fatty acids, primarily through consumption of food products containing PHOs.

In 2010, we prepared an estimate of the intake of industrially-produced *trans* fat using available food consumption data (2003–2006 National Health and Nutrition Examination Survey (NHANES)), market share information, and *trans* fat levels based on label declaration data and analytical data for products that were identified as containing PHOs (Ref. 8). We estimated the 2010 mean *trans* fat intake for the U.S. population aged 2 years or more[8] who consumed one or more of the processed foods identified as containing PHOs[9] to be 1.3 grams per person per day (g/p/d) (0.6 percent of caloric energy). For high-level consumers (represented by the 90th percentile), we estimated the intake to be 2.6 g/p/d (1.2 percent of caloric energy) for the U.S. population aged 2 years or more. Based on this estimate, the mean dietary intake of industrially-produced *trans* fat has decreased significantly since our estimate in the July 2003 final rule.

[5] The non-hydrogenated version of LEAR oil (also known as canola oil) is widely used in foods, and non-hydrogenated menhaden oil is currently used in a limited number of products, primarily to increase the omega-3 fatty acid content of the food. Like other non-hydrogenated refined oils, non-hydrogenated LEAR and menhaden oils, which are also affirmed by FDA as GRAS for use in food, are not significant dietary sources of *trans* fat.

[6] The regulation requires the declaration of the amount of *trans* fat in a product, on a separate line directly below the statement for saturated fat; the declaration must express the amount of *trans* fat as grams per serving to the nearest 0.5 g increment below 5 g and to the nearest gram increment above 5 g. If a serving contains less than 0.5 g, the *trans* fat content may be declared as zero. The regulation also provides that, in certain circumstances, the statement ''Not a significant source of *trans* fat'' may be used instead of a declaration of *trans* fat content. The regulation defines the number of grams of *trans* fat in a serving as the sum of all unsaturated fatty acids that contain one or more isolated (i.e., nonconjugated) double bonds in a trans configuration. If FDA makes a final determination that PHOs are not GRAS, no amount of PHOs would be permitted in food products without prior FDA approval for use as a food additive.

[7] (4.6 g//d × 9 kcal/g × 100)/2,000 kcal/d = 2.0% of energy.

[8] While we did not calculate a mean intake for ages 20 years or more, based on the similarity in the intakes calculated for children aged 2–5 years, teenage boys, and persons aged 2 years or more (Ref. 8), we believe there would not be a significant difference between the intake estimated for persons ages 2 years or more and that for persons ages 20 years or more.

[9] The current estimate indicated that approximately 100 percent of the population consumed one or more of the foods under consideration. This is due to the wide variety of foods that contain *trans* fat from PHOs.

Additionally, scientists at the CDC recently studied the change in levels of four major *trans* fatty acids in the blood of U.S. non-Hispanic white adults from 2000 to 2009, and reported a 58 percent average decrease during that timeframe (Ref. 9).

The data that we collected show that many foods (e.g., frozen potato products, most frozen breaded products) have been reformulated to remove PHOs. However, a number of foods made with PHOs remain on the market. These products fall into one of two categories: Foods for which consumers have alternatives containing lower levels of *trans* fat (e.g., cookies, baked goods, microwave popcorn, frozen pizza, frozen pies, shortening) and foods for which consumers have limited or no choice of an alternative containing a lower level of *trans* fat (e.g., ready-to-use frostings, stick margarine).

In 2010, we also prepared an estimate for a high-intake scenario by assuming that *trans* fat was present at the highest level observed for all foods within a particular food category based on label surveys or analytical data. For this scenario, we estimated the mean intake to be 2.7 g/p/d (1.2 percent of energy) and the 90th percentile intake to be 5.4 g/p/d (2.4 percent of energy) for the U.S. population aged 2 years or more.

In 2012, using label survey data, we updated the 2010 intake estimate of *trans* fats from PHOs for those food categories that were identified as major contributors to the dietary intake of *trans* fat, as well as for those categories where we have noted progress in reformulation. For this most recent estimate, we calculated the mean intake to be 1.0 g/p/d (0.5 percent of energy) and the 90th percentile intake to be 2.0 g/p/d (1.0 percent of energy) for the U.S. population aged 2 years or more (Ref. 10). We also prepared an estimate for a high-intake scenario by assuming that *trans* fat was present at the highest level observed for all foods within a particular food category based on the label survey. For this scenario, we estimated the mean intake to be 2.1 g/p/d (1.0 percent of energy) and the 90th percentile intake to be 4.2 g/p/d (1.9 percent of energy) for the U.S. population aged 2 years or more.

