No. _____

UNITED STATES COURT OF APPEALS FOR THE NINTH CIRCUIT

IN RE BREAST CANCER FUND, CENTER FOR ENVIRONMENTAL HEALTH, CENTER FOR FOOD SAFETY, CENTER FOR SCIENCE IN THE PUBLIC INTEREST, ENVIRONMENTAL WORKING GROUP, and NATURAL RESOURCES DEFENSE COUNCIL, *Petitioners*,

v.

U.S. FOOD AND DRUG ADMINISTRATION and ROBERT M. CALIFF, COMMISSIONER OF THE U.S. FOOD AND DRUG ADMINISTRATION, *Respondents*.

PETITION FOR A WRIT OF MANDAMUS

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CORPORATE DISCLOSURE STATEMENT

Pursuant to Federal Rule of Appellate Procedure 26.1, Petitioners Breast Cancer Fund, Center for Environmental Health, Center for Food Safety, Center for Science in the Public Interest, Environmental Working Group, and Natural Resources Defense Council, Inc., submit that they have no parent corporations. No publicly held corporation holds stock in any of the petitioners.

March 31, 2016

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I. INTRODUCTION

Petitioners Breast Cancer Fund, Center for Environmental Health, Center for Food Safety, Center for Science in the Public Interest, Environmental Working Group, and Natural Resources Defense Council seek a Writ of Mandamus from this Court compelling respondents U.S. Food and Drug Administration and Commissioner Robert M. Califf (collectively, FDA or the agency) to decide petitioners' administrative petition to revoke FDA's approval of perchlorate as a food additive (Petition).[1] *See* Hsieh Decl. ¶¶ 2-4 (ADD 3-4); *id*. Ex. A (ADD 8-84); *id*. Ex. B (ADD 85-106). Perchlorate is an endocrine-disrupting chemical that interferes with the thyroid gland. By inhibiting the thyroid's uptake of iodine, perchlorate impairs hormone production crucial to fetal and infant brain development. Data collected by the Centers for Disease Control and Prevention (CDC) have shown that perchlorate is found in the bodies of virtually all Americans. *See id* Ex. C, at 400 (ADD 108).

[1] A "food additive" includes "any substance the intended use of which results or may reasonably be expected to result, directly or indirectly, in its becoming a component or otherwise affecting the characteristics of any food (including any substance intended for use in . . . packaging . . . or holding food . . .)." 21 U.S.C. § 321(s).

Despite the serious health risks posed by perchlorate, FDA has authorized use of perchlorate in sealing gaskets for food containers since 1962.[2] *See* Closures with Sealing Gaskets for Food Containers, 27 Fed. Reg. 7092 (July 26, 1962) (codified at 21 C.F.R. § 177.1210). The agency approved another food-contact use of perchlorate in 2005, authorizing the chemical's use as an antistatic agent in plastic packaging for dry food products. *See* Hsieh Decl. Ex. D, at 1 (ADD 117); *id*. Ex. E, at 1 (ADD 120). Perchlorate is widespread in the American food supply, appearing in a majority of foods sampled by FDA in 2005 and 2006. *See id*. Ex. A, at 17-18 (ADD 25-26); *id*. Ex. F, at 571, 573, 575 (ADD 123, 125, 127). There are no labeling requirements that mandate disclosure of perchlorate in food packaging, and therefore consumers have no way of knowing when they are being exposed to perchlorate through packaged foods.

Petitioners and other concerned groups filed the Petition in 2014, requesting that FDA rescind its approval of perchlorate as a food additive. The Federal Food, Drug, and Cosmetic Act (Food Act) prohibits the sale of food containing unsafe additives, and the Petition set forth significant data and information demonstrating why the uses of perchlorate authorized by FDA are unsafe. The Food Act requires FDA to issue an order granting or denying a food additive petition within 180 days,

[2] A gasket is a "flat, shaped sheet or ring of rubber, cork, metal composite, or other relatively soft material inserted between adjoining . . . surfaces in order to make the joint airtight or watertight." *Oxford English Dictionary* (online ed. 2016).

and the agency's deadline for deciding the Petition was June 29, 2015. That deadline has come and gone without a final response. FDA's failure to timely decide the Petition contravenes the Food Act's central purpose to protect the public from unsafe food and other products. Petitioners thus ask this Court to find that FDA has unlawfully withheld action on the Petition, and to compel FDA to issue a final order deciding the Petition by a date certain.

II. JURISDICTION

Petitioners bring this case pursuant to Federal Rule of Appellate Procedure 21, which allows parties to petition the Court of Appeals for a writ of mandamus. The Food Act vests exclusive jurisdiction in the Courts of Appeals to review final orders by FDA approving or denying food additive petitions. 21 U.S.C. § 348(g). Although FDA has yet to issue a final order deciding petitioners' food additive petition, the All Writs Act authorizes this Court "to issue mandamus relief necessary to protect [its] 'prospective jurisdiction.'" *In re Cal. Power Exch. Corp.*, 245 F.3d 1110, 1119 (9th Cir. 2001) (quoting *Pub. Util. Comm'r of Or. v. Bonneville Power Admin.*, 767 F.2d 622, 630 (9th Cir. 1985)). The Court therefore has jurisdiction to compel FDA to decide the Petition.

Petitioners have standing to bring this action. To establish standing, petitioners must show that the interests they seek to protect are germane to their organizational purposes, that this litigation will not require their members'

individual participation, and that their members would have standing to sue in their own right. *See Hunt v. Wash. State Apple Adver. Comm'n*, 432 U.S. 333, 343 (1977); *see also Mont. Shooting Sports Ass'n v. Holder*, 727 F.3d 975, 981 (9th Cir. 2013) ("[T]he presence in a suit of even one party with standing suffices to make a claim justiciable . . . ." (quoting *Brown v. City of L.A.*, 521 F.3d 1238, 1240 n.1 (9th Cir. 2008)).

Petitioners satisfy this test. First, protection of human health from unsafe chemical exposures is germane to petitioners' organizational missions. *See* Decl. of Michael F. Jacobson ¶¶ 6-7 (ADD 196-97); Decl. of Andrew Kimbrell ¶¶ 3-8 (ADD 198-201); Decl. of Gina Trujillo ¶¶ 6-7 (ADD 226). Second, this lawsuit does not require the participation of petitioners' individual members, because neither the claims asserted nor the relief sought requires individualized proof. *See Hunt*, 432 U.S. at 344. Third, petitioners' members would have standing to sue on their own because they suffer "injury in fact" that is traceable to FDA's inaction and likely to be redressed by a favorable decision. *See Friends of the Earth, Inc. v. Laidlaw Envtl. Servs. (TOC), Inc.*, 528 U.S. 167, 180-81 (2000) (citing *Lujan v. Defenders of Wildlife*, 504 U.S. 555, 560-61 (1992)).

FDA's failure to decide the Petition inflicts a cognizable procedural injury upon petitioners' members. To show such a cognizable injury, petitioners must demonstrate that: (1) FDA violated a certain procedural rule; (2) that rule protects

the concrete interests of petitioners' members; and (3) it is reasonably probable that FDA's challenged inaction will threaten those interests. *See Ctr. for Food Safety v. Vilsack*, 636 F.3d 1166, 1171 (9th Cir. 2011) (citing *Citizens for Better Forestry v. U.S. Dep't of Agric.*, 341 F.3d 961, 969-70 (9th Cir. 2003)).

This test is satisfied here. First, FDA violated the Food Act's explicit procedural requirement that the agency decide a food additive petition within 180 days. *See* 21 U.S.C. § 348(c)(2); *id*. § 348(i); 21 C.F.R. § 171.100(a). Second, this requirement protects the health interests of petitioners' members by ensuring that FDA promptly considers food additive petitions and, when warranted, takes action to limit the use of a food additive when there is not "reasonable certainty in the minds of competent scientists that the substance is not harmful under the intended conditions of use." 21 C.F.R. § 170.3(i). Third, it is reasonably probable that FDA's violation of the statutory deadline threatens petitioners' members' health. Perchlorate may migrate from plastic packaging into dry food. *See* Hsieh Decl. Ex. A, at 16-17 (ADD 24-25). Once ingested, the chemical disrupts thyroid function, including hormone production. *See id*. at 2 (ADD 10).

Petitioners' members and their families consume dry foods that may have been contaminated with perchlorate; those foods may have been contaminated either directly through contact with perchlorate-containing packaging, or indirectly through inclusion of ingredients that were held in perchlorate-containing

packaging. *See id*. at 10-11 (ADD 18-19); *id*. Ex. D, at 1 (ADD 117); *id*. Ex. E, at 1 (ADD 120); Decl. of Rachel Azzolini ¶ 6 (ADD 160-61); Decl. of Stephanie Cohen ¶¶ 8-9 (ADD 164-65); Decl. of Christopher Davis ¶¶ 15-16, 21 (ADD 172-75); Decl. of Elizabeth Espy ¶¶ 7-9 (ADD 178-79); Decl. of Teresa Hale ¶¶ 10, 12 (ADD 186); Decl. of Thomas Hawkins ¶¶ 9, 12 (ADD 190-91); Decl. of Kirsten Krane ¶ 8 (ADD 205); Decl. of Richard Luczyski ¶¶ 10, 12-13 (ADD 209-10); Decl. of Matthew Rainbow ¶ 5, 7-8 (ADD 215-16); Decl. of Paige Tomaselli ¶¶ 5, 8, 9, 12 (ADD 221-23). Some of petitioners' members have infants and young children, who are likely to have higher exposure to perchlorate through food packaging because they consume more food per unit body weight than adults do, and thus are particularly vulnerable to the health risks posed by ingestion of perchlorate-contaminated foods. *See* Hsieh Decl. Ex. A, at 18 (ADD 26); Azzolini Decl. ¶¶ 4-7 (ADD 160-61); Cohen Decl. ¶¶ 3, 6-7 (ADD 163-64); Espy Decl. ¶¶ 5-7, 10-16 (ADD 178-80); Krane Decl. ¶¶ 4-8 (ADD 204-05); Rainbow Decl. ¶ 4-5, 8-9 (ADD 215-16); *see also* Luczyski Decl. ¶ 13 (ADD 210). Those members include parents who are concerned about exposing their infants to perchlorate through breastmilk or powdered infant formula. *See* Azzolini Decl. ¶ 6 (ADD 160-61); Tomaselli Decl. ¶¶ 4, 6, 10-12 (ADD 220-22); *see also* Hsieh Decl. Ex. C, at 404 (ADD 112) (describing study that reported measurable levels of perchlorate in all samples of breast milk collected). Another subset of petitioners'

members and their families are also especially susceptible to the health risks posed by perchlorate, as they already suffer from hypothyroidism, a condition in which the thyroid produces insufficient hormones. *See* Davis Decl. ¶¶ 7-8 (ADD 169-70); Hale Decl. ¶¶ 4-7, 9, 11 (ADD 184-86); Hawkins Decl. ¶¶ 6-12, 14 (ADD 190-92); Krane Decl. ¶¶ 4-5, 9 (ADD 204-05); Luczyski Decl. ¶¶ 4-6, 11-12 (ADD 208-10); *see also* Hsieh Decl. Ex. G, at 1 (ADD 134) (describing symptoms associated with hypothyroidism, ranging from fatigue to fertility problems).

Furthermore, it is impossible for petitioners' members to avoid consuming food that may have been contaminated with perchlorate for two reasons. First, FDA allows an extremely broad range of foods, including both final consumer products and their constituent ingredients, to be packaged in materials containing perchlorate; those foods include such common staples as flour, sugar, grains, and pasta. *See infra* Section IV.B. Second, food packaging is not labeled to disclose the presence of perchlorate, so petitioners' members lack the information they need to avoid eating perchlorate-contaminated foods. Even if petitioners' members were able to avoid eating foods packaged in plastic at the point of purchase—which they are not—they would have no way of knowing whether those foods, or their component ingredients, had been held in perchlorate-containing packaging at some point in the production and distribution chain. *See* Hsieh Decl. Ex. A, at 10-11 (ADD 18-19); Azzolini Decl. ¶ 6 (ADD 160-61); Cohen Decl. ¶¶ 8-9 (ADD 164-

65); Davis Decl. ¶¶ 15-16 (ADD 172-73); Espy Decl. ¶¶ 9, 15-16 (ADD 179-80); Hale Decl. ¶ 12 (ADD 186); Hawkins Decl. ¶¶ 12-14 (ADD 191-92); Krane Decl. ¶ 8 (ADD 205); Rainbow Decl. ¶ 10 (ADD 216); Tomaselli Decl. ¶ 9 (ADD 221-22); *cf. Nat. Res. Def. Council v. U.S. E.P.A.*, 735 F.3d 873, 879 (9th Cir. 2013) (holding that the Natural Resources Defense Council demonstrated a cognizable injury to its members from the U.S. Environmental Protection Agency (EPA)'s approval of a pesticide, where the "probability of exposure to the risk of harm is quite high" and "the probability that NRDC's members will be able to avoid exposing their children to the risk of harm is quite low").

The Petition presented FDA with information and data explaining how the agency, in approving the challenged uses of perchlorate, underestimated not only consumers' exposure to perchlorate, but also the health risks posed by that exposure. *See generally* Hsieh Decl. Ex. A, at 1-12 (ADD 9-20). The Petition also set forth "significant new information" warranting reconsideration of whether the authorized uses of perchlorate are safe. 21 C.F.R. § 170.39(g); *see generally* Hsieh Decl. Ex. A, at 12-20 (ADD 20-28). FDA's failure to decide the Petition thus threatens petitioners' interests in consuming food free of potentially harmful levels of perchlorate.

"Once plaintiffs seeking to enforce a procedural requirement establish a concrete injury, 'the causation and redressability requirements are relaxed.'"

WildEarth Guardians v. U.S. Dep't of Agric., 795 F.3d 1148, 1154 (9th Cir. 2015) (quoting *W. Watersheds Project v. Kraayenbrink*, 632 F.3d 472, 485 (9th Cir. 2011)). "'Plaintiffs alleging procedural injury must show only that they have a procedural right that, if exercised, *could* protect their concrete interests.'" *Id.* (quoting *Salmon Spawning & Recovery Alliance v. Gutierrez*, 545 F.3d 1220, 1226 (9th Cir. 2008)). FDA's failure to timely decide the Petition subjects petitioners' members to continued risk of exposure to harmful levels of perchlorate through consumption of contaminated foods. If FDA were to decide the Petition, it could agree to ban or limit the uses of perchlorate that injure petitioners' members, thereby protecting their health interests. *See* Cohen Decl. ¶¶ 13-14 (ADD 165-66); Davis Decl. ¶¶ 20-21 (ADD 174-75); Espy Decl. ¶ 20 (ADD 181); Hawkins Decl. ¶¶ 16-17 (ADD 192-93); Luczyski Decl. ¶ 16 (ADD 211); Rainbow Decl. ¶¶ 12, 14 (ADD 216-17); Tomaselli Decl. ¶¶ 14-15 (ADD 223). Alternatively, if FDA were to deny the petition, petitioners would have the right to challenge that decision on the merits; if petitioners were to prevail on such a challenge, this would also protect their members' health interests. *See* Cohen Decl. ¶ 15 (ADD 166); Davis Decl. ¶ 22 (ADD 175); Espy Decl. ¶¶ 21-22 (ADD 181-82); Luczyski Decl ¶¶ 17-18 (ADD 211); Rainbow Decl. ¶ 15 (ADD 217); Tomaselli Decl. ¶ 16 (ADD 223-24).

III. LEGAL FRAMEWORK

The Food Act prohibits the introduction of any "adulterated" food into interstate commerce. 21 U.S.C. § 331(a). A food is "adulterated" if it contains an "unsafe" food additive. *Id*. § 342(a)(2)(C)(i). A food additive may be a "food contact substance," which the Food Act defines as "any substance intended for use as a component of materials used in manufacturing, packing, packaging, transporting, or holding food if such use is not intended to have any technical effect in such food." *Id.* § 348(h)(6). In addition, FDA has defined "[s]afe or safety" to "mean[] that there is a reasonable certainty in the minds of competent scientists that the substance is not harmful under the intended conditions of use." 21 C.F.R. § 170.3(i).

The Food Act requires that a food additive be deemed "unsafe" unless, as relevant here, FDA has approved it by issuing a regulation "prescribing the conditions under which such additive may be safely used." 21 U.S.C. § 348(a). In addition, "[a] substance used in a food-contact article (e.g., food-packaging . . .) that migrates, or that may be expected to migrate, into food will be exempted from regulation as a food additive because it becomes a component of food at levels that are below the threshold of regulation," among other criteria. 21 C.F.R. § 170.39(a); *see also id.* § 170.39(a)(2)(i) (requiring that use of such an exempted substance "has been shown to result in or may be expected to result in dietary concentrations

at or below 0.5 parts per billion, corresponding to dietary exposure levels at or below 1.5 micrograms/person/day"[3]). In determining whether a proposed use of a food additive is safe, FDA must consider, among other relevant factors, "the cumulative effect of such additive in the diet of man or animals, taking into account any chemically or pharmacologically related substance or substances in such diet." 21 U.S.C. § 348(c)(5)(B). In addition, if FDA "receives significant new information that raises questions about the dietary concentration or the safety of a substance that the agency has exempted from regulation, the Food and Drug Administration may reevaluate the substance." 21 C.F.R. § 170.39(g).

Any interested person may submit a food additive petition to FDA asking it to issue, amend, or repeal a food additive regulation. 21 U.S.C. § 348(b)(1), (i); 21 C.F.R. § 171.130. If FDA finds the petition to be deficient or incomplete, the petitioner may supplement and resubmit it. 21 C.F.R. § 171.1(d), (i)(1)(ii). Once the petition has been filed, the agency has ninety days to decide whether or not it will issue, amend, or repeal the relevant regulation. *See* 21 U.S.C. § 348(c)(2), (i); 21 C.F.R. § 171.100(a). FDA can take an additional ninety days if "necessary to enable [the agency] to study and investigate the petition." 21 U.S.C. § 348(c)(2); 21 C.F.R. § 171.100(c). However, FDA "shall" approve or deny a food additive

[3] A microgram is one-millionth of a gram.

petition within 180 days of the petition's filing date. 21 U.S.C. § 348(c)(2); *see id*. § 348(i); 21 C.F.R. § 171.100.

The Food Act sets forth specific actions that FDA must take to approve or deny a food additive petition. In response to a petition to promulgate a new regulation, FDA shall either "by order establish a regulation (whether or not in accord with that proposed by the petitioner) prescribing . . . the conditions under which such additive may be safely used," 21 U.S.C. § 348(c)(1)(A), or "by order deny the petition, and . . . notify the petitioner of such order and of the reasons for such action," *id*. § 348(c)(1)(B). In response to a petition to amend or repeal an existing food additive regulation, FDA must follow a procedure that "conform[s] to the procedure provided . . . for the promulgation of such regulations." *Id*. § 348(i). In other words, the agency must by order amend or repeal the targeted food additive regulation or by order deny the petition. *See id*. § 348(c)(1), (i).

IV. FACTUAL BACKGROUND

A. Perchlorate poses serious human health risks

Perchlorate is a chemical that interferes with the thyroid gland. Hsieh Decl. Ex. A, at 2 (ADD 10). By inhibiting the thyroid's uptake of iodine, perchlorate impairs hormone production. *Id*. Thyroid hormones are, among other things, critical to fetal and infant brain development. *Id*. A pregnant woman's ingestion of perchlorate is especially dangerous during the first two trimesters of pregnancy,

when the fetus's thyroid is not fully functioning and the fetus depends entirely on maternal thyroid hormones. *Id.* Even transient exposures to perchlorate may result in permanent cognitive deficits in children. *Id.*

Risk of harm from perchlorate is particularly high for fetuses carried by pregnant women who already have deficient iodine intake. *Id*. As it is, most pregnant women do not consume sufficient iodine. *Id*. The World Health Organization defines adequacy of iodine intake by the concentration of urinary iodine and sets a concentration of less than 150 μg/L (or micrograms per liter) as inadequate for pregnant women. *Id.* Based on this benchmark and data from the National Health and Nutrition Examination Survey (NHANES) administered by CDC from 2007 to 2010, almost 56% of pregnant women have inadequate iodine intake. *Id*. Risk of harm from maternal perchlorate exposure is particularly high for fetuses carried by the 26.3% of pregnant women with urinary iodine concentrations of less than 100 μg/L, and even more acute for fetuses carried by the 15.7% of pregnant women with concentrations less than 50 μg/L. *Id*.

Exposure to perchlorate is pervasive among Americans. *Id.* Urinary perchlorate levels reflect recent exposure, and a 2001-2002 NHANES survey of 2820 U.S. residents, ages six and older, found detectable levels of perchlorate in all urinary samples. *Id*. Ex. C, at 400 (ADD 108). The samples also showed significantly higher levels of urinary perchlorate in children as compared to adults.

Id. In addition, perchlorate contamination is widespread in the American food supply. *Id*. Ex. A, at 2, 17-18 (ADD 10, 25-26). A 2008 FDA study found that 74% of 285 tested food types had at least one sample containing measurable levels of perchlorate; in addition, about 59% of the 1,065 individual food samples had detectable levels of perchlorate. *Id.* at 17-18 (ADD 25-26); *Id.* Ex. F, at 575 (ADD 127). Recent studies show that there may be substantial migration of perchlorate from plastic packaging into dry foods. *See id*. Ex. A, at 16-17 (ADD 24-25).

In addition to being widely present in the food supply, perchlorate also contaminates drinking water. In 2011, EPA concluded that perchlorate must be regulated under the Safe Drinking Water Act, to protect against health harm by limiting human exposure through drinking water. Drinking Water: Regulatory Determination on Perchlorate, 76 Fed. Reg. 7762, 7762 (Feb. 11, 2011). EPA found that "perchlorate may have an adverse effect on the health of persons" and "is known to occur or there is a substantial likelihood that perchlorate will occur in public water systems with a frequency and at levels of public health concern." *Id*. Accordingly, Americans may be exposed to perchlorate not only through the food they eat, but also the water they drink.

B. FDA has approved two uses of perchlorate as a food additive

In 1962, FDA approved use of the salt potassium perchlorate in closure-sealing gaskets for food containers. *See* Closures with Sealing Gaskets for Food

Containers, 27 Fed. Reg. 7092 (July 26, 1962) (codified at 21 C.F.R. § 177.1210). Closure-sealing gaskets are intended to close food containers hermetically to prevent entry of oxygen, which may otherwise cause discoloration of the packaged product. *See, e.g.*, Hsieh Decl. Ex. H, at 1 (ADD 141). In containers with metal closures, the presence of an electric current can cause corrosion, allowing oxygen to enter. *Id.* Because of its antistatic properties, *see id*. Ex. D., at 1 (ADD 117), perchlorate is presumably used in closure-sealing gaskets for food containers to suppress electric currents that might otherwise lead to corrosion.[4]

In 2005, FDA also granted a "threshold of regulation" exemption (TOR No. 2005-006) allowing use of the compound sodium perchlorate monohydrate as an antistatic agent in plastic packaging for dry solid foods with surfaces containing no free fat or oil. *See id.*; *id*. Ex. E, at 1 (ADD 120); 21 C.F.R. § 170.39(a). Under this exemption, sodium perchlorate monohydrate "may be used at a level not to exceed 1.2 percent by weight of the finished polymer." Hsieh Decl. Ex. D, at 1 (ADD 117). In this capacity, perchlorate reduces the electrostatic charge created during the filling, emptying, and transporting of food containers. *Id*. Ex. A, at 11 (ADD 19); *id*. Ex. J, at 1 (ADD 148). It also decreases the electrostatic charge on film

[4] The Society of the Plastics Industry, the trade association for plastics manufacturers, has represented to FDA that "domestic and foreign producers of perchlorates may not currently manufacture perchlorate for use in closure sealing gaskets for food containers." Hsieh Decl. Ex. I, at 1 (ADD 145). To the extent that perchlorate is still used in food container sealing gaskets, the Society of the Plastics Industry's statement to FDA suggests that superior alternatives exist.

surfaces, preventing dust deposit and preserving the original appearance of packaging. *Id*. Ex. A, at 11 (ADD 19). FDA's exemption permits use of perchlorate in packaging for both raw food ingredients and final consumer products. *See id.* at 10-11 (ADD 18-19). The breadth of the exemption, moreover, allows perchlorate to be used in packaging for an extremely wide range of ingredients and commodities, including not only staples like cereals, grains, beans, and pastas, but also basic substances like flour and sugar. *See id*. Ex. D, at 1 (ADD 117); *id*. Ex. E, at 1 (ADD 120).