We do not consider this to be a significant change in the overall dietary intake of *trans* fat since 2010. However, it suggests a continued downward trend in the dietary intake of *trans* fat. Specifically, there was a decrease observed in the intake of *trans* fat in the refrigerated dough, savory snacks, and frozen pizza categories, consistent with the lower levels of *trans* fat observed in our label survey.

Although *trans* fat intake has decreased overall since our 2003 *trans* fat intake estimate, individuals with certain dietary habits may still consume high levels of *trans* fat from certain brands or certain types of food products (e.g., refrigerated biscuits, ready-to-use frostings, certain brands of frozen pizzas, and certain brands of microwave popcorn), which could contain several grams *trans* fat per serving. As noted previously, for those consumers who consistently choose these products, the daily intake of added *trans* fat is approximately twice as high as that for the consumer who does not choose only the foods containing the highest levels of *trans* fat within a particular category (2.1 g/p/d vs. 1.0 g/p/d).

IV. Safety

In the November 1999 proposed rule, we concluded that dietary *trans* fatty acids have adverse effects on blood cholesterol measures that are predictive of CHD risk, specifically LDL–C levels (64 FR 62746 at 62754). We took final action in the July 2003 final rule based on our evaluation of comments received and on scientific evidence demonstrating that the consumption of *trans* fatty acids increases LDL–C, one of the major risk factors for CHD. The July 2003 final rule cited authoritative reports that recommended limiting intake of *trans* fat to reduce CHD risk, such as the *Dietary Guidelines for Americans,* 2000 (Ref. 11), the American Heart Association Guidelines (Ref. 12), the 2002 IOM/NAS report (Ref. 2), as well as additional studies that had been published since the November 1999 proposal (68 FR 41434 at 41444). In particular, the 2002 IOM/NAS report recognized the positive linear trend between *trans* fat intake, LDL–C concentration, and heart disease, concluded that ''*trans* fatty acids are not essential and provide no known benefit to human health,'' and recommended that ''*trans* fatty acid consumption be kept as low as possible while consuming a nutritionally adequate diet.'' The report did not recommend an upper limit for *trans* fat because it concluded that any incremental increase in *trans* fat consumption increases the risk of CHD.

FDA has summarized findings reported in the literature since the publication of the July 2003 final rule (Refs. 13, 14). Since 2003, both controlled trials and observational human studies published on *trans* fatty acid consumption have consistently confirmed the adverse effects of *trans* fatty acid consumption on intermediary risk factors (e.g., serum lipoproteins) and the increased risk of CHD (Ref. 13). Expert review panels from the IOM/NAS in 2005 (Ref. 2), the American Heart Association (Refs. 15, 16), the American Dietetic Association (Ref. 17), the World Health Organization (Ref. 18), the Dietary Guidelines Advisory Committee (Refs. 19, 20), and the FDA Food Advisory Committee Nutrition Subcommittee (Ref. 21) agree that *trans* fat-mediated changes in lipid metabolism, pro-inflammatory effects, and endothelial dysfunction lead to dose-dependent increases in CHD events in humans. These expert panels all concluded that there is no threshold intake level for industrially-produced *trans* fat that would not increase an individual's risk of CHD, or adverse effects on risk factors for CHD. Moreover, the panels also agree that *trans* fatty acids have a stronger effect on the risk of CHD than saturated fatty acids.

This significant recent evidence demonstrating the increased risk of CHD from consumption of any amount of *trans* fat means that consumption of PHOs, the primary dietary source of *trans* fat, also leads to increased LDL–C levels and an increased risk of CHD. These demonstrated effects support a determination that the consumption of PHOs could be harmful (i.e., increased risk for CHD) under any condition of use in food. Accordingly, we tentatively determine that this evidence erodes any basis to support the GRAS status of these oils, and therefore that there is no longer a consensus among qualified scientific experts that PHOs, the primary dietary source of industrially-produced *trans* fatty acids, are safe under any condition of use in food.