C. Petitioners petitioned FDA to revoke its approval of perchlorate as a food additive, because there is not reasonable scientific certainty that those uses are safe

In 2014, petitioners and other concerned groups submitted a food additive petition to FDA requesting that the agency rescind its approved uses of perchlorate in food packaging. Specifically, the Petition asked FDA to: (1) revoke the exemption, referred to as TOR No. 2005-006, allowing use of sodium perchlorate monohydrate as an antistatic agent in packaging for dry foods; (2) promulgate a new regulation prohibiting use of perchlorate as an antistatic agent in food contact articles; and (3) amend the regulation permitting use of potassium perchlorate in sealing gaskets for food containers, 21 C.F.R. § 177.1210, to prohibit that use. Hsieh Decl. Ex. A, at 1 (ADD 9).

The Petition highlighted significant reasons why there is not "reasonable certainty in the minds of competent scientists that [perchlorate] is not harmful under the intended conditions of use." 21 C.F.R. § 170.3(i). First, it identified serious flaws in the assumptions and analyses underlying FDA's decisions to allow use of perchlorate as a food additive. *See* Hsieh Decl. Ex. A, at 2-12, 19-20 (ADD 10-20, 27-28). For example, FDA failed to consider adequately "the cumulative effect of [perchlorate] in the diet of man or animals." 21 U.S.C. § 348(c)(5)(B). Despite widespread concern about perchlorate contamination in drinking water, the agency did not take into account consumers' exposure to perchlorate through that pathway. Hsieh Decl. Ex. A, at 6 (ADD 14). In other words, in deciding whether exposure to perchlorate from food packaging was safe, FDA ignored the fact that consumers are already exposed to perchlorate through drinking water.

In addition, FDA underestimated the daily intake of perchlorate for infants and young children from food packaging by assuming that infants and young children would ingest no more perchlorate per unit body weight than adults do. *See id.* at 10 (ADD 18). However, infants and adults consume more food per unit of body weight than do adults, and are thus likely to have greater exposure to perchlorate from consumption of contaminated foods. *Id.* FDA neglected to address, moreover, the possibility that a larger proportion of infants' and children's diets may be comprised of perchlorate-contaminated foods, as exemplified by an

infant whose sole source of nutrition is perchlorate-contaminated powdered formula. *Id*. Notably, data confirm that children have significantly higher exposure to perchlorate than do adults. *Id*. at 18 (ADD 26); *see id*. Ex. C, at 400 (ADD 108). Furthermore, FDA failed to consider that perchlorate could enter consumers' diets not only through the packaging of final dry food products sold to consumers, but also through the packaging of the dry food ingredients used in the processing and manufacture of those products. *Id*. Ex. A, at 10-11 (ADD 18-19). FDA also overlooked a mathematical error that underestimated dietary intake of perchlorate by eighty-three times. *Id*. at 7-8 (ADD 15-16).

Next, the Petition presented "significant new information" that warranted reconsideration of whether the FDA-approved uses of perchlorate are safe. 21 C.F.R. § 170.39(g); *see* Hsieh Decl. Ex. A, at 12-19 (ADD 20-27). First, in approving the use of perchlorate as an antistatic agent in food packaging "at a level not to exceed 1.2 percent by weight of the finished polymer," *id*. Ex. D, at 1 (ADD 117), FDA relied on a "reference dose" of 0.7 µg/kg body weight/day (or micrograms per kilogram of body weight per day), meaning that the agency assumed that consumers could safely ingest perchlorate at that rate. *Id*. Ex. A, at 13 (ADD 21). For example, under this reference dose, FDA assumes that a 60 kilogram (or 132 pound) woman could safely consume up to 42 micrograms of perchlorate per day. In 2013, however, EPA's Scientific Advisory Board

concluded that this reference dose is too high and does not provide sufficient protection to susceptible populations, including pregnant women. *Id*. EPA's determination means that sensitive populations could be harmed by consuming perchlorate at a dose of 0.7 µg/kg body weight/day. Because FDA's approval of perchlorate for use in plastic food packaging was based on this inappropriately high reference dose, there is not reasonable certainty that humans can safely consume food held in plastic packaging that contains up to 1.2% perchlorate by weight.

Second, since 2005, research has shown that other chemicals—specifically nitrates and thiocyanates—are pharmacologically-related to perchlorate and have a common mechanism of toxicity: all three interfere with the thyroid's uptake of iodine and its ability to make hormones essential to fetal and infant brain development. *Id*. at 15-16 (ADD 23-24). The widespread presence of these other chemicals, particularly nitrates, in food and food packaging, calls for a new analysis of the cumulative effects of perchlorate's food-additive uses. *Id.* at 16 (ADD 24); *see* 21 U.S.C. § 348(c)(5) (requiring FDA to consider, in determining "whether a proposed use of a food additive is safe," "the cumulative effect of [perchlorate] in the diet of man or animals, taking into account any chemically or pharmacologically related substance or substances in such diet").

Third, FDA's 2008 study finding widespread perchlorate contamination in the American food supply likewise constitutes "significant new information," 21 C.F.R. § 170.39(g), about "the cumulative effect of [perchlorate] in the diet of man," 21 U.S.C. § 348(c)(5). Finally, in approving perchlorate for use as an antistatic agent in food packaging, FDA assumed that only 50 parts per billion (ppb) of the chemical migrates into food—a level described as "virtually nil." Hsieh Decl. Ex. A, at 7, 16-17 (ADD 15, 24-25). However, new research from the European Union shows substantial migration of chemicals from plastic packaging into dry food, and FDA has acknowledged that the 50 ppb migration assumption may be flawed. *Id*. at 16-17 (ADD 24-25). These new data, set forth in the Petition, further negate any reasonable scientific certainty that the approved uses of perchlorate are safe. *See* 21 C.F.R. § 170.3(i).

After written exchanges through which FDA identified alleged deficiencies in the Petition and petitioners responded to the agency's comments, FDA accepted the final version of the Petition for filing on December 31, 2014. *See* Hsieh Decl. Ex. K (ADD 156); Notice of Petition, 80 Fed. Reg. 13508, 13509 (Mar. 16, 2015). On March 31, 2015, FDA requested an additional ninety days to respond to the Petition. *See* Hsieh Decl. Ex. L (ADD 158). FDA's 180-day deadline for approving or denying the Petition expired on June 29, 2015. The agency has yet to decide the Petition.

V. ARGUMENT

FDA has unlawfully withheld action on the Petition in violation of the Administrative Procedure Act (APA), 5 U.S.C. § 706(1), and Food Act, 21 U.S.C. § 348, and the Court should issue a writ of mandamus compelling FDA to decide the Petition by a date certain.

A. FDA has unlawfully withheld agency action by failing to decide the Petition by the Food Act's deadline

The APA authorizes a reviewing court to "compel agency action unlawfully withheld," 5 U.S.C. § 706(1), and an agency's failure to make a mandatory decision by a statutory deadline constitutes action unlawfully withheld, *see Norton v. S. Utah Wilderness Alliance*, 542 U.S. 55, 63-65 (2004). Under the Food Act, FDA "shall" issue an order deciding a food additive petition "not more than one hundred and eighty days after the date of filing of the petition." 21 U.S.C. § 348(c)(2), (i). This statutory deadline is mandatory. *See In re Barr Labs., Inc.*, 930 F.2d 72, 74 (D.C. Cir. 1991) (holding as mandatory a similarly-worded provision of the Food Act stating that FDA "shall" approve or disapprove a generic drug application "within one hundred and eighty days of the initial receipt of an application"); *see also Nat'l Ass'n of Home Builders v. Defenders of Wildlife*, 551 U.S. 644, 661 (2007) (collecting cases that interpret the word "shall" to create mandatory obligations). Because FDA accepted the Petition for filing on December 31, 2014, the Food Act required the agency to decide the Petition by June 29, 2015.

See 21 U.S.C. § 348(c)(2), (i). By failing to issue an order granting or denying the Petition by that deadline, FDA has unlawfully withheld agency action. 5 U.S.C. § 706(1).

B. FDA's failure to publish an order deciding the Petition warrants mandamus relief

1. Petitioners satisfy the Ninth Circuit's general mandamus test, and a writ is appropriate under the circumstances

To determine whether mandamus should issue, the Ninth Circuit generally applies a three-part test: whether "(1) the plaintiff's claim is clear and certain; (2) the duty is ministerial and so plainly prescribed as to be free from doubt; and (3) no other adequate remedy is available." *In re Cal. Power Exch. Corp*., 245 F.3d at 1120 (quoting *Or. Natural Res. Council v. Harrell*, 52 F.3d 1499, 1508 (9th Cir. 1995)); *cf. In re Paralyzed Veterans of Am*., 392 F. App'x 858, 860 (Fed. Cir. 2010) (applying similar test to determine whether court should grant mandamus relief to compel agency action, where agency failed to meet statutory deadline). Mandamus is "an extraordinary remedy justified only in exceptional circumstances," and "[t]he party seeking mandamus relief must establish that its right to issuance of the writ is clear and indisputable." *In re Cal. Power Exch. Corp*., 245 F.3d at 1120 (internal quotation marks omitted). Thus, even when the other prerequisites have been met, "the issuing court, in the exercise of its

discretion, must be satisfied that the writ is appropriate under the circumstances." *In re United States*, 791 F.3d 945, 955 (9th Cir. 2015).

An order compelling FDA to decide the Petition by a prompt deadline is warranted under this test. First, petitioners' claim is "clear and certain," *In re Cal. Power Exch. Corp.*, 245 F.3d at 1120, because the Food Act unambiguously required FDA to approve or deny the Petition within 180 days of the filing of the petition. *See* 21 U.S.C. § 348(c)(2), (i); *see also* 21 C.F.R. §§ 171.100(a), 171.130(a). Second, "[a]n agency 'ministerial act' for purposes of mandamus relief has been defined as a clear, non-discretionary agency obligation to take a specific affirmative action, which obligation is positively commanded and so plainly prescribed as to be free from doubt." *Indep. Mining Co. v. Babbitt*, 105 F.3d 502, 508 (9th Cir. 1997) (internal quotation marks omitted). FDA's duty to decide the Petition is "ministerial," because the Food Act clearly commanded FDA to take one of two discrete actions within 180 days of accepting the Petition for filing: either (1) "by order" establish, amend, or repeal the food additive regulations at issue, or (2) "by order deny the petition." 21 U.S.C. § 348(c)(1); *see id*. § 348(i). Third, no other adequate remedy is available. Neither the Food Act nor its implementing regulations provide any other means by which Petitioners can compel FDA to decide the petition. *Cf. Cole v. U.S. Dist. Court for the Dist. of Idaho*, 366 F.3d 813, 817-18 (9th Cir. 2004) (holding that another adequate remedy

was available where petitioners could have sought reconsideration of magistrate judge's order from district court).

In addition, a writ of mandamus "is appropriate under the circumstances," *In re United States*, 791 F.3d at 955, because a prompt decision on the Petition is necessary to effectuate the Food Act's central purpose. The Supreme Court has recognized that the Food Act "was designed primarily to protect consumers" from unsafe products. *United States v. Sullivan*, 332 U.S. 689, 696 (1948). The deadline mandated by the Food Act for responding to food additive petitions reflects Congress's judgment that timely food safety determinations are critical to protecting public health. *Cf. Mohasco Corp. v. Silver*, 447 U.S. 807, 825-26 (1980) ("By choosing what are obviously quite short deadlines, Congress clearly intended to encourage . . . prompt processing . . . . . [I]n a statutory scheme in which Congress carefully prescribed a series of deadlines measured by numbers of days—rather than months or years—we may not simply interject an additional 60-day period into the procedural scheme."). Time is of the essence, moreover, given the risk of serious and irreparable harm to children's health from exposure to perchlorate in food.

The Supreme Court has underscored that "[t]he high purpose of the [Food Act] [is] to protect consumers who under present conditions are largely unable to protect themselves" in the field of food and drug safety. *Kordel v. United States*,

335 U.S. 345, 349 (1948); *accord United States v. Dotterweich*, 320 U.S. 277, 280 (1943) ("The purposes of this legislation thus touch phases of the lives and health of people which, in the circumstances of modern industrialism, are largely beyond self-protection. Regard for these purposes should infuse construction of the legislation if it is to be treated as a working instrument of government and not merely as a collection of English words."). This admonition is particularly applicable here. Because there are no labeling requirements for disclosure of perchlorate used in food packaging, consumers have no way of knowing when they are being exposed to perchlorate through packaged foods. *See, e.g.*, Cohen Decl. ¶ 8 (ADD 164-65); Davis Decl. ¶ 16 (ADD 173); Espy Decl. ¶¶ 15-16 (ADD 180); Hale Decl. ¶ 12 (ADD 186); Hawkins Decl. ¶ 13 (ADD 191); Rainbow Decl. ¶ 10 (ADD 216). And even if the packaging for final consumer food products were labeled to disclose the presence of perchlorate, consumers would still not know whether any of the component ingredients incorporated into those food products had been held in packaging containing perchlorate.

"[T]he purpose of the [Food Act]—to safeguard the consumer from the time the food is introduced into the channels of interstate commerce to the point that it is delivered to the ultimate consumer—would be substantially thwarted," *United States v. Wiesenfeld Warehouse Co.*, 376 U.S. 86, 92 (1964), by FDA's continued inaction on the Petition. There are thus "exceptional circumstances" here that

justify the "extraordinary remedy" of mandamus. *In re Cal. Power Exch. Corp.*, 245 F.3d at 1120 (internal quotation marks omitted).

2. Alternatively, petitioners are also entitled to mandamus relief under the *Badgley* test

Petitioners see no reason why the Ninth Circuit's general mandamus test would not apply here. Nonetheless, in *Biodiversity Legal Foundation v. Badgley*, 309 F.3d 1166, 1177 (9th Cir. 2002), this Court applied a slightly different framework for determining whether court intervention was warranted to compel agency action unlawfully withheld. In *Badgley*, the Ninth Circuit held that "the test for determining if equitable relief is appropriate is whether an injunction is necessary to effectuate the congressional purpose behind the statute." *Id*. at 1177; *cf. Ctr. for Food Safety v. Hamburg*, 954 F. Supp. 2d 965, 971-72 (N.D. Cal. 2013) (granting injunctive relief to compel FDA to finalize various food safety regulations based on the Food Safety Modernization Act's "evident purpose . . . to ensure the safety of the food supply" when, at the time of the complaint, FDA's regulations were approximately two to eleven months overdue). The *Badgley* standard may not be apposite here, as that case involved a request for injunctive relief, whereas Petitioners seek mandamus relief. *But cf. Fallini v. Hodel*, 783 F.2d 1343, 1345 (9th Cir. 1986) ("When the effect of a mandatory injunction is equivalent to the issuance of mandamus it is governed by similar considerations."); *see also United States v. Carter*, 270 F.2d 521, 524 (9th Cir. 1959) ("'Although

classed as a legal remedy, . . . issuance [of the writ of mandamus] is largely controlled by equitable principles."' (quoting *Duncan Townsite Co. v. Lane*, 245 U.S. 308, 312 (1917)).

Should this Court decide that *Badgley* governs here, Petitioners also satisfy the *Badgley* test for court intervention. Mandamus is warranted under *Badgley* because a prompt decision of the Petition "is necessary to effectuate the congressional purpose behind the statute." 309 F.3d at 1177. As discussed above, the Food Act's central purpose is to protect consumers from unsafe products, and FDA's 180-day statutory deadline for responding to food additive petition reflects Congress's judgment that timely food safety determinations are critical to protecting public health. *See supra* Section V.B.1. The serious and irreparable health risks that perchlorate poses to fetuses, infants, and children further underscore the need for a swift FDA decision on the Petition. Additional delay would hinder the Food Act's primary objective of protecting consumers, particularly given consumers' inability to protect themselves from the health risks posed by perchlorate exposure through food packaging. *See id.*

VI. REQUEST FOR RELIEF

Petitioners request that the Court grant this Petition for a Writ of Mandamus and order FDA to decide the Petition within ninety days of the Court's order.

VII. CONCLUSION

For the foregoing reasons, Petitioners respectfully request that the Court grant this Petition for a Writ of Mandamus.

March 31, 2016

Respectfully submitted,

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STATEMENT OF RELATED CASES

Petitioners are unaware of any related cases within the definition of Circuit Rule 28-2.6.

March 31, 2016

/s/ Margaret T. Hsieh
Margaret T. Hsieh

/s/ Cristina R. Stella
Christina R. Stella

CERTIFICATE OF SERVICE

I hereby certify that on March 31, 2016, I served a copy of the foregoing Petition for a Writ of Mandamus, and Declarations of Margaret T. Hsieh (and Exhibits A-L), Rachel Azzolini, Stephanie Cohen, Christopher Davis, Elizabeth Espy, Teresa Hale, Thomas Hawkins, Michael F. Jacobson, Andrew Kimbrell, Kirsten Krane, Richard Luczyski, Matthew Rainbow, Paige Tomaselli, and Gina Trujillo by placing true copies thereof in sealed envelopes addressed as shown below for service as designated below:

Elizabeth H. Dickinson
Office of the Chief Counsel
U.S. Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993

Robert M. Califf
Office of the Commissioner
U.S. Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993

Brian Stretch
Acting United States Attorney
U.S. Attorney's Office for the
Northern District of California
Federal Courthouse, 11th Floor
450 Golden Gate Avenue
San Francisco, CA 94102

Loretta E. Lynch
United States Attorney General
U.S. Department of Justice
950 Pennsylvania Avenue, NW
Washington, DC 20530

Certified Mail, Return Receipt Requested: I placed the envelopes, sealed with first-class postage fully prepaid, and with certified mail labels and return receipts attached, for collection and mailing at a facility regularly maintained by the United States Postal Service.

I declare under penalty of perjury under the laws of the State of New York that the foregoing is true and correct. Executed this March 31, 2016, in New York, New York.

/s/ Gabriel Levine
Gabriel Levine

ADDENDUM OF DECLARATIONS AND EXHIBITS

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No. _____

UNITED STATES COURT OF APPEALS FOR THE NINTH CIRCUIT

IN RE BREAST CANCER FUND, CENTER FOR ENVIRONMENTAL HEALTH, CENTER FOR FOOD SAFETY, CENTER FOR SCIENCE IN THE PUBLIC INTEREST, ENVIRONMENTAL WORKING GROUP, and NATURAL RESOURCES DEFENSE COUNCIL, *Petitioners*,

v.

U.S. FOOD AND DRUG ADMINISTRATION and ROBERT M. CALIFF, COMMISSIONER OF THE U.S. FOOD AND DRUG ADMINISTRATION, *Respondents*.

DECLARATION OF MARGARET T. HSIEH

I, Margaret T. Hsieh, declare as follows:

1. I serve as counsel for Petitioners Breast Cancer Fund, Center for Environmental Health, Center for Science in the Public Interest, Environmental Working Group, and Natural Resources Defense Council (NRDC) in this case. I am a member in good standing of the bar of this Circuit. I have personal knowledge of the facts stated herein.

2. Attached as Exhibit A is a true and correct copy of the perchlorate food additive petition, dated October 15, 2014, submitted by petitioners Breast Cancer Fund, Center for Environmental Health, Center for Food Safety, Center for Science in the Public Interest, Environmental Working Group, Natural Resources Defense

Council, and other groups. NRDC et al., Perchlorate Food Additive Petition (Oct. 15, 2014), *available at* http://www.regulations.gov/#!documentDetail;D=FDA-2015-F-0537-0004.

3. Attached as Exhibit B is a true and correct copy of the December 5, 2014 supplement to the October 15, 2014 petition, Ex. A, submitted by petitioners and other groups. NRDC et al., Supplement to Perchlorate Food Additive Petition No. 4B4808 (Dec. 5, 2014), *available at* http://www.regulations.gov/#!documentDetail;D=FDA-2015-F-0537-0006.

4. Together, Exhibits A and B constitute the perchlorate food additive petition (Petition) that FDA accepted for filing on December 31, 2014.

5. Attached as Exhibit C is a true and correct copy of an article entitled "Perchlorate Exposure of the US Population, 2001-2002." I downloaded this article from the website of the Journal of Exposure Science & Environmental Epidemiology on March 14, 2016. *See* Benjamin C. Blount et al., *Perchlorate Exposure of the US Population, 2001-2002*, 17 J. Exposure Sci. & Envtl. Epidemiology 400 (2007), *available at* http://www.nature.com/jes/journal/v17/n4/full/7500535a.html.

6. Attached as Exhibit D is a true and correct copy of the FDA's Threshold of Regulation Exemption No. 2005-006 for sodium perchlorate monohydrate, which I downloaded from FDA's website on March 14, 2016. FDA, Threshold of

Regulation Exemption for Sodium Perchlorate Monohydrate, http://www.accessdata.fda.gov/scripts/fdcc/?set=TOR&id=2005-006 (last visited Mar. 16, 2016).

7. Attached as Exhibit E is a true and correct copy of FDA's webpage entitled "Food Types & Conditions of Use for Food Contact Substances," which I downloaded from the agency's website on March 14, 2016. FDA, *Food Types and Conditions of Use for Food Contact Substances*, http://www.fda.gov/Food/IngredientsPackagingLabeling/PackagingFCS/FoodTypesConditionsofUse/default.htm (last visited Mar. 14, 2016).

8. Attached as Exhibit F is a true and correct copy of an article entitled "US Food and Drug Administration's Total Diet Study: Dietary Intake of Perchlorate and Iodine." I downloaded this article from the website of the Journal of Exposure Science & Environmental Epidemiology on March 14, 2016. Clarence William Murray et al., *US Food and Drug Administration's Total Diet Study: Dietary Intake of Perchlorate and Iodine*, 18 J. Exposure Sci. & Envtl. Epidemiology 571 (2008), *available at* http://www.nature.com/jes/journal/v18/n6/full/7500648a.html.

9. Attached as Exhibit G is a true and correct copy of the National Institutes of Health (NIH)'s MedlinePlus entry on hypothyroidism. I downloaded this entry from the NIH's U.S. National Library of Medicine MedlinePlus website on March

14, 2016. Nat'l Insts. of Health (NIH), *Hypothyroidism*, U.S. National Library of Medicine MedlinePlus, https://www.nlm.nih.gov/medlineplus/hypothyroidism.html (last visited Mar. 14, 2016).

10. Attached as Exhibit H is a true and correct copy of U.S. Patent No. 2,689,840 that I downloaded from Google Patents on March 14, 2016. Closure Sealing Gaskets, U.S. Patent No. 2,689,840 (filed Aug. 26, 1952), *available at* https://docs.google.com/viewer?url=patentimages.storage.googleapis.com/pdfs/US2689840.pdf.

11. Attached as Exhibit I is a true and correct copy of a July 10, 2015 Memorandum of Meeting added to the FDA's administrative file for the Petition. I downloaded this memorandum from Regulations.gov on March 14, 2016. Memorandum from Paul Honigfort, Consumer Safety Officer, FDA, to Administrative File FAP 4B4808 (July 10, 2005), *available at* http://www.regulations.gov/#!documentDetail;D=FDA-2015-F-0537-0010.

12. Attached as Exhibit J is a true and correct copy of U.S. Patent Application No. 2004/0004804 A1 that I downloaded from Google Patents on March 14, 2016. Inner Device for Neutralization of Electrostatic Charges from Material in Contact, U.S. Patent Application No. 2004/0004804 A1 (filed Dec. 23, 2002), *available at*

https://docs.google.com/viewer?url=patentimages.storage.googleapis.com/pdfs/US20040004804.pdf.

13. Attached as Exhibit K is a true and correct copy of the letter, dated December 31, 2014, from FDA to NRDC stating that the Petition had been filed and that "[t]he date of this letter is the filing date of your application." Letter from Paul S. Honigfort, Consumer Safety Officer, FDA, to Erik Olson, Senior Strategic Director for Health and Food, NRDC (Dec. 31, 2014), *available at* http://www.regulations.gov/#!documentDetail;D=FDA-2015-F-0537-0007.

14. Attached as Exhibit L is a true and correct copy of the letter, dated March 31, 2015, from FDA to NRDC stating that the agency has "extended scientific review" of the Petition "for an additional 90 days in accordance with section 409(c)(2) of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. § 348(c)(2)]." Letter from Francis Lin, Director, Division of Food Contact Notifications, FDA, to Erik Olson, Senior Strategic Director for Health and Food, NRDC (Mar. 31, 2015) *available at* https://www.regulations.gov/#!documentDetail;D=FDA-2015-F-0537-0015.

I declare under penalty of perjury that the foregoing is true and correct. Executed this 31st day of March, 2016 in New York, New York.

/s/ Margaret T. Hsieh
Margaret T. Hsieh

Exhibit A

Natural Resources Defense Council et al.
Food Additive Petition Seeking Food Additive Regulation Prohibiting the Use of Perchlorate as a Conductivity Enhancer in the Manufacture of Antistatic Agents in Contact with Dry Food and as Additive to Sealing Gaskets for Food Containers (Oct. 15, 2014)

NATURAL RESOURCES DEFENSE COUNCIL
BREAST CANCER FUND
CENTER FOR ENVIRONMENTAL HEALTH
CENTER FOR FOOD SAFETY
CENTER FOR SCIENCE IN THE PUBLIC INTEREST
CHILDREN'S ENVIRONMENTAL HEALTH NETWORK
CLEAN WATER ACTION
ENVIRONMENTAL WORKING GROUP
IMPROVING KIDS' ENVIRONMENT

October 15, 2014

Dr. Dennis Keefe
Director of the Office of Food Additive Safety (HFS-200)
Center for Food Safety and Applied Nutrition
5100 Paint Branch Parkway
College Park, MD 20740-3835

Re: Food additive petition seeking food additive regulation prohibiting the use of perchlorate as a conductivity enhancer in the manufacturer of antistatic agents in contact with dry food and as additive to sealing gaskets for food containers.

Dear Dr. Keefe:

The Natural Resources Defense Council (NRDC), Center for Food Safety, Breast Cancer Fund, Center for Environmental Health, Environmental Working Group, Improving Kids' Environment, Clean Water Action, Center for Science in the Public Interest and Children's Environmental Health Network submit this food additive petition[1], pursuant to section 409(b)(l) of the Federal Food, Drug, and Cosmetic Act (FFDCA) and 21 CFR § 171.130, requesting that the Food and Drug Administration (FDA):

1. Revoke its 2005 approval of "threshold of regulation" (TOR) No. 2005-006 allowing as much as 1.2% sodium perchlorate monohydrate in dry food packaging;[2]
2. Promulgate a new 21 CFR § 189.301 prohibiting the use of perchlorate as a conductivity enhancer in the manufacture of antistatic agents to be used in food contact articles; and
3. Remove potassium perchlorate as an allowed additive in sealing gaskets for food containers in existing 21 CFR § 177.1210.

[1] Draft petition was submitted to FDA on May 18, 2014. FDA assigned it Pre-Notification Consultation (PNC) No. 001447. This petition also addresses concerns raises by FDA in response to a petition filed on July 31, 2014. On August 22, 2014, FDA determined that the petition was not suitable for filing.
[2] See http://www.accessdata.fda.gov/scripts/fdcc/index.cfm?set=TOR&id=2005-006.

The actions we are requesting are necessary because of the well-recognized toxicity of perchlorate, its widespread presence in food and in the bodies of virtually all Americans, and the likelihood that the dietary exposure may cause permanent damage to a fetus' or infant's brain by irreversibly altering its development. The risk is especially significant if a pregnant and nursing woman consumes insufficient iodine.

Perchlorate interferes with the thyroid gland's ability to uptake iodine which is fundamental to make hormones.[3] These thyroid hormones are essential for brain development in infants and in fetuses, especially in the first two trimesters when the fetus' thyroid is not fully functioning and the fetus depends entirely on the pregnant woman for thyroid hormones. Therefore, pregnant women and infants exposed to perchlorate may not absorb sufficient iodine to produce adequate levels of thyroid hormones. Even transient exposures to perchlorate may result in permanent deficits in a child's cognitive ability.[4]

Unfortunately, without regard to perchlorate, most pregnant women and nursing mothers do not consume sufficient iodine.[5,6] The World Health Organization (WHO) defines the adequacy of iodine intake based on the concentration of iodine in urine and sets a level of less than 150 μg/L as inadequate for pregnant women.[7] Based on the National Health and Nutrition Examination Survey (NHANES) results for 2007 to 2010, almost 56% of pregnant women have inadequate iodine intake. [8] For women in their first trimester, the median iodine intake was 129 μg/L with levels increasing in later trimesters. Therefore, the risk of harm from perchlorate is particularly high for the 26.3% of pregnant women with urinary iodine concentrations less than 100 μg/L and even worse for the 15.7% of pregnant women whose levels are below 50 μg/L – one-third of the level deemed inadequate by WHO.[9]

We analyzed the documentation supporting FDA's 2005 decision regarding TOR No. 2005-006 to allow perchlorate in dry food packaging that the agency provided to us in response to NRDC's Freedom of Information Act (FOIA) Request No. 2014-1324 on April 7, 2014.[10] The information makes clear that the agency's decision was improperly made at the time. The company's application contained a mathematical error that underestimated the perchlorate exposure by 83 times. When FDA posted its decision on its website, the agency made an additional mistake that allowed levels 3.3 times higher than the level stated in Ciba's submission. Even without these errors, the analysis was based on long-standing assumptions about the migration of chemicals

[3] EPA Science Advisory Board, SAB advice on approaches to derive a maximum contaminant level goal for perchlorate, 2013, EPA-SAB-13-004.
[4] *Ibid.*
[5] Caldwell KL, Pan Y, Mortensen ME, Makhmdov A, Merrill L, and Moye J, Iodine status in pregnant women in the United States: National Children's Study and National Health and Nutrition Examination Survey, *Thyroid,* 2013, doi: 10.1089/thy.2013.0012.
[6] Note that approximate 70% of salt consumed in the U.S comes from salt consumed from processed and restaurant foods which generally do not use iodized salt. Sixty percent of iodine in the U.S. diet comes from dairy products because of iodine added to cattle feed or from an iodine-based disinfectant used in milking. See Caldwell 2013.
[7] World Health Organization, Assessment of iodine deficiency disorders and monitoring their elimination: a guide for programme managers, 2008.
[8] Caldwell 2013.
[9] *Ibid.*
[10] See Appendix 3.

from packaging into dry food that the agency conceded in 2011 were flawed. In addition, while the approval considered only exposure from final product packaging delivered to consumers, it was so broadly written that it can be – and is – used to allow perchlorate in bulk packaging of any dry food ingredient used in food manufacturing. Finally, FDA issued its approval without considering the agency's own testing showing widespread presence of perchlorate in the food supply.

Our analysis below indicates that the uses allowed by FDA are not safe[11] because there is no longer a reasonable certainty that the perchlorate is not harmful under the intended conditions of use considering: 1) the probable consumption of perchlorate; 2) the cumulative effect of perchlorate after taking into account pharmacologically-related substances, such as thiocyanate and nitrate, in the diet; and 3) additional safety factors necessary to protect the developing brain of fetuses and infants from irreversible harm.

PART I: Request to Revoke TOR No. 2005-006

We request that FDA revoke TOR No. 2005-006 pursuant to 21 CFR § 170.39(g). We justify our request in five sections as follows:

I.A. Summary of FDA's approval of perchlorate in packaging under TOR No. 2005-006
I.B. Flaws in Ciba's exemption request
I.C. FDA's unjustified expansion of request to apply to packaging for all dry foods
I.D. Significant new information after FDA approved the use.
I.E. Disproportionate impact on children's health

We have based our analysis of FDA's response to NRDC's Freedom of Information Act (FOIA) Request No. 2014-1324 on April 7, 2014. NRDC requested documentation related to Ciba Specialty Chemicals Corporation's (Ciba) TOR No. 2005-006. We included the agency's response for reference in Appendix 3. Ciba was purchased by BASF in 2010.[12]

I.A. Summary of FDA's approval of perchlorate in packaging under TOR No. 2005-006

Ciba submitted its request for a threshold of regulation (TOR) exemption pursuant 21 CFR § 170.39 on June 17, 2005.[13] It was the subject of a Pre-Notification Consultation No. 381.

Ciba's submission asked for sodium perchlorate monohydrate (perchlorate) to be formulated with other chemicals whose names were redacted in the FOIA response. The FOIA document did state that Ciba's trade name for the product was Irgastat P18.[14] The perchlorate would have a maximum concentration of 4% by weight in the formulation of Irgastat P18. The mixture would be blended into packaging so the finished article would contain 1.2% perchlorate. Ciba said its

[11] 21 CFR § 170.3(i).
[12] http://en.wikipedia.org/wiki/Ciba_Specialty_Chemicals.
[13] Ciba submission, Memo from Ciba's Neal Earhart to FDA's Vivian Gilliam received on June 22, 2005. See Appendix 3.
[14] Ciba submission, Section 6 – Safety Narrative, page 6. See Appendix 3.

use would be identical to its Food Contact Substance Notification No. 406 which FDA did not object to on July 12, 2004.[15]

The perchlorate formulation would serve "as an antistatic agent for use in polymers in contact with dry foods with surface containing no free fat or oil compliant with 21 CFR § 176.170(c), Table 1, Food Type VIII, such as cereals, flour, macaroni, and sugar."[16] Perchlorate would serve as a conductivity enhancer.

Ciba's submission claimed that the estimated dietary concentration of perchlorate in the diet would be 0.030 parts per billion (ppb) or 0.030 micrograms per kilogram of food (µg/kg). The estimate was calculated by multiplying together the following three variables:

1. 1.2% which is the maximum level of perchlorate in the packaging;
2. 50 ppb using the assumption of "virtually nil" migration of perchlorate from packaging into dry foods per FDA's guidance; and
3. 5% which is the consumption factor FDA recommends in its guidance for the particular type of polymer used in the dry food packaging sold to consumers.[17]

Consistent with FDA's guidance, Ciba calculated the estimated daily intake (EDI) by multiplying the 0.030 ppb dietary concentration by the 3 kg of food a person is assumed to eat per day. This calculation yielded an EDI of 0.09 µg perchlorate/person/day. This level is below the 1.50 µg/person/day threshold of regulation FDA established for additives at 21 CFR § 170.39. Because the EDI was below this threshold, Ciba's submission only needed to show there was no evidence that perchlorate was associated with cancer or other health and safety effects.[18]

Ciba concluded the perchlorate "presents negligible health risks" because the EDI for a 70 kilogram person would be 0.00000129 mg/kg-body weight/day.[19] Based on this result, Ciba determined that its calculated EDI was 542 times smaller than the 0.0007 mg/kg-bw/day reference dose adopted by the U.S. Environmental Protection Agency (EPA) in its Integrated Risk Information System (IRIS) report issued February 18, 2005.[20] Ciba did not consider any sources of perchlorate in the diet other than its product.

FDA's committee handling threshold of regulation exemption submissions reviewed Ciba's document and concluded the product was eligible for the exemption. However, it unilaterally expanded the scope of the request beyond Irgastat P18 to allow sodium perchlorate monohydrate to be used as a conductivity enhancer in the manufacture of any duly authorized antistatic agents for use in contact with dry foods.[21]

[15] See http://www.accessdata.fda.gov/scripts/fdcc/?set=FCN&id=406.
[16] Ciba submission, Section 3 – Conditions of Use, page 3. See Appendix 3.
[17] Ciba submission, Section 5 – Estimated Daily Intake, page 5. See Appendix 3.
[18] Ciba submission, Section 6 – Safety Narrative, page 6. See Appendix 3.
[19] 0.00009 milligrams per person per day divided by 70kg body weight = 0.00000129 milligrams/kg body weight/day
[20] Ciba submission, Section 6 – Safety Narrative, page 6. See Appendix 3.
[21] Memorandum of Conference, FDA Threshold of Regulation Committee, Sept., 15, 2005, page 3.

On November 4, 2005, Mitchell Cheeseman, Director of FDA's Division of Food Contact Notification sent a letter to Ciba approving the exemption request after observing that the firm had "provided worst-case extraction data, safety data, and a categorical exclusion under 21 CFR § 25.32(i) and (j) in support of your request."[22] He concluded

> "that Ciba Specialty Chemical Corporation's intended use of sodium perchlorate monohydrate as a conductivity enhancer in regulated or otherwise authorized antistatic agents at a maximum concentration of 4 percent by weight, which would correlate to 1.2 percent by weight in the finished article for use in contact with dry foods qualifies for an exemption under 21 CFR § 170.39 from the requirement of being the subject of a food additive listing regulation."[23]

FDA announced its decision by posting a notice on its website. As of May 16, 2014, the notice is reprinted in Figure 1.

Figure 1: Reprint of FDA's webpage for its approval of sodium perchlorate[24]

TOR No. 2005-006

Threshold of Regulation Exemptions are generally applicable and are effective for the food contact substance (FCS) for the listed intended use regardless of manufacturer or supplier.

Food Contact Substance:	Sodium perchlorate monohydrate (CAS Reg. No. 7791-07-3)
Use Limitations*:	As a conductivity enhancer in the manufacture of antistati agents at a maximum concentration of 4 percent by weigh in the finished article for use in contact with dry foods.
Requestor:	Ciba Specialty Chemical Corp.

I.B. Flaws in Ciba's exemption request

Ciba's exemption request contained three serious flaws: 1) failure to consider existing FDA approval of perchlorate in food contact articles; 2) failure to consider widespread contamination of the food supply with perchlorate; and 3) mistaken exposure calculation resulting in a dietary concentration estimate 83 times lower than FDA's guidance would allow. FDA appears not to have noticed these flaws.

[22] FDA, Letter to Ciba Specialty Chemicals Corporation regarding Sodium Monohydrate Perchlorate, TOR No. 251, 2005. See Appendix 3.
[23] FDA Letter from Mitchell Cheeseman to Neal Earhart of Ciba Specialty Chemicals Corporation, Nov. 4, 2005. See Appendix 3.
[24] FDA, Threshold of Regulation (TOR) Exemptions, TOR No. 2005-006. Accessed May 16, 2014. See http://www.accessdata.fda.gov/scripts/fdcc/?set=TOR&id=2005-006. Note that the first paragraph in the notice was not included on the webpage on November 6, 2013.

I.B.1. Failure to consider potassium perchlorate exposure allowed as an additive to food contact articles by FDA since 1962

Ciba's exemption request stated that "Sodium perchlorate monohydrate is not FDA regulated." This statement is misleading. A search for "perchlorate" in FDA's "List of Indirect Additives Used in Food Contact Substances"[25] shows that potassium perchlorate is allowed to be used for closures with sealing gaskets for food containers by 21 CFR § 177.1210.

This regulation allows gaskets used to seal food containers to contain up to 1% potassium perchlorate (expressed as percentage by weight of closure-sealing gasket composition). FDA issued this rule on July 20, 1962 in response to a food additive petition filed by Anchor Hocking Glass, W.R. Grace and Company and Chemical Products Corporation. Its decision was effective on July 26, 1962 when it was published in the *Federal Register*.[26]

Ciba's omission is significant because 21 U.S.C. § 348(c)(5) requires FDA to consider "(A) the probable consumption of the additive and of any substance formed in or on food because of the use of the additive" and "(B) the cumulative effect of such additive in the diet of man or animals, taking into account any chemically or pharmacologically related substance or substances in such diet." FDA incorporated these requirements into its definition of safe or safety at 21 CFR § 170.2(i).

While potassium perchlorate and sodium perchlorate monohydrate are different chemicals, they are both salts of perchlorate and would serve a similar function and pose similar health risks. They are chemically-related because in solution the sodium or potassium would disassociate from the perchlorate which would be absorbed and circulate in the body as such. They are also pharmacologically related because they both adversely affect the function of the thyroid gland acting in a similar fashion.

Since Ciba did not consider the exposure from this use of perchlorate, its EDI calculation was flawed. Had this exposure been considered, the proposed use may not have been eligible for the Threshold of Regulation Exemption pursuant to 21 CFR § 170.39.

I.B.2. Failure to consider widespread contamination of food supply with perchlorate

Ciba did not consider the presence of perchlorate as a contaminant in the food supply in its cumulative exposure estimate. At the time the petition was submitted in 2005, there was widespread concern of perchlorate contamination in drinking water.

In response to the concerns, on December 23, 2003, FDA issued a high priority assignment to collect and analyze lettuce and bottled water for perchlorate.[27] Fourteen months later and four months before Ciba submitted its TOR request, the agency expanded the assignment to include

[25] http://www.accessdata.fda.gov/scripts/fcn/fcnNavigation.cfm?filter=perchlorate&sortColumn=&rpt=iaListing.
[26] 27 *Federal Register* 7092 (July 26, 1962).
[27] FDA, Collection and Analysis of Food for Perchlorate – High Priority – DFP#04-11, 2003. See http://www.fda.gov/Food/FoodborneIllnessContaminants/ChemicalContaminants/ucm077780.htm.

broccoli, oranges, orange juice, apples, apple juice, spinach, carrots, cantaloupe, tomatoes, grapes, cornmeal, and oatmeal.[28] This expansion was a clear indication that FDA had found perchlorate in its initial sampling.

As FDA later expanded its testing to include all types of food products, the agency found perchlorate in most samples in all food types and all regions of the country. See section I.D.4 for more information on the sampling results.

Ciba's safety narrative only considered the human exposure to sodium perchlorate resulting from the proposed use of Irgastat P18. This is contrary to 21 U.S.C. § 348(c)(5) and 21 CFR § 170.2(i) because it does not consider the cumulative effect of such additive in the diet of man or animals, taking into account any chemically or pharmacologically related substance or substances in such diet.

I.B.3. Mistaken exposure calculation resulted in estimate exposure that is 83 times lower than FDA's guidance would allow

FDA's guidance recommends the following equation to calculate the dietary concentration (DC) of a food contact substance:

DC = Migration (M) X Consumption Factor (CF)

For food contact substances in contact with dry food, FDA's guidance assumes that the chemical migrates at levels not higher than 50 ppb – a level described as "virtually nil" migration. This 50 ppb migration would result in dry food contamination of 50 µg of perchlorate per kilogram of food (µg/kg).

According to FDA, the consumption factor represents the agency's estimate of "the fraction of the daily diet expected to contact specific packaging materials."[29] For this particular product, the consumption factor was 0.05.

Therefore, the dietary concentration for perchlorate would be:

DC = 0.05 (representing the CF) x 50 µg perchlorate per kilogram of food (representing the migration) = 2.5 µg perchlorate/kg food

The agency then recommends that the estimated daily intake (EDI) is calculated as the product between the DC and the estimated 3 kilograms of food a person consumes per day. This calculation would be:

EDI = DC X 3 kg food

[28] FDA, Collection and Analysis of Food for Perchlorate – High Priority – DFP#05-09, 2005. See http://www.fda.gov/Food/FoodborneIllnessContaminants/ChemicalContaminants/ucm077709.htm.

[29] FDA, Guidance for Industry: Preparation of Premarket Submissions for Food Contact Substances: Chemistry Recommendations," 2002. See Section E.1.A. http://www.fda.gov/Food/GuidanceRegulation/ucm081818.htm. FDA revised the document in 2007 but the revisions did not alter this aspect of the guidance.

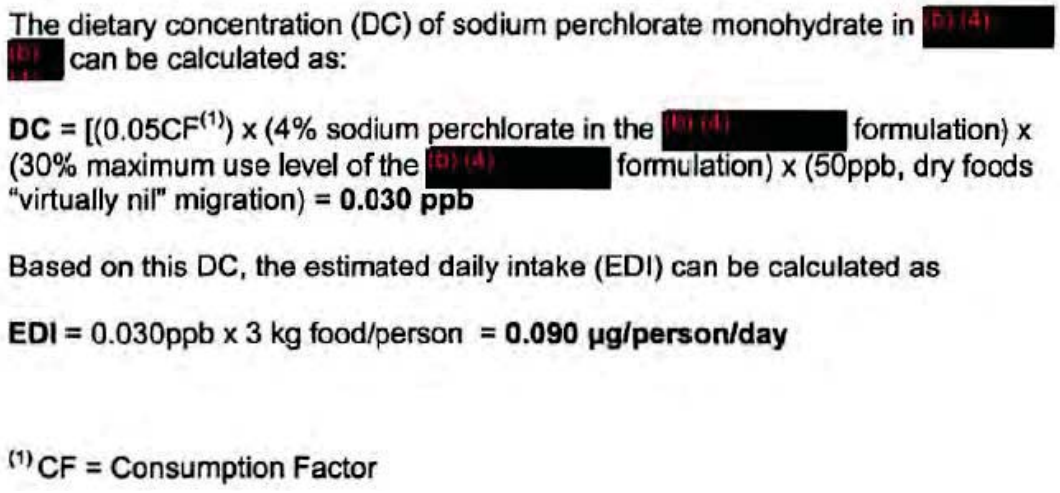
EDI = 2.5 µg perchlorate/kg food X 3 kg food/person/day
EDI = 7.5 µg perchlorate/person/day

In calculating the DC, Ciba varied from FDA's guidance without explanation. In addition to the migration and consumption factor, Ciba inserted the amount of perchlorate in the formulation (4%) and the amount of formulation in the packaging (30%) into the above equation as can be seen in Figure 2 which is an extract of the relevant section from Ciba's submission.

This mistake in the DC estimation led to improperly calculating the EDI. As a result, the calculated EDI of 0.090 µg perchlorate/person/day was 83 times smaller than the EDI of 7.5 µg perchlorate/person/day calculated according to FDA's guidance.

Had Ciba properly calculated the EDI, it would not have been eligible for the threshold of regulation exemption requested because the EDI would have been 5 times larger than the 1.5 µg perchlorate/person/day threshold established in 21 CFR § 170.39.

Figure 2: Extract from "Section 5 – Estimated Daily Intake" (page 5) of Ciba's exemption request



The dietary concentration (DC) of sodium perchlorate monohydrate in [redacted] can be calculated as:

DC = [(0.05CF[1]) x (4% sodium perchlorate in the [redacted] formulation) x (30% maximum use level of the [redacted] formulation) x (50ppb, dry foods "virtually nil" migration) = **0.030 ppb**

Based on this DC, the estimated daily intake (EDI) can be calculated as

EDI = 0.030ppb x 3 kg food/person = **0.090 µg/person/day**

[1] CF = Consumption Factor

I.C. FDA's unjustified expansion of request to apply to packaging for all dry foods

FDA posted on its website a notice of its decision to approve TOR No. 2005-006. See Figure 1 on page 5 for a reprint of FDA's webpage.

Like all TOR exemptions, any supplier or manufacturer, even Ciba's competitors, may rely on this notice and sell packaging and food products consistent with the approval. FDA's website makes this point clear in the first paragraph of Figure 1.

However, in addition to not identifying and correcting the flaws in Ciba's DC and EDI calculations, FDA's public notification of its decision went further than the scope of Ciba's request in six critical ways described below. This conclusion is drawn from our analysis of the agency's response to our FOIA request since FDA does not make publicly available additional information beyond what is posted on its website.

I.C.1. Expanded to all antistatic agents

Despite the narrow request, FDA intentionally and without justification approved the use of perchlorate in any antistatic agent not just Irgastat P18 or that type of plastic. It was not limited to the specific type of plastic used in Ciba's product.

I.C.2. Expanded to all types of dry-food packaging and not just polymers

FDA's letter to Ciba limited the approval to "use in polymers in contact with dry foods."[30] However, the notice on the agency's website does not include such a limitation. Since FDA does not make the approval letter publicly available, manufacturers and suppliers other than Ciba would be unaware of this limitation. Consequently, Ciba's competitors are implicitly authorized to use perchlorate in paper, metal coating, or glass.

I.C.3. Expanded to all dry-food including infant formula and other food for children younger than 2 years old

FDA's guidance for calculating the EDI is based on what an adult eats. For instance, it uses 3 kg of food consumed a day and uses consumption factors based on a wide variety of food products. Therefore, the guidance and Ciba's request are implicitly limited to adults consuming a diverse diet.