We note that, in addition to an increased risk of CHD, *trans* fat consumption (and, accordingly, consumption of food products containing PHOs) has also been connected to a number of other adverse effects on health. Some studies suggest that *trans* fat consumption may worsen insulin resistance, especially in those who are predisposed to the condition (e.g., preexisting insulin resistance, greater adiposity, or lower physical activity levels) (Refs. 22, 23). *Trans* fat may also increase diabetes risk (Refs. 22–26) although this association requires further confirmation. In addition, there is some evidence that fetuses and breastfeeding infants of mothers who regularly consume *trans* fat may be at higher risk for impaired growth (which may be due to inhibition of the synthesis of essential polyunsaturated fatty acids that are needed for their growth and development) (Refs. 27–31). Scientific evidence also shows that, in addition to

increasing LDL–C, *trans* fat intake lowers serum high-density lipoprotein cholesterol (HDL–C), a protective form of serum cholesterol (Refs. 32–39).

V. Other Activities Relating to PHO Consumption

Over the past 5 years, several municipalities, states, and other countries have taken action to reduce the use of PHOs in food. While these actions pertain generally to all products containing *trans* fat, because PHOs are the primary dietary source of *trans* fat, their immediate effect is primarily on food products containing PHOs. For example, the Danish government passed legislation in 2003 that restricted the use of industrially-produced *trans* fat to a maximum of 2 percent of fats and oils used in all processed food products. These required limitations on dietary *trans* fat have nearly eliminated *trans* fat from commercial sources such that industrially-produced *trans* fat is no longer a significant source of intake of *trans* fat in Denmark (Refs. 40–42). Also, in 2007, Canada set voluntary *trans* fat reduction targets of no more than 2 percent *trans* fat in the fat content of vegetable oils and spreadable margarine and no more than 5 percent in all other foods (Ref. 43). Health Canada monitored the industry's actions by analyzing products and reviewing nutrition labels. Canada's monitoring data showed that nutrition labeling regulations are an effective motivator for industry and that many manufacturers reduced the *trans* fat content of foods to meet the voluntary limit of 5 percent total fat as *trans* fat, especially because the monitoring data were posted on Health Canada's Web site. However, Health Canada noted that some sectors (i.e., bakery products, desserts, and cookies) face challenges in reducing the *trans* fat content of their products (Ref. 44).

In the United States, some jurisdictions such as the State of California (California Health and Safety Code, Section 114377), New York City (New York City Health Code, Section 81.08), the City of Baltimore (Baltimore City Health Code Section 6–507), and Montgomery County, MD (County Council for Montgomery County Maryland, Resolution No. 16–134, 2007) have imposed restrictions on the use of *trans* fat ingredients in food service establishments. Generally, these regulations do not permit food service establishments to sell or distribute foods, and in some cases, use ingredients, containing greater than 0.5 g *trans* fat per serving. In New York City, by 2008 an estimated 98 percent of restaurants were not using ingredients containing industrially-produced *trans* fat, compared with 50 percent in 2005 (Ref. 45).

We have also received two citizen petitions regarding the safety of PHOs. In 2004, FDA received a citizen petition from the Center for Science in the Public Interest (CSPI) requesting that we revoke the GRAS status of PHOs, and consequently declare that all of these oils are food additives. The petition also asks FDA to revoke the safe conditions of use for partially hydrogenated products that are currently considered food additives,[10] to prohibit the use of partially hydrogenated vegetable oils that are prior sanctioned (FDA is not aware of any), and to initiate a program to encourage manufacturers and restaurants to switch to more healthy oils. The petition excluded *trans* fat that occurs naturally in meat from ruminant animals and dairy fats, and that forms during the production of non-hydrogenated oils. It also does not include fully hydrogenated oils, which contain negligible amounts of *trans* fat, and PHOs that may be produced by new technologies that result in negligible amounts of *trans* fat in the final product. CSPI's petition states that *trans* fat promotes CHD by increasing LDL–C and also by lowering HDL–C, and therefore has greater adverse effects on serum lipids (and possibly CHD) than saturated fats. CSPI also states that, beyond its adverse effects on serum lipids, *trans* fat may promote heart disease in additional ways. Based on these findings, CSPI asserts that PHOs can no longer be considered GRAS.[11]