The guidance could grossly underestimate exposure of an infant relying on powdered formula as the sole source of nutrition – as is common for infants younger than six months of age. If the formula packaging used the perchlorate as an antistatic agent to allow the powder to flow more fully and freely from the container, then the infant would have much greater exposure to perchlorate. Also, infants and children consume more food per body weight than adults, adding to a higher exposure.[31]

I.C.4. Expanded to include bulk packaging for raw materials

FDA's consumption factors are based on packaging for consumer products. Its guidance states the factors represent "the fraction of the daily diet expected to contact specific packaging materials."[32] It goes on to state that the "values were derived using information on the types of food consumed" and by implication not the ingredients used as raw materials in food production.[33]

In an October 5, 2011 speech at a seminar organized by an industry-sponsored law firm, FDA's Michael Adams, a supervisory chemist in the food contact notifications division at the time, described the sources of information FDA uses to estimate consumption factors and discussed potential changes to its guidance. The next day, Food Chemical News summarized his speech as follows:

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[30] FDA Letter from Mitchell Cheeseman to Neal Earhart of Ciba Specialty Chemicals Corporation, Nov. 4, 2005. See Appendix 3.
[31] EPA, Children Are Not Little Adults! Accessed at http://www2.epa.gov/children/children-are-not-little-adults on July 27, 2014.
[32] FDA, Guidance for Industry: Preparation of Premarket Submissions for Food Contact Substances: Chemistry Recommendations," 2002. See Section E.1.A. http://www.fda.gov/Food/GuidanceRegulation/ucm081818.htm. FDA revised the document in 2007 but the revisions did not alter this aspect of the guidance.
[33] *Ibid*.

"Additionally, the agency has signed new contracts with data mining companies Food Essentials, Mintel Corp. and Gladson Corp. to determine consumption factors for various polymers." They mainly do packaging surveys around the world," he reported. "We can get photos of packages from all over the world. We can find out what the package is made of. Our package analysis can feed into a database. If we set it up right, we'll be able to update it regularly." Food Chemical News, October 6, 2011.

As far as we can discern, these three data mining companies are evaluating only final products sold to consumers.

However, FDA's approval of TOR No. 2005-006 referred only to "finished article" (Figure 3, Use limitations). In this context, "finished article" applies to packaging for raw materials throughout the supply chain and not solely food products sold to the consumer. This issue is significant since food manufacturers typically prefer to store and transport materials as dry powders or solids rather than as liquids to reduce costs and to allow longer storage without spoilage.

Therefore, consistent with FDA's broad public statement, whenever a dry food ingredient came in contact with the Irgastat P18, perchlorate would be likely to migrate into it. Even if FDA's assumption of 50 ppb migration levels from the packaging were correct, perchlorate could be entering any food through the manufacturing process and not just from the final packaging of dry food sold to the consumer.

As evidence that these exposures from multiple sources must be cumulatively assessed, consider the following two resources:

1. In 2004, the U.S. Patent Office issued patent US2004/0004804 A1 for "a mechanism for use in a Flexible Intermediate Bulk Container (FIBC), which enables the immediate neutralization of the electrostatic charges generated during filling, emptying or transporting of the FIBC. **FIBCs are used to carry bulk solid powders**, such as **sugar, flour, starch** and chemical substances." The patent application states that "[t]hese fibers for neutralizing the electrostatic charges preferably include permanent antistatic additives such as **IRGASTAT P18** or IRGASTAT P22 manufactured by **Ciba Geigy**® at a ratio of %6-%20 preferably." *Emphasis added.* The IRGASTAT P18 is the same product that FDA approved to contain perchlorate as a conductivity enhancer pursuant to TOR No. 2005-006 a year later.
2. In 2013, BASF, which bought Ciba in 2010, published a brochure specifically targeted for food manufacturers called "Solutions for Food Packaging".[34] It states that "**Irgastat® P18 FCA features:** • Anti-dust protection – the use of a permanent anti-static agent reduces the electrostatic charge on film surfaces, avoiding dust deposit and preserving the original appearance of the package. The product is approved and used for **bulk and industrial food and non-food contact packaging**." *Emphasis added.* We found the

[34] BASF, Solutions for Food Packaging, 2013. See http://chinaplas.basf.com/sites/default/files/brochure/Solutions%20for%20Food%20Packaging_English_2013_lo.pdf.

document at a BASF website – chinaplas.basf.com – that focused on the China plastics market.

I.C.5. Expanded to allow perchlorate in repeated use packaging

The bulk packaging described above may be reused. While FDA's guidance has special procedures to consider migration from repeated use packaging, Ciba did not rely on those sections.[35] However, FDA's approval did not contain any limitation to single use packaging.

I.C.6. Expanded to levels of up to 4% in antistatic agents

FDA's letter to Ciba limited the approval to "1.2 percent by weight in the finished article for use in contact with dry foods."[36] However, the notice on its website only limits the perchlorate levels to 4% in the finished article (Figure 1, Use limitations). As a result, food in packaging from a Ciba competitor who is unaware of this limitation could have exposures that are 3.3 times greater than Ciba's products thus further increasing the health risk for consumers.

I.D. Significant new information after FDA approved the use.

If FDA receives significant new information that raises questions about the dietary concentration or the safety of a substance that the agency has exempted from regulation, 21 CFR § 170.39(g) authorizes the agency to reevaluate the substance. If FDA tentatively concludes that the information that is available about the substance no longer supports an exemption for the use of the food-contact material from the food additive regulations, the agency should notify any persons that requested an exemption for the substance of its tentative decision. The requestors will be given an opportunity to show why the use of the substance should not be regulated under the food additive provisions of the act. If the requestors fail to adequately respond to the new evidence, the agency will notify them that further use of the substance in question for the particular use will require a food additive regulation. Because other manufacturers and suppliers may rely on the notice, FDA will notify them by means of a *Federal Register* notice of its decision to revoke an exemption issued for a specific use of a substance in a food contact article.

In our review of the scientific literature and other sources of information since the agency's approval of the exemption in 2005, we identified four types of significant new information that would warrant a reevaluation of the decision. First, additional research shows that the endpoint used in the decision was not the most appropriate or sensitive one to protect fetuses and infants from permanent brain damage. Second, it is now known that nitrates and thiocyanates are pharmacologically-related to perchlorate and, therefore, must be considered in any safety evaluation of perchlorate as an additive. Third, in 2011, FDA acknowledged that the 50 ppb

[35] FDA, Guidance for Industry: Preparation of Premarket Submissions for Food Contact Substances: Chemistry Recommendations," 2002. See Appendix II Section 4. http://www.fda.gov/Food/GuidanceRegulation/ucm081818.htm.

[36] FDA Letter from Mitchell Cheeseman to Neal Earhart of Ciba Specialty Chemicals Corporation, Nov. 4, 2005. See Appendix 3.

migration to dry-food default assumption ("virtually nil" migration) may be flawed based on research evidence from Europe. Fourth, FDA has demonstrated that there is widespread contamination of the food supply with perchlorate that must be considered.

I.D.1. Additional research identified a more sensitive and appropriate endpoint to assess perchlorate risk in pregnant women, fetuses and to infants.

Ciba's submission uses EPA's IRIS document issued a few months earlier to conclude that their estimated perchlorate migration from Irgastat P18 (using the flawed assumption of 50 ppb as discussed below) was more than two orders of magnitude lower than the IRIS reference dose of 0.7 micrograms/kg body weight/day and, therefore, did not pose a health risk. The same year, a National Research Council (NRC) report confirmed that reference dose.

In 2013, EPA's Science Advisory Board (SAB) considered the latest science regarding perchlorate. The SAB disagreed with NRC's reference dose because it does not provide sufficient protection to susceptible populations. The SAB questioned NRC's use of hypothyroidism in pregnant women as the most sensitive indicator of perchlorate health effects. Instead, it recommended that the safe level be based on "maternal hypothyroxinemia (without hypothyroidism)."[37] Hypothyroxinemia is a low level of thyroxine or T4 hormone without elevated thyroid-stimulating hormone (TSH).

SAB stated that hypothyroxinemia is a more sensitive indicator of the adverse effects on a fetus' or infant's brain development and based its recommendation on its conclusion that

> "Although adverse neurodevelopmental effects of perchlorate in infants and children have not been reported in the literature, the risk of adverse effects can be reasonably inferred from perchlorate's mode of action and the known role of thyroid hormone on human brain development." [38]

We agree with the SAB's conclusion that hypothyroxinemia is a more sensitive indicator of perchlorate health effects. Its conclusion warrants deference because it was developed through a robust and transparent process that involved public comment, public meetings and peer review. The SAB also recommended that the EPA expand the available physiologically-based pharmacokinetic/pharmacodynamics model to explicitly incorporate predictions of thyroid hormone insufficiencies and sensitive life stages to develop a maximum contaminant level goal.

Recently published research published in the Journal of Clinical Endocrinology and Metabolism reinforces the strength of SAB's conclusions. The authors undertook a retrospective analysis of 487 mother-child pairs in mothers who were hypothyroid/hypothyroxinemic during pregnancy. They found that children of women with perchlorate levels in the highest 10% in the first

[37] EPA Science Advisory Board, SAB Advice on Approaches to Derive a Maximum Contaminant Level Goal for Perchlorate, 2013. See page 10
[38] *Ibid* at page 2 of the cover letter.

trimester had increased odds of being in the lowest 10% IQ at 3 years of age.[39] The greater negative impact was in verbal performance with odds ratio of 3.14 (95%CI 1.42, 6.9) and p value of 0.005. This study supports the SAB recommendation of using hypothyroxinemia as a more sensitive indicator of the adverse effects of perchlorate exposure brain development.

Regarding a no-observe-adverse-effect level (NOAEL) for this new endpoint, we have not identified one that was developed taking into consideration the most sensitive endpoint and life stages as recommended by the SAB and that we support. Two articles regarding models for a NOAEL or Reference Dose have been published, one led by FDA's National Center for Toxicological Research and the other one led by EPA's scientists; however, both are incomplete.

Using a model originally developed by AEgis Technologies Group for the Air Force, FDA published a model of perchlorate's impact on pregnant women and fetuses in the third trimester of pregnancy.[40] The model considers both maternal endpoints: hypothyroidism and hypothyroxinemia and various iodine intake levels. It calculated that a daily intake of 4.2 µg perchlorate/kg body weight was necessary to reduce free T4 serum levels to a hypothyroxinemic state in women with a low iodine intake of 75 µg/day.

Although a good attempt to tackle a difficult problem, the model has several shortcomings including only considering pre-term women and fetuses, not considering NHANES biomonitoring data and using assumptions without supporting rationale, and not considering the nitrate and thiocyanate in the pharmacologically-related substances in the diet. See Appendix 4 for a detailed description of the model's deficiencies we submitted to EPA on February 2014. FDA and EPA have been collaborating to expand the model to represent all three trimesters as well as for a formula-fed or breast-fed infant. The model has not yet been published or made available for peer review.

In 2014, EPA's scientists published their analysis of the available models using a six-step framework for PBPK model evaluation.[41] The authors did not consider the SAB recommendation of hypothyroxinemia as the most sensitive endpoint to protect the most vulnerable populations. However, they still found that the models have several limitations including 1) not considering the effect of thiocyanate and nitrate on iodide uptake inhibition and the flux of dietary iodine, and 2) being insufficiently protective of newborns. It is worth noting that the models reviewed by EPA had additional limitations including not considering first and second trimester or women with iodine deficiency.

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[39] Taylor PN, Okosieme OE, Murphy R, Hales C, Chiusano E, Maina A, Joomun M, Bestwick JP, Smyth P, Paradice E, Channon S, Braveman LE, Dayan CM, Lazarus JH, Pearce EN. Maternal perchlorate levels in women with borderline thyroid function during pregnancy and the cognitive development of their offspring; Data from the Controlled Antenatal Thyroid Study. J Clin Endocrinol Metab. 2014. Jul 24:jc20141901.

[40] Lumen A, Mattie DR, and Fisher JW, Evaluation of Perturbations in Serum Thyroid Hormones During Human Pregnancy Due to Dietary Iodide and Perchlorate Exposure Using a Biologically Based Dose-Response Model, *Toxicological Sciences,* 2013, 133(2), 320–341.

[41] McLanaham ED, White P, Flowers L, Schlosser PM. The use of PBPK models to inform human health risk assessment: Case study on perchlorate and radioiodide human life stages models. Risk Analysis 2014. 34(2):356-366

This information is significant because it raises questions about the safe level of exposure to perchlorate relied on by Ciba when the agency approved TOR No. 2005-006.

I.D.2. Since 2005, research shows that nitrates and thiocyanates are pharmacologically-related to perchlorate

When FDA approved TOR No. 2005-006, it did not consider the contribution of chemicals that were pharmacologically but not structurally-related to perchlorate such as thiocyanate and nitrates. Research since 2005 has made clear that these chemicals have a common mechanism of toxicity with perchlorate: all three disrupt the sodium/iodide symporter and interfere with the thyroid's uptake of iodine and its ability to make hormones essential to fetal and infant brain development.[42,43] This same symporter is found elsewhere in the body, most notably in the mammary gland in production of breast milk.[44]

The amount needed to disrupt the symporter mechanism likely varies for each of the three chemicals. However, the levels of the other chemicals in the body are also likely to be greater than perchlorate.

One particularly useful study on the issue was published by researchers at the Centers for Disease Control and Prevention (CDC) and their colleagues.[45] They measured levels of all three chemicals (perchlorate, thiocyanate and nitrate) in the urine of more than 200 infants younger than one year old in Philadelphia and correlated the levels with the infant's nutrition source. Table 1 summarizes the findings.

Table 1. Comparison of levels of three contaminants in urine based on the nutrition source for infants younger than one year old.

Nutrition source for infant	Perchlorate	Nitrate	Thiocyanate
Breast milk (n = 92)	4.97 ppb	18,350 ppb	189 ppb
Cow milk-based formula (n = 51)	2.89 ppb	29,330 ppb	151 ppb
Soy-based formula (n = 63)	1.07 ppb	32,070 ppb	70 ppb
Adapted from Table 1 of Valentin-Blasini, 2011.			

The information is significant because the 21 U.S.C. § 348(c)(5)(B) and 21 CFR § 170.2(i) requires FDA to consider "the cumulative effect of such additive in the diet of man or animals, taking into account any chemically or pharmacologically related substance or substances in such diet."

[42] Steinmaus C, Miller MD, Cushing L, Blount BC, Smith AH, Combined effects of perchlorate, thiocyanate, and iodine on thyroid function in the National Health and Nutrition Examination Survey 2007-08, Environ Res. 2013 May;123:17-24. doi: 10.1016/j.envres.2013.01.005.
[43] EPA SAB 2013.
[44] Dasgupta PK, Kirk AB, Dyke JV, Ohira S, Intake of Iodine and Perchlorate and Excretion in Human Milk, *Environ. Sci. Technol.* 2008**,** *42,* 8115–8121.
[45] Valentin-Blasini L, Blount BC, Otero-Santos S, Cao Y, Bernbaum JC, and Rogan WJ, Perchlorate exposure and dose estimates in infants, Environ. Sci. Technol. 2011, 45, 4127–4132, dx.doi.org/10.1021/es103160j.

Another recent study[46] evaluated the potential associations between urinary perchlorate, nitrate and thiocyanate and serum free T4 (the hormone associated with hypothyroxinemia) in individuals with low urinary iodine levels in two NHANES cycles: 2001-2002 and 2007-2008. Low iodine levels were defined as those less than 100 µg/L. The authors found that in a meta-analysis, urinary perchlorate, nitrate, and thiocyanate were significant predictors of serum free T4 in non-pregnant women. They concluded that "risk assessment for perchlorate exposure should consider co-exposure to nitrate and thiocyanate."

Given the widespread use of these chemicals, particularly nitrates,[47] in food or food packaging, this new information must be taken into account when evaluating their cumulative effect on the thyroid in pregnant women and children. This, together with new epidemiological data that children exposed to perchlorate during the first trimester of gestation have impaired neurodevelopment, constitute new scientific evidence that should lead FDA to reconsider TOR No. 2005-006.

I.D.3. In 2011, FDA acknowledged that 50 ppb migration assumption may be flawed

Ciba based its request on FDA's *Guidance for Industry – Preparation of Food Contact Notifications and Food Additive Petitions for Food Contact Substances* issued in 2002.[48] For dry food with surfaces containing no free fat or oil, the guidance states that:

> "Dry foods with the surface containing no free fat or oil typically exhibit little to no migration, although some studies have shown migration of certain adjuvants into dry foods (*e.g.*, volatile or low molecular weight adjuvants in contact with porous or powdered foods). If the FCS is intended for use *only* with dry foods with surface containing no free fat or oil, **a migration of 50 ppb may be assumed**. This migration level can then be multiplied by the appropriate food-type distribution factor and consumption factor to obtain an estimated dietary concentration. If the intended use for the FCS includes other food types (*e.g.,* acidic, aqueous, or fatty foods), in addition to dry foods with surface containing no free fat or oil, then the migration studies conducted for those food types will subsume any migration for a dry food with surface containing no free fat or oil. If you desire to conduct migration studies for dry foods containing no free fat or oil, consult with FDA for recommended migration protocols."[49] ***Emphasis added.***

FDA has acknowledged that the long-standing 50 ppb assumption needs to be reconsidered based on European Union studies showing substantial migration of chemicals into dry food. In

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[46] Suh M, Abraham L, Hixon JG, Proctor DM. The effects of perchlorate, nitrate, and thiocyanate on free thyroxine for potentially sensitive subpopulations of the 2001-2002 and 2007-2008 National Health and Nutrition Examination Surveys. J Expo Sci Environ Epidemiol. 2013. Published ahead of print on Oct 23. Doi: 10.1038/jes.2013.67

[47] Nitrates are allowed by 21 C.F.R. §§ 172.160, 172.170, 172.175, 173.310, 175.105, 176.180, 176.320, 181.33, 181.34.

[48] FDA, Guidance for Industry: Preparation of Premarket Submissions for Food Contact Substances: Chemistry Recommendations," 2002. See Appendix II Section 13. http://www.fda.gov/Food/GuidanceRegulation/ucm081818.htm. It was revised in 2007 but the changes do not affect the recommendations relied upon by Ciba.

[49] *Ibid.*

an October 5, 2011 speech at a seminar organized by an industry-sponsored law firm, FDA's Michael Adams, a supervisory chemist in the food contact notifications division at the time, described these concerns. The next day, Food Chemical News summarized his speech as follows:

> "Much of the data used in FDA [food contact] recommendations is showing its age," Adams said. "New analytical techniques, new products and new markets must be accommodated."
>
> "Maybe we need to look at the science behind our assumptions," Adams said, acknowledging that many of the agency's recommendations, such as chemical residue levels "of no consequence," rely on data from the 1970s and 1980s. "How do we handle these numbers?" he asked.
>
> Adams noted that FDA doesn't require migration tests for packaging adhesives. Instead, the agency uses a default assumption of 50 parts per billion that he said apparently "came out of the ether. For some adhesives, 50 ppb might be okay, but with 'hot melts' and rubber adhesives, migration may be very high."
>
> Adams noted that FDA's standing assumption has been that there is no migration of polymers from packaging into dry food. Exposure is based on a default dietary concentration of 50 parts per billion. However, evidence from EU lab studies shows substantial migration into dry food, more than 50 ppb in some cases."
>
> "We're contemplating a change to require migration studies for dry foods," he said. "We'll put out some guidance when we put it all together."
>
> Noting that FDA has recently received some grants for its research, Adams concluded, "Hopefully, we'll be able to bring our science into the 21st century."[50]

We believe the 50 ppb migration assumption is particularly flawed for a chemical like perchlorate whose function in the package is to chemically-interact with the dry food by neutralizing the static charge. Unlike others, packaging made with perchlorate-laden Irgastat P18 is not intended to simply be an inert barrier.

To our knowledge, FDA has not updated its guidance despite these statements.

I.D.4. Information on widespread contamination

As noted earlier, Ciba's submission did not consider the possibility that perchlorate was already widely present in the food and drinking water supply despite FDA's public steps to investigate the issue.

In 2008, FDA published the results of its investigation into perchlorate contamination of the food supply.[51] It found that 625 of the 1065 (59%) samples it tested had detectable levels of

[50] Food Chemical News, October 6, 2011.

perchlorate and 211 of the 285 (74%) food types had at least one sample containing measurable levels of perchlorate. Children between six months and 6 years old had the greatest average exposures ranging from 0.25 to 0.39 micrograms per kilograms of body weight per day (µg/kg-bw/day). Compared to the 2005 Reference Dose (RfD) used by Ciba of 0.7 µg/kg-bw/day based on the less sensitive endpoint of hypothyroidism, the average young child would be exposed to about half of the acceptable daily intake.

While in its 2008 publication of perchlorate contamination FDA did not estimate the 90th percentile of exposure, typically, the 90th percentile is twice the mean. FDA's guidance for estimating the EDI recommends using the more protective 90th percentile value, not just the average. If the 90th percentile was used, some children may already be exposed above the 2005 RfD (which may not be sufficiently protective of fetuses and infants during their critical stages of brain development).

If the more sensitive endpoint of hypothyroxinemia were considered as EPA's SAB now recommends, many more children would be at risk of permanent harm to their brain from even transient exposure to perchlorate.

Samples of infant milk formula collected from October 2004 to July 2005, before FDA made a decision on Ciba's application had levels as high as 3.6 µg perchlorate/kg infant formula with all regions having levels in milk-based formula greater than 1.2 µg/kg.[52]

Because the FDA perchlorate dietary contamination results are from samples taken from October 2004 to July 2006, they most likely do not reflect the contribution from Ciba's product since FDA approved it in November 2005 because it would take time for the manufacturer of Irgastat P18 and its competitors to make significant new inroads into this market.

FDA's survey published in 2008 represents significant new information that warrants a reassessment of its approval in 2005 of TOR No. 2005-006.

I.E. Disproportionate impact on children's health

EPA, EPA's Science Advisory Board, and FDA's evaluations of perchlorate in recent years make clear that infants are likely to be disproportionately impacted by perchlorate because their brains are undergoing development in the womb and in their younger years. Therefore, FDA has an obligation under Executive Order 13045 regarding protection of children from environmental health risks and safety risk[53] to ensure its policies, programs, activities and standards specifically address these risks. The order expressly applies to food and drink.

[51] Murray, Egan, Kim, Beru, and Bolger, US Food and Drug Administration's Total Diet Study: Dietary intake of perchlorate and nitrate, *Journal of Exposure Science and Environmental Epidemiology* (2008) 18, 571–580.
[52] *Ibid*.
[53] See http://yosemite.epa.gov/ochp/ochpweb.nsf/content/whatwe_executiv.htm.

Because perchlorate is associated with potentially irreversible harm to pre-natal and post-natal brain development, we believe that FDA should use additional safety factors designed to protect children beyond the default of 100-fold recommended by the agency at 21 CFR § 170.22.

PART II: Request to Prohibit Use of Perchlorate as Conductivity Enhancer

We understand that FDA would publish a *Federal Register* notice announcing its revocation of TOR No. 2005-006 should it accept Part I of this petition. However, in light of the magnitude of the errors and the significance of the potential risk to pre-natal and post-natal brain development, we believe that notice is insufficient to alert industry to the change. Many companies have relied on the nine-year old decision and may miss the notice. Therefore, we request that FDA promulgate a new 21 CFR § 189.301 prohibiting the use of perchlorate as a conductivity enhancer in the manufacture of antistatic agents to be applied to food contact articles. We propose language for that new section in Appendix 2.

PART III: Request to Remove Perchlorate as Additive to Sealing Gaskets

Existing 21 CFR § 177.1210 allows more than 75 chemicals to be added to sealing gaskets for food containers. Potassium perchlorate is one of them with gaskets allowed to contain up to 1% potassium perchlorate (expressed as percentage by weight of closure-sealing gasket composition). FDA issued this rule on July 20, 1962 in response to a food additive petition filed by Anchor Hocking Glass, W.R. Grace and Company and Chemical Products Corporation. Its decision was effective on July 26, 1962 when it was published in the *Federal Register.*[54]

While potassium perchlorate and sodium perchlorate monohydrate are different chemicals, they are both salts of perchlorate, serve a similar function, and pose similar health risks. They are chemically-related because in solution the sodium or potassium would disassociate from the perchlorate which would be absorbed and circulate in the body as such. Pursuant to U.S.C. § 348(c)(5), and pharmacologically related because they affect the same sodium iodine symporter in the thyroid gland. Therefore, FDA must consider potassium perchlorate when evaluating perchlorate exposures.