In 2009, we received a citizen petition from Dr. Fred Kummerow requesting that we ban partially hydrogenated fat from the American diet. Dr. Kummerow cited studies linking the intake of industrially-produced *trans* fatty acids to the prevalence of CHD in the United States. The petition also asserts that *trans* fat may be passed to infants via breast milk and that the daily intake of *trans* fat related to the health of children has been ignored since children do not exhibit overt heart disease. Dr. Kummerow further states that inflammation in the arteries is believed to be a risk factor in CHD and studies have shown that *trans* fatty acids elicit an inflammatory response.[12]

VI. Tentative Determination

As discussed previously, for a substance to be GRAS, there must be a consensus among qualified experts that the substance is safe under the intended conditions of use. In accordance with the process in FDA's regulations in § 170.38, the Agency on its own initiative or on the petition of any interested person, under 21 CFR part 10, may publish a notice in the **Federal Register** determining that a substance is not GRAS and is a food additive subject to section 409 of the FD&C Act. In accordance with this process, we will normally allow a period of 60 days during which any interested person may file comments, and we will evaluate all comments received (§ 170.38(b)). If we conclude that there is a lack of convincing evidence that the substance is GRAS or is otherwise exempt from the definition of a food additive in section 201(s) of the FD&C Act, we will publish a notice thereof in the **Federal Register**.

Based on current scientific evidence discussed in section IV of this document regarding the health risks associated with the consumption of *trans* fat, opinions of expert panels, as well as the IOM's recommendation to limit *trans* fat consumption as much as possible, we have tentatively determined that there is not a consensus that PHOs, the primary dietary source of industrially-produced *trans* fatty acids, are safe for use in food. The fact that a substance was commonly used in food prior to 1958 is not sufficient to support continued GRAS status if there is no longer a scientific consensus that the substance is safe for the intended use in food.

FDA has prepared a memorandum attempting to estimate the potential costs and benefits associated with removing PHOs from the food supply (Ref. 46). Where possible we have used publicly available information to make these estimates; however, in many cases we have very limited data to support our rough estimates. We estimate the initial costs of removing PHOs from the food supply to be about $8 billion, although those costs may not be borne all in one year if FDA provides a multi-year compliance period; we seek comment on that idea as part of this notice. We estimate the 20-year net present value of costs to be between $12 and $14 billion, where the upper and lower estimates are calculated at 3 and

[10] The petition from CSPI provided, as an example, partially hydrogenated methyl ester of rosin, which is approved as a food additive for use as a synthetic flavoring substance (32 FR 7946, June 2, 1967; 21 CFR 172.515) and as a masticatory substance in chewing gum base (29 FR 13894, October 8, 1964; 21 CFR 172.615). Partially hydrogenated methyl ester of rosin is not a PHO; accordingly, this document does not address this substance.

[11] The CSPI petition may be accessed at *http://www.regulations.gov* and is identified as Docket No. FDA–2004–P–0279.

[12] The petition from Dr. Kummerow may be accessed at *http://www.regulations.gov* and is identified as Docket No. FDA–2009–P–0382.

7 percent discount rates. Using the same method, we estimate benefits between $117 and $242 billion. Our memorandum is part of the administrative record and can be found on *http://www.regulations.gov* as Reference 46 to this document. As discussed in the memorandum, our analysis focused on processed foods and food prepared at home. There may, however, be additional costs to small businesses associated with removing PHOs from food. Our intent is not to create an undue burden on these entities. Therefore, we are specifically requesting comment on the costs to small businesses and any special considerations that might be made in order to minimize the burden on these entities. We request comment on what types of special considerations for small business would be possible if FDA makes a final determination that PHOs are not GRAS.

VII. Request for Comments and for Scientific Data and Information

We are seeking comments and additional scientific data and information related to this action and, in particular, we request comment on the following:

1. Should FDA finalize its tentative determination that PHOs are no longer GRAS?

2. Are there data to support other possible approaches to addressing the use of PHOs in food, such as by setting a specification for *trans* fat levels in food?