We do not know how common perchlorate is used in these gaskets and what the cumulative exposure is from their use. Presumably the 1962 food additive petition contained an estimate because the agency could not have approved it without considering "the probable consumption of the additive and of any substances formed in or on food because of the use of the additive" as required by 21 U.S.C. § 348(c)(A). Since the agency has that information in its possession, there is no need for us to submit a Freedom of Information Act request and submit it back to the agency once we get it.

[54] 27 *Federal Register* 7092 (July 26, 1962).

Whatever exposure estimate FDA used to approve it in 1962, we believe the use is unnecessary in light of the existing perchlorate exposures and the significance of the potential risk to pre-natal and post-natal brain development. Therefore, we request that FDA delete the potassium perchlorate listing in Table 1 of 21 CFR § 177.1210.

Conclusion

Based on all the new evidence we just introduced, we ask that FDA:

1. Revoke its 2005 approval of "threshold of regulation" (TOR) No. 2005-006 allowing as much as 1.2% sodium perchlorate monohydrate in dry food packaging;[55]
2. Promulgate a new 21 CFR § 189.301 prohibiting the use of perchlorate as a conductivity enhancer in the manufacture of antistatic agents to be used in food contact articles; and
3. Remove potassium perchlorate as an allowed additive in sealing gaskets for food containers in existing 21 CFR § 177.1210.

See Appendix 1 for additional details on the petition and Appendix 2 for the specific changes we seek in the regulation. Appendix 3 provides the agency's response to NRDC's FOIA request.

Please note that this letter and all appendices and references constitute our complete petition. Please note that this is NOT a citizens petition. We have enclosed three copies per 21 CFR § 171.1.

If you have questions or comments, please contact Erik D. Olson at eolson@nrdc.org or 202-289-2415.

Sincerely,

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[55] See http://www.accessdata.fda.gov/scripts/fdcc/index.cfm?set=TOR&id=2005-006.

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Appendices

1. Responses to Elements Required by 21 CFR § 171.1
2. Requested New 21 CFR § 189.301
3. FDA Response to NRDC FOIA Request No. 2014-1324, April 7, 2014
4. NRDC Comments to EPA regarding FDA model for perchlorate

Appendix 1
Responses to Elements Required by 21 CFR § 171.1

Per 21 CFR § 171.1, we provide responses to the requested elements of a food additive petition with one element per page.

Name and Pertinent Information Concerning Food Additive
The identity of the food additive is as follows:

Name	Chemical Formula	Formula Weight	CAS No.
Perchlorate	ClO_4^-	99.451	14797-73-0
Sodium Perchlorate	$NaClO_4^-$	122.44	7601-89-0
Sodium Perchlorate Monohydrate	$NaClO_4 \cdot H_2O$	140.46	7791-07-3
Potassium Perchlorate	$KClO_4^-$	138.55	7778-74-7
Ammonium Perchlorate	$NH_4ClO_4^-$	117.49	7790-98-9
Perchloric Acid	$HClO_4^-$	100.46	7601-90-3

Directions, Recommendations, and Suggestions Regarding Proposed Use

We are asking FDA to prohibit the use of any form of perchlorate to enhance the conductivity of any antistatic agent in contact with food and to remove potassium perchlorate as an allowed additive to sealing gaskets for food containers. Since there is no use being proposed, we do not have any directions, recommendations or suggestions regarding proposed uses.

Data establishing that food additive will have intended physical or other technical effect. We are asking FDA to prohibit the use of any form of perchlorate to enhance the conductivity of any antistatic agent in contact with food and to remove potassium perchlorate as an allowed additive to sealing gaskets for food containers. As a result, there should be no intended physical or technical effect from the absence of perchlorate as a food additive.

Description of practicable methods to determine the amount of the food additive in the food
We are asking FDA to prohibit the addition of any form of perchlorate to enhance the conductivity of any antistatic agent in contact with food and to remove potassium perchlorate as an allowed additive to sealing gaskets for food containers. As a result, there should be no detectable amount of the food additive in the food.

Full reports of investigations made with respect to the safety of the food additive
Our cover letter identified the key investigations. Specifically, we reference 11 recent comprehensive evaluations of perchlorate:

1. EPA Science Advisory Board, SAB advice on approaches to derive a maximum contaminant level goal for perchlorate, 2013, EPA-SAB-13-004. See http://yosemite.epa.gov/sab/sabproduct.nsf/0/86E44EE7F27EEC1A85257B7B0060F364/$File/EPA-SAB-13-004-unsigned2.pdf.
2. EPA, Life Stage Considerations and Interpretation of Recent Epidemiological Evidence to Develop a Maximum Contaminant Level Goal for Perchlorate, 2012. See http://yosemite.epa.gov/sab/SABPRODUCT.NSF/PeopleSearch/D3BB75D4297CA4698525794300522ACE/$File/Final+Perchlorate+White+Paper+05.29.12.pdf.
3. Murray, Egan, Kim, Beru, and Bolger, US Food and Drug Administration's Total Diet Study: Dietary intake of perchlorate and nitrate, *Journal of Exposure Science and Environmental Epidemiology* (2008) 18, 571–580.
4. Caldwell KL, Pan Y, Mortensen ME, Makhmdov A, Merrill L, and Moye J, Iodine status in pregnant women in the United States: National Children's Study and National Health and Nutrition Examination Survey, *Thyroid,* 2013, doi: 10.1089/thy.2013.0012.
5. World Health Organization, Assessment of iodine deficiency disorders and monitoring their elimination: a guide for programme managers, 2008.
6. Lumen A, Mattie DR, and Fisher JW, Evaluation of Perturbations in Serum Thyroid Hormones During Human Pregnancy Due to Dietary Iodide and Perchlorate Exposure Using a Biologically Based Dose-Response Model, *Toxicological Sciences,* 2013, 133(2), 320–341.
7. Steinmaus C, Miller MD, Cushing L, Blount BC, Smith AH, Combined effects of perchlorate, thiocyanate, and iodine on thyroid function in the National Health and Nutrition Examination Survey 2007-08, Environ Res. 2013 May;123:17-24. doi: 10.1016/j.envres.2013.01.005.
8. Dasgupta PK, Kirk AB, Dyke JV, Ohira S, Intake of Iodine and Perchlorate and Excretion in Human Milk, *Environ. Sci. Technol.* 2008**,** *42,* 8115–8121.
9. Valentin-Blasini L, Blount BC, Otero-Santos S, Cao Y, Bernbaum JC, and Rogan WJ, Perchlorate exposure and dose estimates in infants, Environ. Sci. Technol. 2011, 45, 4127–4132, dx.doi.org/10.1021/es103160j.
10. McLanahan, White, Flowers, and Schlosser, The Use of PBPK Models to Inform Human Health Risk Assessment: Case Study on Perchlorate and Radioiodide Human Lifestage Models, *Risk Analysis,* 0272-4332/13/0100-0001, 2013.
11. Aycock, Heinemann, Lanier-Christensen, and Larr, Dietary Risk Assessment of Perchlorate, Case Studies in Risk Assessment and Environmental Policy, Columbia University Mailman School of Public Health, 2014

The following evaluates five key studies published since EPA's SAB that are relevant to ingestion of perchlorate.

Study #1: Maternal perchlorate levels in women with borderline thyroid function during pregnancy and the cognitive development of their offspring; Data from the Controlled Antenatal Thyroid Study. Taylor PN , Okosieme OE, Murphy R, Hales C, Chiusano E, Maina A, Joomun M, Bestwick JP, Smyth P, Paradice R, Channon S, Braverman LE, Dayan CM, Lazarus JH, Pearce EN., J Clin Endocrinol Metab. 2014 Jul 24:jc20141901. [Epub ahead of print]

Abstract

Objective: Thyroid dysfunction is associated with impaired cognitive development. Perchlorate decreases thyroidal iodine uptake, potentially reducing thyroid hormone production. It is unclear whether perchlorate exposure in early life affects neurodevelopment.

Design: Historical cohort analysis. Patients: During 2002-2006, 21,846 women at gestational age <16 weeks recruited from antenatal clinics in Cardiff, UK and Turin, Italy were enrolled in the Controlled Antenatal Thyroid Screening Study (CATS). We undertook a retrospective analysis of 487 mother-child pairs in mothers who were hypothyroid/hypothyroxinemic during pregnancy and analyzed whether first trimester maternal perchlorate levels in the highest 10% of the study population were associated with increased odds of offspring IQ being in the lowest 10% at age 3 years.

Main Outcome Measures: Maternal urinary perchlorate, offspring IQ. Results: Urine perchlorate was detectable in all women (median 2.58μg/liter); iodine levels were low (median 72μg/liter). Maternal perchlorate levels in the highest 10% of the population increased the odds of offspring IQ being in the lowest 10% OR=3.14 (95%CI 1.38, 7.13) p=0.006 with a greater negative impact observed on verbal OR=3.14 (95%CI 1.42, 6.90) p=0.005 than performance IQ. Maternal levothyroxine therapy did not reduce the negative impact of perchlorate on offspring IQ.

Conclusions: This is the first study using individual-level patient data to study maternal perchlorate exposure and offspring neurodevelopment and suggests that high-end maternal perchlorate levels in hypothyroid/hypothyroxinemic pregnant women have an adverse effect on offspring cognitive development, not affected by maternal levothyroxine therapy. These results require replication in additional studies, including in the euthyroid population.

Petitioners' analysis: The purpose of this study was to assess whether perchlorate exposure in early life affects neurodevelopment. A group of 487 mother-child pairs were analyzed where the mothers were hypothyroid/hypothyroxinemic during the first trimester of pregnancy. Levels of perchlorate in maternal urine were measured; IQ tests were performed in children at age 3 years. The study showed that all women had measurable levels of perchlorate in urine. However, children of women with perchlorate levels in the highest 10% in the first trimester had statistically significant increased odds of being in the lowest 10% IQ. The greater negative impact was in verbal performance. It is clear from the data that perchlorate exposure in pregnant women with low thyroid hormone is associated with impaired neurodevelopment in their children.

Study #2: The effects of perchlorate, nitrate, and thiocyanate on free thyroxine for potentially sensitive subpopulations of the 2001-2002 and 2007-2008 National Health and Nutrition Examination Surveys. Suh M , Abraham L, Hixon JG, Proctor DM., J Expo Sci Environ Epidemiol. 2013 Oct 23. doi: 10.1038/jes.2013.67. [Epub ahead of print]

Abstract
Among women with urinary iodine concentration <100 μg/l in the 2001-2002 National Health and Nutrition Examination Survey (NHANES), urinary perchlorate was associated with significant changes in thyroid stimulating hormone and total thyroxine (T4). Although perchlorate, nitrate, and thiocyanate all potentially act to inhibit iodide uptake, free T4 was not found to be associated with exposure to these chemicals in the same data. Fetuses of pregnant mothers with iodine deficiency are thought to be a sensitive subpopulation for perchlorate exposure, but the potential associations between free T4 and exposure to these chemicals among pregnant mothers in NHANES 2001-2002 and 2007-2008 have not been specifically evaluated to date. This study investigates the potential associations between urinary perchlorate, nitrate, and thiocyanate and serum free T4 in individuals with low urinary iodine levels and pregnant women. Multivariate regression models of free T4 were conducted and included urinary perchlorate, nitrate, thiocyanate, and covariates known to have an impact on the thyroid (anti-thyroid peroxidase (TPO) antibodies, age, race/ethnicity, body mass index, and hours of fasting). Meta-analyses were also conducted on non-pregnant and on pregnant women from the two survey cycles. Urinary nitrate was associated with serum free T4 in non-pregnant women of NHANES 2001-2002 who had urinary iodine ≥100 μg/l. In the meta-analysis, urinary perchlorate, nitrate, and thiocyanate were significant predictors of serum free T4 in non-pregnant women. No association was found in men and pregnant women. TPO antibodies were significant predictors of free T4 among non-pregnant women only when the models included urinary perchlorate, nitrate, or thiocyanate. Risk assessment for perchlorate exposure should consider co-exposure to nitrate and thiocyanate.

Petitioners' analysis: The purpose of this study was to investigate potential associations between urinary perchlorate, nitrate and thiocyanate and serum free T4 (thyroxine) in individuals with low urinary levels of iodine and pregnant women. The study used biomonitoring data from two cycles of NHANES. In a meta-analysis, all three chemicals were significant predictors of serum free T4 in non-pregnant women; the lack of significant association in pregnant women is likely due to a smaller sample size. This study is important because it highlights the need to perform cumulative risk assessment for pharmacologically-related chemicals.

Study #3: Combined effects of perchlorate, thiocyanate, and iodine on thyroid function in the National Health and Nutrition Examination Survey 2007-08. Steinmaus C , Miller MD, Cushing L, Blount BC, Smith AH., Environ Res. 2013 May;123:17-24. doi: 10.1016/j.envres.2013.01.005. Epub 2013 Mar 7.

Abstract
Perchlorate, thiocyanate, and low iodine intake can all decrease iodide intake into the thyroid gland. This can reduce thyroid hormone production since iodide is a key component of thyroid hormone. Previous research has suggested that each of these factors alone may decrease thyroid hormone levels, but effect sizes are small. We hypothesized that people who have all three factors at the same time have substantially lower thyroid hormone levels than people who do not, and the effect of this combined exposure is substantially larger than the effects seen in analyses focused on only one factor at a time. Using data from the 2007-2008 National Health and Nutrition Examination Survey, subjects were categorized into exposure groups based on their urinary perchlorate, iodine, and thiocyanate concentrations, and mean serum thyroxine concentrations were compared between groups. Subjects with high perchlorate (n=1939) had thyroxine concentrations that were 5.0% lower (mean difference=0.40 μg/dl, 95% confidence interval=0.14-0.65) than subjects with low perchlorate (n=2084). The individual effects of iodine and thiocyanate were even smaller. Subjects with high perchlorate, high thiocyanate, and low iodine combined (n=62) had thyroxine concentrations 12.9% lower (mean difference=1.07 μg/dl, 95% confidence interval=0.55-1.59) than subjects with low perchlorate, low thiocyanate, and adequate iodine (n=376). Potential confounders had little impact on results. Overall, these results suggest that concomitant exposure to perchlorate, thiocyanate, and low iodine markedly reduces thyroxine production. This highlights the potential importance of examining the combined effects of multiple agents when evaluating the toxicity of thyroid-disrupting agents.

Petitioners' analysis: This study looked at whether people who have perchlorate, thiocyanate and low iodide levels in their urine at the same time will have substantially lower thyroid hormone levels compared to those who don't, and their combined effect is larger than the effect of an individual factor alone. The authors used NHANES biomonitoring data. Individuals with high perchlorate, high thiocyanate and low iodine combined had 13% reduction in thyroid hormone compared to those with low perchlorate, low thiocyanate and adequate iodine. The individual effect of perchlorate was 5% and greater than both thicyanate and iodine. This study clearly shows that the potential adverse effect is greater when all the factors associated with thyroid hormone production are combined than when assessed individually.

Study #4: The Use of PBPK Models to Inform Human Health Risk Assessment: Case Study on Perchlorate and Radioiodide Human Lifestage Models. Eva D. McLanahan, Paul White, Lynn Flowers, and Paul M. Schlosser, *Risk Analysis, Vol. 34, No. 2, 2014* DOI: 10.1111/risa.12101

Abstract

Physiologically-based pharmacokinetic (PBPK) models are often submitted to or selected by agencies, such as the U.S. Environmental Protection Agency (U.S. EPA) and Agency for Toxic Substances and Disease Registry, for consideration for application in human health risk assessment (HHRA). Recently, U.S. EPA evaluated the human PBPK models for perchlorate and radioiodide for their ability to estimate the relative sensitivity of perchlorate inhibition on thyroidal radioiodide uptake for various population groups and lifestages. The most well-defined mode of action of the environmental contaminant, perchlorate, is competitive inhibition of thyroidal iodide uptake by the sodium-iodide symporter (NIS). In this analysis, a six-step framework for PBPK model evaluation was followed, and with a few modifications, the models were determined to be suitable for use in HHRA to evaluate relative sensitivity among human lifestages. Relative sensitivity to perchlorate was determined by comparing the PBPK model predicted percent inhibition of thyroidal radioactive iodide uptake (RAIU) by perchlorate for different lifestages. A limited sensitivity analysis indicated that model parameters describing urinary excretion of perchlorate and iodide were particularly important in prediction of RAIU inhibition; therefore, a range of biologically plausible values available in the peer-reviewed literature was evaluated. Using the updated PBPK models, the greatest sensitivity to RAIU inhibition was predicted to be the near-term fetus (gestation week 40) compared to the average adult and other lifestages; however, when exposure factors were taken into account, newborns were found to be populations that need further evaluation and consideration in a risk assessment for perchlorate.

Petitioners' analysis: In this study, the authors applied a six-step framework for PBPK model evaluation to inform human health risk assessment on perchlorate exposures using the uptake of radionuclear iodine as an endpoint. The authors concluded that the two published models were suitable for use in human health risk assessment. Although the greatest sensitivity to uptake inhibition was found in the near-term fetus, newborns were found to be further evaluated in a risk assessment for perchlorate.

Study #5: Evaluation of Perturbations in Serum Thyroid Hormones During Human Pregnancy Due to Dietary Iodide and Perchlorate Exposure Using a Biologically Based Dose-Response Model, Annie Lumen, David R. Mattie, and Jeffrey W. Fisher, Toxicological Sciences 133(2), 320‑341 2013, doi:10.1093/toxsci/kft078

A biologically based dose-response model (BBDR) for the hypothalamic pituitary thyroid (HPT) axis was developed in the near-term pregnant mother and fetus. This model was calibrated to predict serum levels of iodide, total thyroxine (T4), free thyroxine (fT4), and total triiodothyronine (T3) in the mother and fetus for a range of dietary iodide intake. The model was extended to describe perchlorate, an environmental and food contaminant, that competes with the sodium iodide symporter protein for thyroidal uptake of iodide. Using this mode-of-action framework, simulations were performed to

determine the daily ingestion rates of perchlorate that would be associated with hypothyroxinemia or onset of hypothyroidism for varying iodide intake. Model simulations suggested that a maternal iodide intake of 75 to 250 µg/day and an environmentally relevant exposure of perchlorate (~0.1 µg/ kg/day) did not result in hypothyroxinemia or hypothyroidism. For a daily iodide-sufficient intake of 200 µg/day, the dose of perchlorate required to reduce maternal fT4 levels to a hypothyroxinemic state was estimated at 32.2 µg/kg/day. As iodide intake was lowered to 75 µg/day, the model simulated daily perchlorate dose required to cause hypothyroxinemia was reduced by eightfold. Similarly, the perchlorate intake rates associated with the onset of subclinical hypothyroidism ranged from 54.8 to 21.5 µg/kg/day for daily iodide intake of 250‑75 µg/day. This BBDR-HPT axis model for pregnancy provides an example of a novel public health assessment tool that may be expanded to address other endocrine-active chemicals found in food and the environment.

Petitioners' analysis: This study describes the development of a biologically based dose-response model for the hypothalamic pituitary thyroid axis in the near-term pregnant mother and fetus. The model calculated the daily intake of perchlorate that would be associated with hypothyroxinemia or hypothyroidism (measured as maternal free T4 levels) for varying iodide intake. Simulations showed that in a low iodine intake scenario much lower levels of perchlorate were needed to cause hypothyroxinemia. Although a good step forward, this model has a number of shortcomings that are explained in detail in Appendix 4.

Proposed tolerances for the food additive
We are asking FDA to prohibit the use of any form of perchlorate to enhance the conductivity of any antistatic agent in contact with food and to remove potassium perchlorate as an allowed additive to sealing gaskets for food containers. As a result, no tolerance is needed.

Regarding a no-observe-adverse-effect level (NOAEL) for this new endpoint, we have not identified one that was developed taking into consideration the most sensitive endpoint and life stages as recommended by the SAB and that we support. Two articles regarding models for a NOAEL or Reference Dose have been published, one led by FDA's National Center for Toxicological Research and the other one led by EPA's scientists; however, both are incomplete.

Using a model originally developed by AEgis Technologies Group for the Air Force, FDA published a model of perchlorate's impact on pregnant women and fetuses in the third trimester of pregnancy.[56] The model considers both maternal endpoints: hypothyroidism and hypothyroxinemia and various iodine intake levels. It calculated that a daily intake of 4.2 µg perchlorate/kg body weight was necessary to reduce free T4 serum levels to a hypothyroxinemic state in women with a low iodine intake of 75 µg/day.

Although a good attempt to tackle a difficult problem, the model has several shortcomings including only considering pre-term women and fetuses, not considering NHANES biomonitoring data and using assumptions without supporting rationale, and not considering the nitrate and thiocyanate in the pharmacologically-related substances in the diet. See Appendix 4 for a detailed description of the model's deficiencies we submitted to EPA on February 2014. FDA and EPA have been collaborating to expand the model to represent all three trimesters as well as for a formula-fed or breast-fed infant. The model has not yet been published or made available for peer review.

In 2014, EPA's scientists published their analysis of the available models using a six-step framework for PBPK model evaluation.[57] The authors did not consider the SAB recommendation of hypothyroxinemia as the most sensitive endpoint to protect the most vulnerable populations. However, they still found that the models have several limitations including 1) not considering the effect of thiocyanate and nitrate on iodide uptake inhibition and the flux of dietary iodine, and 2) being insufficiently protective of newborns. It is worth noting that the models reviewed by EPA had additional limitations including not considering first and second trimester or women with iodine deficiency.

[56] Lumen A, Mattie DR, and Fisher JW, Evaluation of Perturbations in Serum Thyroid Hormones During Human Pregnancy Due to Dietary Iodide and Perchlorate Exposure Using a Biologically Based Dose-Response Model, *Toxicological Sciences,* 2013, 133(2), 320–341.
[57] McLanaham ED, White P, Flowers L, Schlosser PM. The use of PBPK models to inform human health risk assessment: Case study on perchlorate and radioiodide human life stages models. Risk Analysis 2014. 34(2):356-366

Full information on each proposed change to the original regulation
See Appendix 2 for the specific changes requested to 21 CFR §189.301. Text in strikethrough font is to be deleted.

We also ask that FDA delete the potassium perchlorate listing in Table 1 of 21 CFR § 177.1210.

Environmental impact statement

This food additive petition is categorically excluded from the need to prepare an Environmental Assessment under 21 CFR 25.32(m) for actions to prohibit or otherwise restrict or reduce the use of a substance in food, food packaging, or cosmetics. The proposed action complies with the categorical exclusion criteria. No extraordinary circumstances exist which would require the submission of an Environmental Assessment or Environmental Impact Statement.

Appendix 2
Request New 21 CFR § 189.301

The Natural Resources Defense Council (NRDC) petitions the Food and Drug Administration (FDA) to adopt a new section 189.301 to 21 CFR Part 189 that would ban the addition of perchlorate in antistatic agents. The new section would read as follows:

New section 21 CFR **§**189.301 would read as follows:

> TITLE 21--FOOD AND DRUGS
> CHAPTER I--FOOD AND DRUG ADMINISTRATION, DEPARTMENT OF HEALTH AND HUMAN SERVICES
> SUBCHAPTER B--FOOD FOR HUMAN CONSUMPTION
> PART 189 -- SUBSTANCES PROHIBITED FROM USE IN HUMAN FOOD
> Subpart D--Substances Prohibited From Indirect Addition to Human Food Through Food-Contact Surfaces
>
> Sec. 189.301 Perchlorate.
> (a) Perchlorate is an ion with the molecular formula, $ClO4^-$ commonly manufactured in solid form with sodium, potassium or ammonium or in liquid form as perchloric acid. It has been used in gaskets to seal containers or as an antistatic agent in packaging for dry food. It is also produced as a contaminant from degradation of hypochlorite solutions used to make sanitizing solutions.
>
> (b) Food contact articles containing perchlorate as a food contact substance in antistatic agents are deemed to be adulterated in violation of the act.

Food and Drug Administration
College Park, MD 20740

April 7, 2014

Tom Nelter
Natural Resources Defense Council
1152 15th Street,
Suite 300
Washington, DC 20005

Re: FOI Request No. 2014-1324

Dear Mr. Nelter:

This is in response to your request of February 10, 2014, requesting records regarding Threshold of Regulation Submission No. 05-006 regarding sodium perchlorate monohydrate. Your request was forwarded to the Office of Food Additive Safety in the Center for Food Safety and Applied Nutrition.

__X__ Enclosed are the records you requested.

__X__ Certain material has been deleted from the records furnished to you because a preliminary review of the records indicated that the deleted information is not required to be publicly disclosed and that disclosure is not appropriate. FDA has taken this approach to facilitate the process of responding to you. If you dispute FDA's preliminary determination with respect to these records and would like FDA to reconsider any particular deletion, please let us know in writing at the following address: Food and Drug Administration, Division of Freedom of Information, HFI-35, 5600 Fishers Lane, Rockville, MD 20857 within 30 days from the date of this letter. If we do not receive a response in that time period, we will consider the matter closed with respect to these records. If you do request further consideration and if the agency then formally denies your request for any or all of the previously-withheld information, you will have the right to appeal that decision. Any letter of denial will explain how to make this appeal.

The following charges for this request to date may be included in a monthly invoice:

Reproduction $ 0.00 Search $0.00 Review $46.00 Other $1.00 (CD) Total $47.00

THE ABOVE TOTAL MAY NOT REFLECT THE FINAL CHARGES FOR THIS REQUEST. **PLEASE DO NOT SEND PAYMENT** UNTIL YOU RECEIVE AN INVOICE FOR THE TOTAL MONTHLY FEE.

Sincerely Yours,

Sharon R. Dodson
Program Analyst
Office of Food Additive Safety
Center for Food Safety
and Applied Nutrition

Enclosure

TOR #251

IS

Ciba Specialty Chemicals Corporation
Ciba® Expert Services
Neal J. Earhart, Ph.D.
Sr. Compliance Applications Specialist
540 White Plains Road, PO Box 2005
Tarrytown, NY 10591-9005
E-mail: neal.earhart@cibasc.com
Tel: 914-785-4518 Fax: 914-785-4147

Ciba

2005-3767

June 17, 2005

Vivian Gilliam
Office of Food Additive Safety, HFS-275
Center for Food Safety & Applied Nutrition
Food and Drug Administration
5100 Paint Branch Parkway
College Park, MD 20740

Subject: Prenotification Consultation #381

Dear Ms. Gilliam:

Ciba Specialty Chemicals Corporation is submitting the enclosed Threshold of Regulation (TOR) document for an exemption from the food additive regulations under 21 CFR 170.39 for Sodium Perchlorate Monohydrate, CASRN 7719-07-3, to be used as a "conductivity enhancer" in (b) (4) a commercially available permanent antistatic agent.

The request for exemption of regulation is based on the dietary concentration (DC) of sodium perchlorate monohydrate, at the maximum proposed use level of (b) (4)® (b) of 30% in the finished article, to be calculated as 0.030 ppb, with a resulting estimated daily intake (EDI) of 0.09µg/p/d. The dietary concentration is less than 0.5 ppb and therefore qualifies for a Threshold of Regulation submission.

This TOR is the subject of Prenotification Consultation #381.

Should you have any questions, please do not hesitate to contact the undersigned at (914) 785-4518, or e-mail at neal.earhart@cibasc.com.

(b) (6)

Neal J. Earhart, Ph.D.
Sr. Compliance Applications Specialist
Ciba® Expert Services

Anna
Mike
Akinjoke

000001

Comprehensive Summary

Comprehensive Summary

Ciba Specialty Chemicals Corporation commercially markets (b) (4) a permanent antistatic agent. (b) (4) is formulated blend of the following:

CAS Number	Component	% by weight
(b) (4)		
7791-07-3	Sodium perchlorate monohydrate	4

(b) (4)
(b) (4)
. Sodium perchlorate monohydrate is not FDA regulated.

(b) (4)

The maximum concentration of sodium perchlorate monohydrate to be used in the (b) (4) formulation would be 4% (wt.), which would correlate to 1.2% (wt) in the finished article.

Sodium Perchlorate Monohydrate is a commodity inorganic chemical produced by various manufacturers worldwide such as:

Manufacturer *	Chemical Description	Purity
ABCR	Sodium Perchlorate Monohydrate p.a.	99%
Calibrechem	Sodium Perchlorate Monohydrate	98.5%
Lancaster	Sodium Perchlorate Monohydrate 98%	98%
Loba chemie	Sodium Perchlorate Monohydrate granules	98%

Table of Contents

* Representative technical data sheets from the above manufacturers are included in Section 8 of this submission. Purity of sodium perchlorate monohydrate ranges between 98% - 99%.

The primary chemical process used in the commercial manufacturing of sodium perchlorate monohydrate involves electrochemical oxidation of lower valence chlorine-containing compounds, mainly sodium chlorate.

Ciba Specialty Chemicals will be purchasing sodium perchlorate monohydrate from a variety of manufacturers based on volume pricing.

(b) (4) is incorporated into the polymer during processing and develops a conductive network within the polymer matrix. This conductive network dissipates any acquired static charge. Sodium perchlorate monohydrate is used in the (b) (4) formulation as a "conductivity enhancer."

The proposed use of (b) (4) is identical to the FDA regulated product (b) (4) (FCN 000406), as an antistatic agent for use in polymers in contact with dry foods with surface containing no free fat or oil compliant with 21 CFR 176.170 (c), Table 1, Food type VIII, such as cereals, flour, macaroni, and sugar.

Per the FDA's Guidance for Industry - *Preparation of Food Contact Notifications and Food Additive Petitions for Food Contact Substances: Chemistry Recommendations, Final Guidance, April 2002, Appendix II, Section 13*, migration testing is not required and for non-fatty dry foods a "virtually nil" migration (50ppb) may be assumed.

Based on the maximum use level and the minimum consumption factor (CF) of 0.05 for all exposure estimates, the dietary concentration (DC) for sodium perchlorate monohydrate can be calculated as 0.030 ppb, with a resulting estimated daily intake (EDI) of 0.09μg/p/d.

Ciba Specialty Chemicals believes that sodium perchlorate monohydrate, as a component of the (b) (4) formulation to be used as an antistatic agent in polymers in contact with dry foods with surface containing no free fat or oil, would be exempt from regulation by the agency, due to the very low dietary concentration that will not be detected by an analytical technique and a negligible risk to human heath in the proposed end-use application.

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Sections 1-7

Section 1 – Chemical Composition

Sodium Perchlorate Monohydrate a commodity inorganic chemical produced by various manufacturers worldwide such as:

Manufacturer *	Chemical Description	Purity
ABCR	Sodium Perchlorate Monohydrate p.a.	99%
Calibrechem	Sodium Perchlorate Monohydrate	98.5%
Lancaster	Sodium Perchlorate Monohydrate 98%	98%
Loba chemie	Sodium Perchlorate Monohydrate granules	98%

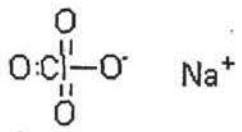
* Representative technical data sheets from the above manufacturers are included in this submission. Purity of sodium perchlorate monohydrate ranges between 98% - 99%.

See Section 8 – Attachment #1 – Representative Manufacturers' Data Sheets for Sodium Perchlorate Monohydrate

Chemical Name:
Sodium Perchlorate Monohydrate

CAS Reg. No.:
7791-07-3

Structure:



Molecular Formula::
$NaClO_4 \cdot H_2O$

Molecular Weight:
140.45 g/mol

Density:
2.02 g/ml

Melting Point:
130 °C

Section 2 – Intended Technical Effect

The Food Contact Substance (FCS) Sodium Perchlorate Monohydrate is added during the manufacture of [redacted], a commercially available permanent antistatic agent. The FCS functions as a "conductivity enhancer" in the [redacted]® [redacted] formulation.

Section 3 – Conditions of Use

Sodium Perchlorate Monohydrate will be used in (b) (4) at a maximum level of 4% by weight, which corresponds to 1.2% by weight of the finished article. (b) (4) will be used in polymers at concentrations of up to 30 % by weight of the polymer in contact with dry foods with surface containing no free fat or oil compliant with 21 CFR 176.170 (c), Table 1, Food type VIII, such as cereals, flour, macaroni, and sugar, and under temperature conditions of use E through G. The proposed use of (b) (4) is identical to the FDA regulated use for product (b) (4) (FCN 000406)

Section 4 – Basis of Request for Exemption

This threshold of regulation request is based on the fact that given the maximum use level of [redacted] and using a minimum consumption factor (CF) of 0.05 for all exposure estimates, the dietary concentration (DC) for sodium perchlorate monohydrate can be calculated as 0.030 ppb. The dietary concentration is less than 0.5 ppb and therefore qualifies for a Threshold of Regulation submission.

Section 5 – Estimated Daily Intake

Per the FDA's Guidance for Industry - *Preparation of Food Contact Notifications and Food Additive Petitions for Food Contact Substances: Chemistry Recommendations, Final Guidance, April 2002, Appendix II, Section 13*, migration testing is not required and for non-fatty dry foods a "virtually nil" migration (50ppb) may be assumed.

The dietary concentration (DC) of sodium perchlorate monohydrate in (b) (4) (b) can be calculated as:

DC = [(0.05CF[1]) x (4% sodium perchlorate in the (b) (4) formulation) x (30% maximum use level of the (b) (4) formulation) x (50ppb, dry foods "virtually nil" migration) = **0.030 ppb**

Based on this DC, the estimated daily intake (EDI) can be calculated as

EDI = 0.030ppb x 3 kg food/person = **0.090 µg/person/day**

[1] CF = Consumption Factor

Section 6 – Safety Narrative

The estimated dietary concentration (DC) of sodium perchlorate in [redacted] is 30 parts per trillion (30 nanograms per kg of food). Based on this DC, the following human dose is calculated:

30 ng/kg (ppt in food) x 3 kg food/person = **90** ng/person/day

90 ng/person/day ÷70 kg bw = 1.29 ng/kg/day
= 0.00129 µg/kg/day
= **0.00000129** mg/kg/day

EPA (IRIS) has recently published (2/18/2005) an Oral RfD for Perchlorate and perchlorate salts (including sodium perchlorate). The RfD is based on a study with human subjects.[1, 2] The RfD (lifetime safe oral exposure level) is 0.0007 mg/kg/day.

The dietary exposure for sodium perchlorate here determined for this use of Irgastat P18 is much less than the RfD:

RfD ÷DC = **0.0007** mg/kg/day ÷ **0.00000129** mg/kg/day = 542

We conclude, therefore, that the human exposure to sodium perchlorate resulting from the proposed use of [redacted] presents negligible health risks.

---

[1] Greer, M.A., Goodman, G., Pleuss, R.C., Greer, S.E. 2002. Health effect assessment for environmental perchlorate contamination: The dose response for inhibition of thyroidal radioiodide uptake in humans. Environ. Health Perspect. 110:927-937.

Greer et al. (2002) studied 21 healthy women and 16 healthy men (mean age 38 years, range 18-57 years) who were given potassium perchlorate in doses of 0.007, 0.02, 0.1 and 0.5 mg perchlorate/kg body weight per day for 14 days. The dose was administered in 400 ml of water with instructions that 100 ml be consumed four times each day. Thyroid uptake of radioiodide was measured at 8 and 24 hours after radioiodide administration: at baseline, on days 2 and 14 of perchlorate administration, and 15 days after cessation of dosing. The human subjects research ethics of the study were approved by the Oregon Health & Science University Institutional Review Board (IRB). On day 14 of administration, the mean 24-hour radioiodide uptake was 98.2% of the baseline value in the seven subjects given 0.007 mg/kg/day, a non-statistically significant decrease of 1.8% (standard error of the mean 8.3%). The day-14 24-hour radioiodide uptake value was 83.6% of the baseline value (16.4% decrease; n=10) in the subjects given 0.02 mg/kg/day, 55.3% of the baseline value (44.7% decrease; n=10) in those given 0.1 mg/kg/day, and 32.9% of the baseline value (67.1% decrease; n=10) in those given 0.5 mg/kg/day.

The effects of perchlorate in these healthy adult humans did not change over time, as indicated by very similar results for thyroid radioiodide uptake measurements on day 2 of perchlorate administration compared to day 14 in the three higher dose groups (uptake was not measured on day 2 in the lowest dose group). The 8-hour thyroid radioiodide uptake values 15 days after exposure were very similar to the baseline values, indicating rapid disappearance of inhibition on cessation of dosing. The results were similar in the women and men. The statistical no observed effect level (NOEL) for perchlorate-induced inhibition of thyroid iodide uptake was 0.007 mg/kg/day. An Uncertainty Factor of 10 was applied to the NOEL to obtain the RfD value.

[2] NRC. 2005. Health Implications of Perchlorate Ingestion. National Research Council of the National Academies. National Academies Press, Washington, D.C.

Section 7 – Environmental Assessment

A - CLAIM OF CATEGORICAL EXCLUSION

1. Cite the specific section of the CFR under which the categorical exclusion is claimed 21 CFR 25.32 (i) and (j)

Class of Action	Description
(i)	Approval of a food additive petition or GRAS affirmation petition, the granting of a request for exemption from regulation as a food additive under Sec. 170.39 of this chapter, or allowing a notification submitted under 21 U.S.C. 348(h) to become effective, when the substance is present in finished food-packaging material at not greater than 5 percent-by-weight and is expected to remain with finished food-packaging material through use by consumers or when the substance is a component of a coating of a finished food-packaging material.
(j)	Approval of a food additive petition or GRAS affirmation petition, the granting of a request for exemption from regulation as a food additive under Sec. 170.39 of this chapter, or allowing a notification submitted under 21 U.S.C. 348(h) to become effective, when the substance is to be used as a component of a food-contact surface of permanent or semipermanent equipment or of another food-contact article intended for repeated use.

2. Does your proposed food-contact use comply with the categorical exclusion criteria?

Yes

3. To the best of your knowledge are there any extraordinary circumstances that would require your submission of an EA

No

Attachment 1

Representative Manufacturers' Data Sheets for
Sodium Perchlorate Monohydrate

Manufacturers Listed in Order:

1 – ABCR

2 – Calibrechem

3 – Lancaster

4 - Loba chemie

16

deutsch english >> HOME

Search Criteria

Search Help [?] Search

Name:

Productno.:

Formular:

CAS:

Name:	SODIUM PERCHLORATE MONOHYDRATE, 99%, WHITE POWDER
Productno.:	S93-1170
Formular:	$NACLO_4H_2O$
CAS:	[7791-07-3]
Formular weight:	122,44
Density:	2,02
Melting point:	130°C
R:	9-22
S:	13-22-27
UN:	1502
EINECS:	231-511-9

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ADD 62

R.B. Chemicals & Agro Industries Pvt. Limited
A Calibre Group Company mail@calibrechem.com

Sodium Perchlorate Monohydrate

(Perchloric Acid, Sodium Salt - Hydrated)
$NaClO_4.H_2O$ **M.W. 140.46**

Product Data Sheet
SPM-02-R3
Effective 1/04/04

Appearance	:	White deliquescent crystals
Specifications	:	Sodium Perchlorate (as $NaClO_4.H_2O$): 98.5% (Minimum) (as $NaClO_4$) : 86.0% (Minimum) Chlorides (as NaCl) : 0.1% (Maximum) Chlorates (as $NaClO_3$) : 0.5% (Maximum) Sulphates (as SO_4^{--}) : 0.05% (Maximum) Free Moisture (as H_20) : 1.5% (Maximum)
Physical Properties	:	Melting Point : 482 °C Boiling Point : - Decomposition : Starts losing water of hydration above 130 °C; decomposition starts at 482 °C. Solubility : Very soluble in water Particle Density : 2.02 grams/cc Bulk Density : About 1.3 grams/cc
Packing - Domestic	:	25 Kg net laminated HDPE woven bags with separate inner LDPE bag.
- Exports	:	25 Kg nett certified UN performance standard HDPE bags with LDPE inner bags.
Storage & Handling	:	Store in cool dry place away from direct sunlight and heat. Keep away from organic and readily oxidizable materials. In case of spillage, flush with *plenty* of water.
Uses	:	In manufacture of PVC stabilizers and explosives. In chemical synthesis. In perchloric acid and other perchlorates production.
Shipping Information	:	CAS No. : 7791-07-3 EINECS Nr. : 231 – 511 - 9 UN No. : 1502 Packing Group: II IMDG Code: Proper Shipping Name : Sodium Perchlorate Hydrate Hazard Class : 5.1 Oxidizing Substance EmS No. : 5.1-06 MFAG Table No.: 745 Label : Oxidizer 5.1 Subsidiary Risk Label : None

Committed to Better Chemistry

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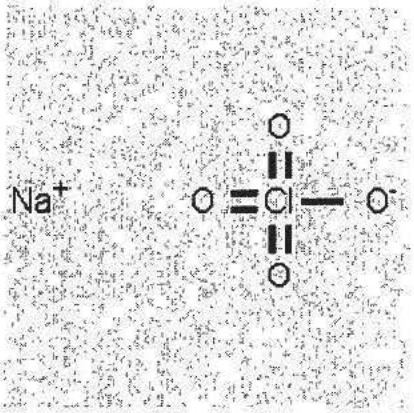
Product Details

Catalogue Number:	**14315**
Name:	**Sodium perchlorate monohydrate**
Structure: (To enlarge the structure double-click the structure and then resize the window)	
Pack sizes:	100g, 500g
Grade:	98
Melting Point:	
Molecular Formula:	ClNaO4.H2O
Molecular Weight:	140.46
CAS number:	7791-07-3
EINECS number:	231-511-9
UN number:	1502
Air Freight Status:	P
Hazard Storage:	OXIDISING HARMFUL HYGROSCOPIC
Safety Phrases:	S:13-22-27
Risk Phrases:	R:9-22
RTECS:	SC9850000
TSCA:	Y
Merck:	13,8726

5954
SODIUM NITRITE GR 500 gm
$NaNO_2$ M.W. 69.00 10 x 500 gm
Minimum assay 98.0% 50 kg
Maximum Limits of Impurities:
Insoluble matter 0.003%
Chloride (Cl) 0.005%
Sulphate (SO_4) 0.005%
Arsenic (As) 0.00004%
Calcium (Ca) 0.002%
Copper (Cu) 0.0005%
Iron (Fe) 0.001%
Lead (Pb) 0.0005%
Magnesium (Mg) 0.002%
Potassium (K) 0.001%

SODIUM NITROSO PENTACYANO FERRATE (III)
(See Sodium Nitro prusside LR/GR)

5956
SODIUM NITROPRUSSIDE 100 gm
EXTRA PURE 10 x 100 gm
$Na_2[Fe(CN)_5NO].2H_2O$ M.W. 297.95 500 gm
Minimum assay 98% 10 x 500 gm
Maximum Limits of Impurities:
Ferricyanide 0.02%
Ferrocyanide 0.1%
Sulphate (SO_4) 0.05%

5958
SODIUM NITROPRUSSIDE GR 100 gm
(Reagent for the detection of many organic 10 x 100 gm
compounds such as acetone aldehyde also 500 gm
of alkali sulphides etc.) 10 x 500 gm
$Na[Fe(CN)_5NO].2H_2O$ M.W. 297.95
Minimum assay 99%
Maximum Limits of Impurities:
Insoluble matter 0.01%
Chloride (Cl) 0.01%
Ferricyanide ($Fe(CN_6)$] 0.01%
Ferrocyanide ($Fe(CN_6)$] 0.02%
Sulphate (SO_4) 0.01%

5958 - D
SODIUM OLEATE pure 1 Kg
(Oleic acid sodium salt)
$C_{18}H_{33}NaO_2$ M.W. 304.50
Minimum Assay (GC) >99.0%
Maximum Limits of Impurities
Assay of fatty acid >82%
Free alkali (as NaOH) <0.5%
Heavy metals (as Pb) <0.005%
Chloride (Cl) <0.2%

5959
tri-SODIUM ORTHOPHOSPHATE 500 gm
(DODECAHYDRATE)EXTRA PURE 50 kg
$Na_3PO_4.12H_2O$ M.W. 380.12
Minimum assay (acidimetric) 98%
Chloride (Cl) 0.1%
Sulphate (SO_4) 0.05%
Sodium hydroxide (Na) 2.0%
Iron (Fe) 0.04%

5960
tri-SODIUM ORTHOPHOSPHATE GR 500 gm
(DODECAHYDRATE) 10 x 500 gm
$Na_3PO_4.12H_2O$ M.W. 380.12 50 kg
Minimum assay 98%
Maximum Limits of Impurities:
Insoluble matter 0.005%
Free alkali (NaOH) 2.0%
Chloride (Cl) 0.001%
Nitrogen compounds (N) 0.001%
Sulphate (SO_4) 0.005%
Calcium (Ca) 0.002%
Copper (Cu) 0.0005%
Iron (Fe) 0.001%
Lead (Pb) 0.0005%
Magnesium (Mg) 0.002%
Potassium (K) 0.005%

5961
SODIUM OXALATE EXTRA PURE 500 gm
$(COONa)_2$ M.W. 134.00 10 x 500 gm
Minimum assay (oxidimetric) 99.5% 50 kg
Chloride (Cl) 0.005%
Sulphate (SO_4) 0.03%
Iron (Fe) 0.005%
Potassium (K) 0.02%

5962
SODIUM OXALATE GR 500 gm
$C_2Na_2O_4$ M.W. 134.00 10 x 500 gm
Assay (manganometric) 99.8% 50 kg
pH 3% water 7.5-8.5
Maximum Limits of Impurities:
Chloride (Cl) 0.002%
Sulphate (SO_4) 0.002%
Total nitrogen (N) 0.001%
Heavy metals (as Pb) 0.001%
Iron (Fe) 0.0005%
Potassium (K) 0.005%
Loss on drying (105°C) 0.01%

5964
SODIUM PERBORATE 1 kg
(TRIHYDRATE) PURE 10 x 1 kg
$NaBO_2.H_2O_2.3H_2O$ M.W. 153.86 25 kg
Minimum assay (by iodometry) 98%
Maximum Limits of Impurities:
Chloride (Cl) 0.1%
Sulphate (SO_4) 0.05%
Heavy metals (as Pb) 0.003%
Iron (Fe) 0.001%

5965
SODIUM PERCHLORATE GR 500 gm
(Monohydrate) 10 x 500 gm
$NaClO_4.H_2O$ M.W. 140.46
Minimum assay (by argentometric) 99%
pH (5% water) 4.5-7
Maximum Limits of Impurities:
Chloride & Chlorate (as Cl) 0.002%
Sulphate (SO_4) 0.002%
Total nitrogen (N) 0.0005%
Iron (Fe) 0.0003%
Heavy metals (as Pb) 0.0005%
Calcium (Ca) 0.002%
Potassium (K) 0.005%

5967
SODIUM (META)PERIODATE 100 gm
EXTRA PURE 10 x 100 gm
$NaIO_4$ M.W. 213.89 500 gm
Assay (iodometric) minimum 98% 10 x 500 gm
Maximum Limits of Impurities:
Bromate, bromide, chlorate
and chloride (as Cl) 0.01%
Sulphate (SO_4) 0.005%
Manganese (Mn) 0.0005%

5968
SODIUM (META)PERIODATE GR 100 gm
(For the colorimetric determination 10 x 100 gm
of tri-glycerides) 500 gm
$NaIO_4$ M.W. 213.89 10 x 500 gm
Minimum assay of $NaIO_4$ 99.8%
Maximum Limits of Impurities:
Chloride chlorate bromide
and bromate (as Cl) 0.01%
Sulphate (SO_4) 0 005%
Manganese (Mn) 0.0001%

5969
SODIUM PEROXIDE for synthesis 500 g
(granular)
Na_2O_2 M.W. 77.98
Minimum Assay (by manganometry) >95%

000020

ADD 65

FD

MEMORANDUM OF CONFERENCE
THRESHOLD OF REGULATION COMMITTEE
Date: September 15, 2005

COMMITTEE MEMBERS

Michael VanDerveer	HFS-275
Adejoke Ogungbesan	HFS-275
Anna Shanklin	HFS-275
Julius Smith	HFS-275

Project 1
CSO:V. Gilliam
CTS #: 2005-3767
TOR # 251

Ciba Specialty Chemicals Corp. - Use of sodium perchlorate monohydrate as a conductivity enhancer in (b) (4), a commercially available permanent antistatic agent.