3. How long would it take producers to reformulate food products to eliminate PHOs from the food supply? Are there likely to be differences in reformulation time for certain foods or for certain types of businesses?

4. If FDA makes a final determination that PHOs are not GRAS and does not otherwise authorize their use in food, FDA intends to provide for a compliance date that would be adequate for producers to reformulate any products as necessary and that would minimize market disruption. We welcome comments on what would be an adequate time period for compliance.

5. Are there any special considerations that could be made to reduce the burden on small businesses that would result from removal of PHOs from foods, such as additional time for reformulation? Would those considerations be consistent with a final determination that PHOs are not GRAS?

6. Are there other challenges regarding the removal of PHOs from foods? Are there products that may not be able to be reformulated? If so, what sorts of products and what challenges are faced?

7. Is there any knowledge of an applicable prior sanction for the use of PHOs in food?

We anticipate that some interested persons may wish to provide FDA with certain comments, research, data, and information that they consider to be trade secret or confidential commercial information (CCI) that would be exempt under Exemption 4 of the Freedom of Information Act (5 U.S.C. 552). You may claim information that you submit to FDA as CCI or trade secret by clearly marking both the document and the specific information as ''confidential.'' Information so marked will not be disclosed except in accordance with the Freedom of Information Act and FDA's disclosure regulations (21 CFR part 20). For electronic submissions to *http://www.regulations.gov* indicate in the ''comments'' box of the appropriate docket that your submission contains confidential information. You must also submit a copy of the comment that does not contain the information claimed as confidential for inclusion in the public version of the official record. Information not marked confidential will be included in the public version of the official record without prior notice.

VIII. Comments

Interested persons may submit either electronic comments and scientific data and information to *http://www.regulations.gov* or written comments and scientific data and information to the Division of Dockets Management (see **ADDRESSES**). It is only necessary to send one set of comments. Identify comments with the docket number found in brackets in the heading of this document. Received comments may be seen in the Division of Dockets Management between 9 a.m. and 4 p.m., Monday through Friday, and will be posted to the docket at *http://www.regulations.gov.*

IX. References

We have placed the following references on display in the Division of Dockets Management (see **ADDRESSES**). You may see them between 9 a.m. and 4 p.m., Monday through Friday. FDA has verified the Web site addresses, but FDA is not responsible for any subsequent changes to the Web sites after this document publishes in the **Federal Register**.

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Dated: November 5, 2013.

Leslie Kux,

Assistant Commissioner for Policy.

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DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

Proposed Collection; 60-Day Comment Request: Incident HIV/Hepatitis B Virus Infections in South African Blood Donors: Behavioral Risk Factors, Genotypes and Biological Characterization of Early Infection

Summary: In compliance with the requirement of Section 3506(c) (2) (A) of the Paperwork Reduction Act of 1995, for opportunity for public comment on proposed data collection projects, the National Heart, Lung, and Blood Institute (NHLBI), the National Institutes of Health (NIH), will publish periodic summaries of proposed projects to the Office of Management and Budget (OMB) for review and approval.

Written comments and/or suggestions from the public and affected agencies are invited on one or more of the following points: (1) Whether the proposed collection of information is necessary for the proper performance of the function of the agency, including whether the information will have practical utility; (2) The accuracy of the agency's estimate of the burden of the proposed collection of information, including the validity of the methodology and assumptions used; (3) Ways to enhance the quality, utility, and clarity of the information to be collected; and (4) Ways to minimize the burden of the collection of information on those who are to respond, including the use of appropriate automated, electronic, mechanical, or other technological collection techniques or other forms of information technology.

To Submit Comments and For Further Information: To obtain a copy of the data collection plans and instruments, submit comments in writing, or request more information on the proposed project, contact: Simone Glynn, MD, Project Officer/ICD Contact, Two Rockledge Center, Suite 9142, 6701 Rockledge Drive, Bethesda, MD 20892, or call 301–435–0065, or Email your request, including your address to: *glynnsa@nhlbi.nih.gov.* Formal requests for additional plans and instruments must be requested in writing.

Comments Due Date: Comments regarding this information collection are best assured of having their full effect if received within 60 days of the date of this publication.

Proposed Collection: Incident HIV/Hepatitis B virus (HBV) infections in South African blood donors: Behavioral risk factors, genotypes and biological