Ciba Specialty Chemicals Corporation (CSCC) submits this TOR request for an exemption from the need for a food additive listing regulation for the use of sodium perchlorate monohydrate as a conductivity enhancer in (b) (4), a commercially available antistatic agent. The maximum concentration of sodium perchlorate monohydrate (CAS Reg. No. 7791-07-3) proposed for use in (b) (4) formulation is 4 percent by weight, which would correlate to 1.2 percent by weight in the finished article for use in contact with dry foods.

CSCC states that the request for an exemption is based on the dietary concentration (DC) of sodium perchlorate monohydrate, at the maximum proposed use level of (b) (4) of 30% in the finished article, which can be calculated as 0.030 ppb, with a resulting estimated daily intake (EDI) of 0.09 µg/p/d.

Chemistry
CSCC commercially markets (b) (4) as a permanent antistatic agent and is a formulated blend of the following substances:

CAS Number	Component	Wt. %
(b) (4)		
7791-07-3	Sodium perchlorate monohydrate	4

000021

(b) (4) [redacted] Sodium perchlorate monohydrate is not FDA regulated.

(b) (4) [redacted]

The maximum concentration of sodium perchlorate monohydrate to be used in the (b) (4) formulation would be 4% (wt.), which would correlate to 1.2% (wt) in the finished article.

The primary chemical process used in the commercial manufacturing of sodium perchlorate monohydrate involves electrochemical oxidation of lower valence chlorine-containing-compounds, mainly sodium chlorate.

(b) (4) is incorporated into the polymer during processing and develops a conductive network within the polymer matrix. This conductive network dissipates any acquired static charge. Sodium perchlorate monohydrate is used in the (b) (4) formulation as a "conductivity enhancer."

The proposed use of (b) (4) is identical to the FDA regulated product (b) (4) (FCN 000406), as an antistatic agent for use in polymers in contact with dry foods with surface containing no free fat or oil compliant with 21 CFR 176.170 (c), Table 1, Food type VIII, such as cereals, flour, macaroni, and sugar.

Based on the maximum use level and the minimum consumption factor (CF) of 0.05 for all exposure estimates, the dietary concentration (DC) for sodium perchlorate monohydrate can be calculated as 0.030 ppb, with a resulting estimated daily intake (EDI) of 0.09 µg/p/d.

Estimated Daily Intake

The dietary concentration (DC) of sodium perchlorate monohydrate in (b) (4) (b) can be calculated as:

DC = [(0.05 CF) x (4% sodium perchlorate in (b) (4) formulation) x (30% maximum use level of the (b) (4) formulation) x (50 ppb, dry foods "virtually nil" migration) = 0.030 ppb

Based on this DC, the estimated daily intake (EDI) can be calculated as

EDI = 0.030 ppb x 3 kg food/person = 0.09 µg/person/day

Toxicology (Safety Narrative)
As stated above, the estimated DC for sodium perchlorate monohydrate in [redacted] is 30 parts per trillion (ppt). Based on the fact that the DC of this compound is less that 50 ppt, in addition to lack of carcinogenicity data, toxicology has no safety concerns for the proposed use of this compound at the level of dietary exposure indicated.

Environmental

A claim of categorical exclusion under 21 CFR 25.32 (i) and (j) is included in the submission, including CSCC's statement that there are no extraordinary circumstances that would require the submission of an EA.

Conclusion

The Committee agrees with the requestor's conclusion that this action qualifies for a categorical exclusion from the need to prepare an Environmental Assessment in accordance with 21 CFR 25.32(i) and (j).

Review of the available toxicity data indicates that the proposed use of sodium perchlorate monohydrate does not raise any safety concerns at the above exposure level. Also, the Committee is not aware of any study showing sodium perchlorate monohydrate, itself, to be carcinogenic in humans or in animals.

The Committee notes that the FCS will be used in the manufacture of an antistatic agent, consisting of [redacted] intended for use in polymers in contact with dry foods. Because the FCS is intended for use in contact with dry foods only, the Committee has no reason to limit use of the FCS to only in the manufacture of [redacted] as mentioned in the submission. Therefore, the Committee concludes that the FCS may be used as a conductivity enhancer in the manufacture of an antistatic agent that are duly authorized (by regulation, FCN, TOR, etc) for use in contact with dry foods.

Therefore, based on the above findings, the Committee concludes that Ciba Specialty Chemical Corporation should be issued a letter indicating that the use of sodium perchlorate monohydrate as a conductivity enhancer in regulated or otherwise authorized antistatic agents at a maximum concentration of 4 percent by weight, which would correlate to 1.2 percent by weight in the finished article for use in contact with dry foods qualifies for an exemption under 21 CFR 170.39 from the requirement of being the subject of a food additive listing regulation. (TR/05-006)

Julius Smith

Reviewed by:

M.VanDerveer:HFS-275 9-29-05
A.Ogungbesan:HFS-275:9-29-05
A.Shanklin:HFS-275:9:28-05
J.Smith:HFS-275:9-30-05
E.Machuga:HFS-275:10-3-05

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Public Health Service

Food and Drug Administration
College Park, MD 20740

Sept 23, 2005

Dr. Neal Earhart
Ciba Expert Services
540 White Plains Road
Tarrytown, NY 10591

Dear Dr. Earhart:

This correspondence is in response to your letter, dated June 17, 2005, requesting an exemption from regulation as a food additive the use of sodium perchlorate monohydrate, as a conductivity enhancer in [redacted], a commercially available antistatic agent for use in polymers in contact with dry foods, under 21 CFR 170.39 ***Threshold of regulation for substances used in food-contact articles***.

We have reviewed your claim of categorical exclusion under 21 CFR 25.32(i) and (j) and have determined that it is incomplete as submitted. A claim of categorical exclusion should include a citation of the CFR section under which the exclusion is warranted, a statement of compliance with the categorical exclusion criteria, and a statement that to the submitter's knowledge that there are no extraordinary circumstances that will require the preparation of an environmental assessment (EA). In your claim you do cite the CFR section under which the categorical exclusion is claimed, however we have noted the following deficiencies:

1) A statement of compliance with the categorical exclusion criteria is not included in your submission.

2) A statement that to your knowledge there are no extraordinary circumstances that will require the preparation of an EA is not included in your submission.

You need to provide the above information in order to completely satisfy the criteria for a categorical exclusion from preparation of an EA.

If you have any questions concerning this matter, please do not hesitate to contact us.

Sincerely,

[redacted]

Vivian Gilliam.
Consumer Safety Officer
Division of Food Contact Notifications, HFS-275
Office of Food Additive Safety
FDA/Center for Food Safety and Applied Nutrition

BEST ORIGINAL COPY

Section 7 – Environmental Assessment

A - CLAIM OF CATEGORICAL EXCLUSION

1. Cite the specific section of the CFR under which the categorical exclusion is claimed 21 CFR 25.32 (i) and (j)

Class of Action	Description
(i)	Approval of a food additive petition or GRAS affirmation petition, the granting of a request for exemption from regulation as a food additive under Sec. 170.39 of this chapter, or allowing a notification submitted under 21 U.S.C. 348(h) to become effective, when the substance is present in finished food-packaging material at not greater than 5 percent-by-weight and is expected to remain with finished food-packaging material through use by consumers or when the substance is a component of a coating of a finished food-packaging material.
(j)	Approval of a food additive petition or GRAS affirmation petition, the granting of a request for exemption from regulation as a food additive under Sec. 170.39 of this chapter, or allowing a notification submitted under 21 U.S.C. 348(h) to become effective, when the substance is to be used as a component of a food-contact surface of permanent or semipermanent equipment or of another food-contact article intended for repeated use.

2. Does your proposed food-contact use comply with the categorical exclusion criteria?

Yes

3. To the best of your knowledge are there any extraordinary circumstances that would require your submission of an EA

No

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Public Health Service

Food and Drug Administration
College Park, MD 20740

Sept 23, 2005

Dr. Neal Earhart
Ciba Expert Services
540 White Plains Road
Tarrytown, NY 10591

Dear Dr. Earhart:

This correspondence is in response to your letter, dated June 17, 2005, requesting an exemption from regulation as a food additive the use of sodium perchlorate monohydrate, as a conductivity enhancer in [redacted] a commercially available antistatic agent for use in polymers in contact with dry foods, under 21 CFR 170.39 ***Threshold of regulation for substances used in food-contact articles***.

We have reviewed your claim of categorical exclusion under 21 CFR 25.32(i) and (j) and have determined that it is incomplete as submitted. A claim of categorical exclusion should include a citation of the CFR section under which the exclusion is warranted, a statement of compliance with the categorical exclusion criteria, and a statement that to the submitter's knowledge that there are no extraordinary circumstances that will require the preparation of an environmental assessment (EA). In your claim you do cite the CFR section under which the categorical exclusion is claimed, however we have noted the following deficiencies:

1) A statement of compliance with the categorical exclusion criteria is not included in your submission.

2) A statement that to your knowledge there are no extraordinary circumstances that will require the preparation of an EA is not included in your submission.

You need to provide the above information in order to completely satisfy the criteria for a categorical exclusion from preparation of an EA.

If you have any questions concerning this matter, please do not hesitate to contact us.

Sincerely,

Vivian Gilliam.
Consumer Safety Officer
Division of Food Contact Notifications, HFS-275
Office of Food Additive Safety
FDA/Center for Food Safety and Applied Nutrition

FileName:TOR251DEF
R/D: VGilliam:HFS-275:09/23/05
F/T:HFS-275:VGilliam:sgg:9/23/05

Section 7 – Environmental Assessment

Upon review, it has been determined that Sodium Perchlorate Monohydrate qualifies for a claim of Categorical Exclusion under 21 CFR 25.32 classes of action (i) and (j).

Class of Action	Description
(i)	Approval of a food additive petition or GRAS affirmation petition, the granting of a request for exemption from regulation as a food additive under Sec. 170.39 of this chapter, or allowing a notification submitted under 21 U.S.C. 348(h) to become effective, when the substance is present in finished food-packaging material at not greater than 5 percent-by-weight and is expected to remain with finished food-packaging material through use by consumers or when the substance is a component of a coating of a finished food-packaging material.
(j)	Approval of a food additive petition or GRAS affirmation petition, the granting of a request for exemption from regulation as a food additive under Sec. 170.39 of this chapter, or allowing a notification submitted under 21 U.S.C. 348(h) to become effective, when the substance is to be used as a component of a food-contact surface of permanent or semipermanent equipment or of another food-contact article intended for repeated use.

M

Earhart Neal PX US

From: Earhart Neal PX US
Sent: Friday, September 23, 2005 11:46 AM
To: 'Gilliam, Vivian M'
Subject: RE: Formal Response for TOR 251...
Importance: High
Attachments: NaCl04_TOR_EA.doc

Dear Ms. Gilliam,

Attached is the additional Environmental Assessment information as requested by the FDA in support of the Threshold of Regulation Exemption for the use of sodium perchlorate monohydrate, as a conductivity enhancer in (b) (4) , a commercially available antistatic agent for use in polymers in contact with dry foods.

The attached page is a replacement page for page 7 of the TOR document.

If you have any questions upon review, please contact me at your convenience.

Best regards,
Neal

Neal J. Earhart, Ph.D.
Regulatory Services
Ciba® Expert Services
540 White Plains Road
Tarrytown, NY 10591
Telephone: (914) 785-4518
Fax: (914) 785-4147
http://www.cibasc.com/index/exs-index.htm

-----Original Message-----
From: Gilliam, Vivian M [mailto:Vivian.Gilliam@cfsan.fda.gov]
Sent: Thursday, September 22, 2005 3:05 PM
To: Earhart Neal PX US
Subject: Formal Response for TOR 251...

September 23, 2005

Neal Earhart
Ciba Expert Services
540 White Plains Road
Tarrytown, NY 10591

000025

Dear Dr. Earhart:

This correspondence is in response to your letter, dated June 17, 2005, requesting an exemption from regulation as a food additive the use of sodium perchlorate monohydrate, as a conductivity enhancer in [redacted], a commercially available antistatic agent for use in polymers in contact with dry foods, under 21 CFR 170.39 ***Threshold of regulation for substances used in food-contact articles.***

We have reviewed your claim of categorical exclusion under 21 CFR 25.32(i) and (j) and have determined that it is incomplete as submitted. A claim of categorical exclusion should include a citation of the CFR section under which the exclusion is warranted, a statement of compliance with the categorical exclusion criteria, and a statement that to the submitter's knowledge that there are no extraordinary circumstances that will require the preparation of an environmental assessment (EA). In your claim you do cite the CFR section under which the categorical exclusion is claimed, however we have noted the following deficiencies:

1) A statement of compliance with the categorical exclusion criteria is not included in your submission.

2) A statement that to your knowledge there are no extraordinary circumstances that will require the preparation of an EA is not included in your submission.

You need to provide the above information in order to completely satisfy the criteria for a categorical exclusion from preparation of an EA.

If you have any questions concerning this matter, please do not hesitate to contact us.

Sincerely,

Vivian Gilliam.
Consumer Safety Officer
Division of Food Contact Notifications, HFS-275
Office of Food Additive Safety
Center for Food Safety
and Applied Nutrition

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
Food and Drug Administration

Memorandum

FD

Date: September 26, 2005

From: Environmental Review Group (ERG)
Threshold of Regulation Committee, Environmental Review Chemist via ERG
Division of Chemistry Research and Environmental Review (HFS-246)

Subject: TOR 251 (CTS# 2005-3767) – Sodium perchlorate monohydrate as a conductivity enhancer in antistatic agent for use in polymers in contact with dry foods. Ciba Specialty Chemicals

To: Division of Food Contact Notifications (HFS-275)
Threshold of Regulation Committee
Attention: Julius Smith
Through: Annette McCarthy, Ph.D., ERG [redacted]

CC: Division of Food Contact Notifications (HFS-275)
Attention: Vivian Gilliam, Consumer Safety Officer

I have reviewed the claim of categorical exclusion for the above referenced Threshold of Regulation submission and have concluded that categorical exclusion is warranted. The food additive to be exempt from regulation under 21 CFR 170.39 is to be used as a conductivity enhancer in [redacted], a commercially available antistatic agent for use in polymers in contact with dry foods. The claim of categorical exclusion cites the section under which categorical exclusion is warranted, 21 *CFR* 25.32 (i) and (j), states compliance with the categorical exclusion criteria, and states that no extraordinary circumstances exist that would require the submission of an environmental assessment.

Please let me know if there is any change in the identity or use of the food contact substance.

Anna P. Shanklin, Ph.D.

cc:
HFS-246 File: TOR No. 251 (CTS 2005-3767)

HFS-246:APShanklin:aps:09/27/05 H:
FT: APShanklin:aps:09/27/05 p:\EIS Documents\MEMOS\TOR251_E_CatEx.doc

FD

November 4, 2005

TR 2005-006

Neal J. Earhart, Ph.D.
Sr. Compliance Applications Specialist
Ciba Expert Services
Ciba Specialty Chemicals Corporation
540 White Plains Road, PO Box 2005
Tarrytown, NY 10591-9005

Re: Sodium Perchlorate Monohydrate
TOR No 251

Dear Dr. Earhart:

This is in response to your letter of June 17, 2005, and amended on September 23, 2005, requesting an exemption under 21 CFR 170.39 for the safe use of sodium perchlorate monohydrate (CAS Reg. No. 7719-07-3) as a conductivity enhancer in the manufacture of antistatic agents at a maximum concentration of 4 percent by weight, which would correlate to 1.2 percent by weight in the finished article for use in contact with dry foods.

We note that sodium perchlorate monohydrate will be used in the manufacture of an antistatic agent, (b) (4) [redacted] intended for use in polymers in contact with dry foods. You have provided worst-case extraction data, safety data, and a claim of categorical exclusion under 21 CFR 25.32(i) and (j) in support of your request.

We have completed our review of your submission and conclude that the dietary concentration for sodium perchlorate monohydrate resulting from its intended use would be below the threshold of regulatory concern. Also, we are not aware of any study showing this copolymer to be carcinogenic to humans or animals.

Additionally, we have reviewed your claim of categorical exclusion and conclude that this action qualifies for a categorical exclusion from the requirement to submit an environmental assessment pursuant to 21 CFR 25.32(i) and (j).

Therefore, based on the above findings, we conclude that Ciba Specialty Chemical Corporation's intended use of sodium perchlorate monohydrate as a conductivity enhancer in regulated or otherwise authorized antistatic agents at a maximum concentration of 4 percent by weight, which would correlate to 1.2 percent by weight in the finished article for use in contact with dry foods qualifies for an exemption under 21 CFR 170.39 from the requirement of being the subject of a food additive listing regulation.

000032

FILE COPY

OFFICE	SURNAME	DATE	OFFICE	SURNAME	DATE	OFFICE	SURNAME	DATE
HFS-276	(b) (6) [redacted]	11/4/05						
HFS-225	[redacted]	11/4/05						

We trust that this letter is responsive to your inquiry. If you have additional questions, please feel free to contact us.

Sincerely yours,

Mitchell A. Cheeseman, Ph.D.
Director
Division of Food Contact Notificatioin, HFS-275
Center for Food Safety and Applied Nutrition

cc: HFS-200
HFS-275(2)
TR 2005-06
E. Machuga (HFS-275) Letter No. 20053767
Named: Earhart
R/D: J.Smith:HFS-275:11-2-05
Init: E.Machuga:HFS-275:11-2-05
F/T: sgg:11/4/2005

NATURAL RESOURCES DEFENSE COUNCIL

February 28, 2014

By Electronic Delivery

Dr. Peter Grevatt, Director
Office of Ground Water and Drinking Water
USEPA Headquarters
William Jefferson Clinton Building
1200 Pennsylvania Avenue, N. W.
Mail Code: 4601M
Washington, DC 20460

Re: NRDC concerns with FDA's perchlorate biologically based dose-response model

Dear Dr. Grevatt:

As the EPA Office of Ground Water and Drinking Water is working to develop a Maximum Contaminant Level Goal (MCLG) and a national primary drinking water standard for perchlorate, we are very concerned that EPA may be weakening the perchlorate Reference Dose (RfD) to make it less health-protective by relying on a flawed model. Overall, we think the model is a strong starting point, but EPA needs to make the following improvements:

- Expand the model to include the first two trimesters in addition to infants. The current model is based only on the end of the third trimester when the fetus has a functioning thyroid.
- Ensure the model considers iodide levels at the 95th and 99th percentiles of pregnant women, not just the 90th percentile.
- Reevaluate affinity constants for iodide and perchlorate to ensure they are based on a robust data set and are calculated consistently.
- Incorporate thiocyanate and nitrate in the model as recommended by EPA's Science Advisory Board since they also inhibit iodide uptake in a manner similar to perchlorate.
- Justify the selection of 10 pmol/L of maternal free T4 as the threshold for hypothyroxinemia.
- Compare the model results to NHANES monitoring data.

Background

In 2005, EPA adopted a Reference Dose (RfD) of 0.7 µg/kg/day, which is posted on its public IRIS database.[1] It is derived from a No Observed Effect Level (NOEL) of 7 µg/kg/day for the critical effect of radioactive iodide update inhibition in the thyroid, with a 10-fold uncertainty factor for differences between humans. EPA felt that this would protect the most sensitive population, the fetuses of pregnant women who might have hypothyroidism or iodide deficiency.

[1] http://www.epa.gov/iris/subst/1007.htm

Because the principal study was of humans – healthy adults - not laboratory animals, no additional uncertainty factor was used for interspecies differences.[2]

EPA based its IRIS assessment and RfD on the recommendations of the National Research Council (NRC) perchlorate report (2005). The IRIS assessment sums up the NRC approach and recommendations as follows:

> The NRC (2005) reviewed a number of benchmark dose models for the radioiodide uptake inhibition point of departure, as developed by the U.S. EPA (2003), California Environmental Protection Agency (CalEPA 2004) and Crump and Goodman (2003). The NRC (2005) concluded that these analyses used different models, approaches, parameters, response levels, and input data, making the comparison of results difficult. Although the NRC Committee recognized that BMD modeling can be an improvement over the use of the NOAEL or LOAEL as a point of departure, there appeared to be no consensus on the criteria for choosing one BMD approach over another. Because no clear justifications were provided with the individual analyses of the Greer et al. (2002) data that allowed selection of one set of results over another, the NRC Committee concluded that using the NOEL (0.007 mg/kg/day) for iodide inhibition from Greer et al. (2002) as the point of departure provided a reasonable and transparent approach to perchlorate risk assessment.[3]

In 2012, EPA convened its Scientific Advisory Board (SAB) to advise the Office of Water on how to consider sensitive life stages, the physiologically-based pharmacokinetic (PBPK) modeling efforts, available epidemiologic and biomonitoring data, and approaches to integrate these data to derive an MCLG for perchlorate.

In its final 2013 report to EPA the SAB recommended the following:[4]

- EPA should derive a perchlorate MCLG that addresses sensitive life stages through PBPK/pharmacodynamics modeling based on the mode of action. The SAB preferred this approach over using the RfD with specific chemical exposure parameters.
- EPA should expand its models to account for thyroid hormone perturbations and potential adverse neurodevelopmental outcomes from perchlorate exposure.
- Clinical thyroid literature is relevant to identify the degree of iodide uptake inhibition required for onset of hypothyroxinemia in a pregnant woman.
- In developing the pharmacodynamics aspects of the model, EPA should consider information on potential adverse health effects due to thyroid hormone perturbations, regardless of the cause, to document and support the model.

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[2] Greer, M.A., Goodman, G., Pleus, R.C., Greer, S.E. 2002. Health effect assessment for environmental perchlorate contamination: The dose response for inhibition of thyroidal radioiodide uptake in humans. Environ. Health Perspect. 110:927-937.

[3] http://www.epa.gov/iris/subst/1007.htm

[4] EPA-SAB-13-004, May, 2013. Available at: http://yosemite.epa.gov/sab%5CSABPRODUCT.NSF/86E44EE7F27EEC1A85257B7B0060F364/$File/EPA-SAB-13-004-unsigned2.pdf

- EPA must consider specific adverse effects on brain development due to inadequate iodide update or low thyroid hormone levels vary at different life stages, but are especially critical during the early formative stages of brain development, when the human brain most needs thyroid hormone.

NRDC's Concerns with the FDA Model

We are concerned that EPA may be considering adoption – in whole or in part – of a perchlorate biologically based dose-response model (BBDR) developed by U.S. Food and Drug Administration (FDA) scientists. The FDA model is published as Lumen A, Mattie DR, Fisher JW. *Evaluation of perturbations in serum thyroid hormones during human pregnancy due to dietary iodide and perchlorate exposure using a biologically based dose-response model*. Toxicol Sci. 2013 Jun;133(2):320-41.

According to the FDA model, the intakes of perchlorate required to alter maternal thyroid levels enough to induce hypothyroxinemic conditions are 6-fold greater than the current reference dose, and for hypothyroid conditions are 31-fold greater (Lumen et al, Table 8), making the model predictions much less protective than EPA's current RfD.

We understand that EPA's adaptions of the above FDA model may include consideration of infant exposure from breastfeeding and from bottle feeding. While we agree with this, we also believe that the FDA model should be expanded to cover the first two trimesters and infant exposure. The FDA model is based on pregnant women in weeks 37 to 40 – the late third trimester just before giving birth. By the third trimester, the fetus has a functioning thyroid that is contributing thyroid hormones. However, in the previous two trimesters, the thyroid does not exist or is not functioning. The 2011 Guidelines of the American Thyroid Association for the Diagnosis and Management of Thyroid Disease During Pregnancy and Postpartum make clear that the fetus needs greater levels of thyroxin (T4) in the first trimester than in the third.[5] Given this and other differences, the model needs to include the first and second trimesters as well in addition to the planned modeling for the infant.

If EPA relies on the FDA model, then it should be expanded to protect all women. The model uses 75 µg/day as the lowest iodide intake without any explanation. By back-calculating the relationship between daily intake and urinary concentrations from NHANES, it seems that this dose corresponds to only the 90th percentile of pregnant women, leaving 10% of women unaddressed by FDA's model. [6] [7] [8] The potential for irreversible damage to a child's brain

[5] Stagnaro-Green A, Abalovich M, Alexander E, Azizi F, Mestman J, Negro R, Nixon A, Pearce EN, Soldin OP, Sullivan S, Wiersinga W; American Thyroid Association Taskforce on Thyroid Disease During Pregnancy and Postpartum. Guidelines of the American Thyroid Association for the diagnosis and management of thyroid disease during pregnancy and postpartum. Thyroid. 2011 Oct;21(10):1081-125. doi:10.1089/thy.2011.0087. Epub 2011 Jul 25. PubMed PMID: 21787128; PubMed Central PMCID: PMC3472679.

[6] Blount BC, L Valentin-Blasini, JD Osterloh, JP Mauldin, and JL Pirkle. 2007. Perchlorate exposure of the US population, 2001-2002. J Expo Sci Environ Epidemiol. 17(4):400-7.

[7] Based on NHANES biomonitoring data from 2005 to 2008, 11.5% of pregnant women had urinary iodide concentrations of < 50 µg/L and 5.2% had < 20 µg/L. At 90%, a 75 µg/day uptake corresponds to 67.5 µg/day excretion in urine. Assuming mean daily urine output of 1.5 L per day in the third trimester (Thorp et al 1995), the concentration of perchlorate in the urine would be 45 µg/L, representing approximately 10% of pregnant women.

[8] Thorp, J. M., Jr, Norton, P. A., Wall, L. L., Kuller, J. A., Eucker, B., and Wells, E. (1999). Urinary incontinence in pregnancy and the puerperium: A prospective study. Am. J. Obstet. Gynecol. 181, 266–273.

warrants protecting all pregnant women. The model should include iodide levels for the 95th and 99th percentiles of pregnant women.

Perchlorate binds and inhibits the sodium/iodide symporter (NIS) that is meant to transport iodide into the thyroid gland, where it is used to produce thyroid hormone. Therefore, the affinity of perchlorate and iodide for the NIS – which one binds more strongly and replaces the other – must be accurate in the model. The model uses an affinity constant of 3.15×10^4 nmol/L for iodide in both the mother and fetus, and 1.5×10^3 nmol/L for perchlorate in both the mother and fetus (Lumen et al Table 2). Lumen et al cite three sources[9,10,11] for these affinity constants.

It is unclear how any of these articles could support the derivation of an NIS affinity constant in pregnant mothers and their fetuses. Gluzman et al is a comparison between normal and diseased thyroid tissue from 1983. The constant for iodide in normal human thyroid was given as 3.12×10^{-5} mol/L with a standard deviation of 0.98 relying on only five samples. After adjusting the units to be consistent, the number is similar but not exactly the same as the one used in the model (3.12 in the article v. 3.15 in the model).

Kosugi et al from 1996 uses hamster-derived cell line with no consideration of women, pregnancy, or fetal tissue kinetics. Tonacchera et al from 2004 focused on the expression and cell localization of the NIS in diseased thyroid tissue, and did not provide information regarding NIS uptake kinetics or affinity constants.

EPA should reevaluate affinity constants for iodide and perchlorate to ensure they are based on a robust data set and are calculated consistently. If the Gluzman et al data is used, given the wide standard deviation, the high (4.10×10^{-5} mol/L) and low (2.14×10^{-5} mol/L) levels should be evaluated.

It is interesting to note that Kosugi et al – the hamster cell line study – not only provided an affinity constant for perchlorate, but also estimated the affinity constant of thiocyanate at 1.6×10^2 nmol/L – ten times greater than perchlorate. Because thiocyanate acts like perchlorate on the same target, EPA should incorporate thiocyanate into its MCLG determination. Thiocyanate is naturally present in some foods and is also found in cigarette smoke. FDA also allows ionic forms of thiocyanate to be used as an indirect additive in adhesives; 25 organic thiocyanates are approved by FDA for food uses, primarily as flavors, which would contribute to human dietary exposures that the EPA should consider an MCLG.

The perchlorate model recently published by EPA's Office of Research and Development, (McLanahan et al 2014) notes that nitrate is also known to competitively inhibit iodide uptake by

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[9] Gluzman, B. E., and Niepomniszcze, H. (1983). *Kinetics of the iodide trapping mechanism in normal and pathological human thyroid slices*. Acta Endocrinol. 103, 34–39.

[10] Kosugi, S., Sasaki, N., Hai, N., Sugawa, H., Aoki, N., Shigemasa, C., Mori, T., and Yoshida, A. (1996). *Establishment and characterization of a Chinese hamster ovary cell line, CHO-4J, stably expressing a number of Na+/I- symporters*. Biochem. Biophys. Res. Commun. 227, 94–101.

[11] Tonacchera, M., Viacava, P., Fanelli, G., Agretti, P., De Marco, G., De Servi, M., Di Cosmo, C., Chiovato, L., Pinchera, A., and Vitti, P. (2004). *The sodium-iodide symporter protein is always present at a low expression and confined to the cell membrane in nonfunctioning nonadenomatous nodules of toxic nodular goitre*. Clin. Endocrinol. (Oxf) 61, 40–45.

the thyroid using the same mechanism as perchlorate.[12] Given its extensive use in food, and widespread presence in drinking water, EPA should also include nitrate exposure in its MCLG determination.

The use of <10 pmol/L of maternal free T4 threshold (fT4) in the model is unfounded (see Lumen et al page 329 and Table 8). The model authors reference Moleti et al (2011) as the basis of the 10 picomolar cut-off for fT4 for maternal hypothyroxinemia. [13] However, when we reviewed the reference, it does not provide a specific cut-off value of fT4 for either hypothyroxinemia or hypothyroidism. Table 1 in the Moleti article summarizes criteria used by various researchers but there is no consensus on a particular concentration. Moleti states that the fT4 values depend on the population's iodide intake, the trimester, and the methodology used to measure the hormone. Therefore, it is clear that a single value for the cut-off of fT4 is not appropriate.

In setting a MCLG, EPA also needs to consider the impact of perchlorate on the fetus' thyroid in addition to its existing plans to include infants. The FDA model indicates that perchlorate levels in the fetus serum (19.8 µg/L) are 50% higher than in the mother's serum (12.4 µg/L) (Lumen et al, page 332). The effects of these higher levels on fetal thyroid do not appear to be considered in the model. Although during the first trimester the fetus is reliant on maternal thyroid hormone, in the second and third trimester the fetus can synthesize its own thyroid hormone in limited amounts. Studies have shown that the cognitive development of the fetus is impaired in mothers with even mild disruptions in thyroid hormone levels, prompting the medical community to recommend thyroid hormone replacement therapy for pregnant women who are found to have sub-clinical hypothyroidism (mildly elevated TSH but normal T4).[14] At a minimum, EPA should ensure the fT4 levels in the fetus do not exceed the threshold for maternal fT4.

The FDA model results need to be compared to the NHANES monitoring data. The model is calibrated for high perchlorate exposures based on a longitudinal epidemiological study of 184 pregnant women in three Chilean cities from 2002 to 2004.[15] Other researchers have raised concerns with the conclusions being drawn from this study, particularly because some residents moved from city-to-city. In contrast, NHANES has data on thousands of people, including pregnant woman with information on maternal levels of iodide, perchlorate, thyroid hormones, as

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[12] McLanahan ED, White P, Flowers L, Schlosser PM. The Use of PBPK Models to Inform Human Health Risk Assessment: Case Study on Perchlorate and Radioiodide Human Lifestage Models. Risk Anal. 2014 Feb;34(2):356-66.

[13] Moleti M, Trimarchi F, Vermiglio F. Doubts and Concerns about Isolated Maternal Hypothyroxinemia. J Thyroid Res. 2011;2011:463029. doi:10.4061/2011/463029. Epub 2011 Jun 15. PubMed PMID: 21765991; PubMed Central PMCID: PMC3134327.

[14] Cooper, D. 2004. Sub-clinical thyroid disease: consensus or conundrum. Clinical Endocrinology 60 (410-412); Haddow JE, Palomake GE, Allan, WC, Williams JR, Knight GJ, and Gagnon J, et al. Maternal thyroid deficiency during pregnancy and subsequent neuropsychological development of the child. New England Journal of Medicine 1999: 341: 549-555; Pop VJ, Kuijpens J., van Baar, AL, Verkert, G. et al. 1999. Low maternal free thyroxine concentrations during early pregnancy are associated with impaired psychomotor development in infancy. Clinical Endocrinology 50 (149); Surks M., Ortiz E., Daniels G., Sawin C., Col N., Cobin R., Franklyn J. Hershman J., Burman K., Denke M., Gorman C., Cooper R., Weissman N. 2004. Subclinical Thyroid Disease. Subclinical Thyroid Disease. Journal of the American Medical Association 2004: 228-238.

[15] Téllez Téllez R, Michaud Chacón P, Reyes Abarca C, Blount BC, Van Landingham CB, Crump KS, Gibbs JP. Long-term environmental exposure to perchlorate through drinking water and thyroid function during pregnancy and the neonatal period. Thyroid. 2005 Sep;15(9):963-75. PubMed PMID: 16187904.

well as thiocyanate.[16] Therefore, EPA should use the data from the NHANES survey rather than the flawed Chilean cities study.

Again, we appreciate the opportunity to provide you with these comments and would like to discuss them in more detail as EPA works with FDA to fix the problems we described above in the model.

If you have any questions, please contact me at tneltner@nrdc.org.

Sincerely,

Tom Neltner
Senior Attorney

Maricel Maffini
Senior Scientist

cc: Eric Burneson, Acting Director, Standards and Risk Management Division
Mae Wu, Program Attorney, NRDC

[16] Blount BC, L Valentin-Blasini, JD Osterloh, JP Mauldin, and JL Pirkle. 2007. Perchlorate exposure of the US population, 2001-2002. J Expo Sci Environ Epidemiol. 17(4):400-7.

Exhibit B

Natural Resources Defense Council et al.
Food Additive Petition: Supplemental Material (Dec. 5, 2014)

December 5, 2014

Paul Honigfort, Ph.D., Consumer Safety Officer
Division of Food Contact Notifications, HFS-275
Office of Food Additive Safety
Center for Food Safety and Applied Nutrition
U.S. Food and Drug Administration
5100 Paint Branch Parkway
College Park, MD 20740

Re: Perchlorate Food Additive Petition (FAP) No. 4B4808: Supplemental Material

Dear Dr. Honigfort,

We received your November 7, 2014 letter informing us that Food and Drug Administration (FDA) was not filing our Perchlorate Food Additive Petition (FAP) No. 4B4808 submitted on October 15, 2014. Your letter identified five "deficiencies" in the petition as justification for its decision.

We also received your November 24, 2014 letter providing us with feedback on our May 18, 2014 draft perchlorate food additive petition you reviewed pursuant to Pre-Notice Consultation (PNC) No. 001447. Your letter made a number of recommendations to improve the draft petition submitted six months earlier. We remain confused as to why it took more than six months to provide this feedback when the agency's goal is one month, but, nonetheless, we appreciate the feedback.

In response to both documents, we submit this letter and attachments as supplementary material to FAP No. 4B4808 pursuant to 21 CFR 171.1(i)(1)(ii). We respond to the "deficiencies" raised in the November 7, 2014 letter in Attachment 1. We respond to recommendations you made in the November 24, 2014 letter in Attachment 2. Where the letters both addressed the same or similar issue, we made the detailed response in Attachment 1.

We want to raise one general concern with FDA's recommendations in the November 24, 2014 letter. You state that "Put plainly, 21 CFR 171.130 requires a risk assessment on the allowed uses, and §§ 171.1 and 171.100 specify the data necessary to support that risk assessment" and "the burden of demonstrating safety (*i.e,* that the intended use is safe, or that the allowed use is unsafe) is on the petitioner – the petition must include a risk assessment on the food additive use as well as adequate data to support the conclusions of that risk assessment."

However, 21 CFR 171.130 makes no reference to a risk assessment and only requires "showing that new information exists with respect to the food additive or that new uses have been developed or old uses abandoned, that new data are available as to toxicity of the chemical, or that experience with the existing regulation or exemption may justify its amendment or repeal." A risk assessment is one way to accomplish that and we provide that analysis in Attachment 1.

As petitioners, under 21 C.F.R. 171.130, we merely need to , "assert[] facts, supported by data, showing that new information exists … [or] that new data are available as to toxicity of the chemical, or that experience with the existing regulation or exemption *may justify* its amendment or repeal." Thus, our petition simply needs to provide data indicating that there may no longer be a "reasonable certainty in the minds of competent scientists that the substance is not harmful under the intended conditions of use" pursuant to 21 CFR 170.3(i) and that our proposed use will provide that reasonable certainty. Irrespective of where the burden of proof lies, we have provided strong evidence that FDA's decision to approve perchlorate as a food contact substance may have caused harm to children's brain development, even though we have no obligation under the law or FDA's rules to demonstrate that the use causes harm in our petition. In our October 15, 2014 petition, we presented new scientific information (both toxicology and exposure) that shows there is no longer a reasonable certainty of no harm with the approved use. Without a reasonable certainty of no harm, it is FDA's obligation under the FFDCA to no longer allow these uses. Our proposed ban is the only effective way we have been able to identify for the agency to fulfill its legal obligation to ensure safety.

We also ask that you immediately correct the acknowledged error in FDA's posting of its decision on Threshold of Regulation (TOR) No. 2005-006 that allowed up to 4% perchlorate in dry food packaging. As of November 27, 2014, more than six months after we alerted FDA to it, the error remains on its official announcement, and, as a result, manufacturers may be adding more than 3.3 times the allowed amount of perchlorate to their packaging.

Also, please ensure that in all future communications regarding this petition in the future that you contact both me and Tom Neltner (you can reach him at tneltner@gmail.com or 317-442-3973; his address is 1701 Tilton Dr., Silver Spring, MD 20902.) Please also copy Dr. Maricel Maffini at drmvma@gmail.com on all correspondence.

Thank you in advance for your consideration of these issues.

Erik D. Olson, Director, Health Program and
Senior Strategic Director for Health and Food
Natural Resources Defense Council
1152 15th St. NW, Suite 300
Washington, DC 20005

Attachment 1: Response to FDA's Concerns Raised in its November 7, 2014 Letter with October 15, 2014 Perchlorate Food Additive Petition (FAP No. 4B4808)

Attachment 2: Response to FDA's Concerns Raised in its November 24, 2014 Letter with May 18, 2014 Draft Perchlorate Food Additive Petition (PNC No. 001447)

Attachment 1
Response to FDA's Concerns Raised in its November 7, 2014 Letter with October 15, 2014 Perchlorate Food Additive Petition (FAP No. 4B4808)

Concern #1: "FAP 4B4808 provides information on exposure to sodium perchlorate monohydrate as a result of the use subject to TOR 2005-006, but this exposure is not compared to available toxicity data to support an assertion that the allowed use is unsafe."

No one really knows the exposure that results from the use subject to TOR 2005-006. In the petition, we demonstrate that Ciba's estimate of 0.09 µg[1] of perchlorate/person/day is so seriously flawed that any additional estimate based on the reported exposure is only a guess.

If the exposure calculation would have been done following FDA's guidance, the correct estimated dietary intake (EDI) would be 7.5 µg perchlorate/person/day, which is 83.3 times higher than Ciba's estimates. For a 70 kg person, this exposure corresponds to 0.11 µg/kg-body weight (bw)/day.

Then, Ciba used the perchlorate reference dose, which is essentially the acceptable daily intake (ADI), adopted by the U.S. Environmental Protection Agency's (EPA) Integrated Risk Information System (IRIS), to compare against its estimated exposure. Ciba concluded that the estimated 0.00129 µg/kg-bw/day was 542 times smaller than the IRIS 0.7 µg/kg-bw/day, thus providing a substantial margin of safety. However, because the exposure calculated by Ciba was flawed, the difference between the correct exposure estimate and the reference dose cited in the petition is 6 times smaller, not 542 times smaller (as reported in the petition.)

An additional error made by the FDA in its publication of TOR 2005-006's approval also resulted in an incorrectly understated estimated exposure. Ciba petitioned using perchlorate at a 1.2% level in the packaging. FDA listed the approved uses at 4% in the finished article, thus adding 3.3-fold more perchlorate allowed to be used. Thus, the correctly-estimated exposure of 7.5 µg perchlorate/person/day would translate into 25 µg perchlorate/person/day, or 0.36 µg perchlorate/kg bw/day. Assuming no other sources of exposure to perchlorate in the diet, this exposure alone would comprise more than half of the reference dose of 0.7 µg/kg-bw/day. And as discussed below, FDA has ample evidence from its own sampling of food and water that there are other substantial sources of perchlorate in the diet, which cause the correctly-estimated dietary intake to exceed the acceptable daily intake (calculated using the EPA IRIS reference dose), clearly indicating that a reasonable certainty of no harm is lacking.

It is worth mentioning that the cited reference dose has also been regarded inadequate and not sufficiently protective of susceptible populations such as pregnant women and fetuses by the EPA's own Science Advisory Board. Although a new more protective reference dose has not been determined yet, it will certainly be below the current 0.7 µg/kg-bw/day which would likely push the correctly-estimated exposure above the acceptable daily intake.

[1] We understand that FDA's unit of choice is milligrams. In the interest of simplifying the text, we chose to use micrograms. Readers should divide by 1000 to convert microgram into milligram units.

These are just two flaws in the petition and approval of TOR 2005-006. In FAB No. 4B4808, we documented additional flaws that in combination make it virtually impossible for FDA to be reasonably certain that the approved use would cause no harm. These flaws include:

- FDA's assumption that migration of packaging chemicals into dry food is "virtually nil" and use of 50 parts per billion (ppb) as recommended migration level. FDA acknowledged in 2011 that the 50 ppb assumption may be flawed. The agency's expert referred to European Union studies showing migration may exceed 50 ppb. The agency has yet to update its guidance or justify why its prior acknowledgement of a flawed assumption was incorrect.
- FDA's formula to estimate exposure considered only exposure in final packaging. However, we demonstrated that the product containing perchlorate was being marketed for bulk shipments of dry food raw materials. Therefore, Ciba never included exposure from storage, processing and handling of raw materials. Since most raw materials are handled as dry food, the exposure estimate may more appropriately be several times higher and well over the safe dose if the cumulative exposure from all sources is taken into account.
- FDA knew that food was already contaminated with perchlorate and failed to consider this exposure in its evaluation. In December 2003, FDA began testing lettuce and bottled water for contamination. Before the TOR was approved, it had expanded the testing to include a broader array of produce and had evidence in hand that most food was contaminated. Contrary to the Federal Food, Drug and Cosmetic Act and FDA rules, the agency never considered these exposures. Ultimately, it found that children had the greatest exposure with levels ranging as high as 0.39 µg/kg-bw/day. If this level is added to the corrected exposure estimate of 0.36 µg/kg-bw/day, the exposure exceeds ADI (0.7 µg/kg-bw/day).
- Neither Ciba nor FDA considered the exposure to use of perchlorate in rubber gaskets pursuant to 21 CFR 177.1210. Because FDA does not make this information publicly available, we cannot estimate the exposure from this use, but it would only make the EDI further exceed the ADI.

After correcting for Ciba's and FDA's many errors, we demonstrated that the estimated exposure from TOR 2005-006 exceeds Ciba's reported ADI. And we now know, as explained below and in the petition, that Ciba's reported ADI was insufficient to protect children's brains from harm.

Concern #2: "The petition also notes the expectation that the Agency would have considered exposure to potassium perchlorate from the use listed in 21 CFR 177.1210, but the petition does not specify this exposure or compare it to available toxicity data to support an assertion that the allowed use is unsafe."

We cannot compare exposure to perchlorate from use allowed in 21 CFR 177.1210 to available toxicity data because the agency has not made the information publicly available. As the Department of Justice has made clear, "publicly available" does not mean that a Freedom of Information Act (FOIA) request must be submitted to get said information.[2] FDA has the information from the petition it approved on July 20, 1962. Since we demonstrated that the estimated exposure due to perchlorate contamination of the food supply coupled with the exposure from the use of perchlorate pursuant to TOR 2005-006 already exceeds the ADI, the additional exposure resulting 21 CFR 177.1210 only increases the risk to human health, in particular to harm children's brain development.

In addition, 21 CFR 170.1(c)(G) states that "If submitting petition to modify an existing regulation issued pursuant to section 409(c)(1)(A) of the Act, full information on each proposed change that is to be made in the original regulation must be submitted. The petition may omit statements made in the original petition concerning which no change is proposed." Our petition asks FDA to modify the existing 21 CFR 177.1210. Therefore, we do not need to repeat statements made in the original petition.

Put simply, it is unreasonable for FDA to expect a petitioner to evaluate information that the agency has chosen not to make publicly available. As is customary with food additive petitions, we submitted a draft petition on perchlorate to FDA on May 2014. Upon receipt of the draft, FDA's consumer safety officer indicated that the agency would review it and send feedback; however, the agency never provided the promised evaluation of the draft despite the passage of six months. If FDA believed that the information it now requests was essential to the petition, it should have alerted us to this view and made the relevant information publicly available.

[2] U.S. Department of Justice, Guide to the Freedom of Information Act, 2009. See page 9 which states that "Proactive disclosures -- where agencies make their records publicly available without waiting for specific requests from the public -- are an integral part of the Freedom of Information Act."

Concern #3: "The petition also notes that new data on perchlorate contamination in food has become available since TOR 2005-006 became effective or the listing for potassium perchlorate in 21 CFR 177.1210 was promulgated, as well as data indicating that nitrates and thiocyanates are pharmacologically-related to perchlorate. However, the petition does not calculate cumulative exposure to perchlorates, nitrates, or thiocyanates in the diet, nor is exposure to these substances in the diet compared to available toxicity data to support an assertion that the allowed uses are unsafe."

In Table 1 of the petition, we estimated cumulative exposure to perchlorate, nitrates and thiocyanates in the diet of infants younger than one year old. Because an infant's brain is developing, the infant is particularly vulnerable to these exposures. **Note**: these chemical inhibit the transport of iodine into the thyroid gland; iodine is fundamental in the synthesis of thyroid hormone, a key hormone during brain development. In the extreme cases, the lack of thyroid hormone, either maternal or post-natal, leads to mental retardation and a clinical condition known as cretinism.

As required by 21 CFR 171.18, we consider perchlorate, nitrates, and thiocyanates to be regarded as a class because they cause toxicity by affecting the same biological mechanism. The regulation calls for us to assume that the toxic effects are additive; however, there is evidence indicating that perchlorate's affinity for the iodine transporter is higher than that of nitrates and thiocyanates.

In 2004, Tonacchera et al.[3] calculated the relative potency of these chemicals in the inhibition of iodine uptake. This *in vitro* study on Chinese hamster ovary cells showed that perchlorate was 15 times greater inhibitor than thiocyanate and 240 times greater than nitrates. We have found no study that challenges or contradicts these conclusions.[4]

Beyond 21 CFR 171.18, we could not find any guidance from FDA on how to assess the cumulative exposure of pharmacologically-related substances in the diet. Due to the lack of agency's methods, below is our attempt to perform such an assessment.

1. Table 1 of the petition was the basis for the exposure calculation to the class of chemicals.
2. We adjusted the nitrate and thiocyanate levels to "perchlorate equivalents" by dividing their concentrations by the relative symporter inhibitory capacity compared to perchlorate. For instance the nitrate urinary levels were divided by 240 and the thiocyanate levels were divided by 15. Using similar "units" facilitates estimating a cumulative exposure to this class of endocrine disruptors. Table A below lists the adjusted urinary concentrations. While infants fed solely breast milk had the greatest

[3] Tonacchara, Pinchera, Dimida, Ferrarini, Agretti, Vitti, Santini, Crump, and Gibbs. Relative Potencies and Additivity of Perchlorate, Thiocyanate, Nitrate, and Iodide on the Inhibition of Radioactive Iodide Update by the Human Sodium Iodide Symporter. Thyroid, 14:12, 2004.

[4] We cannot explain why both FDA and Ciba failed to consider cumulative exposure to thiocyanate and nitrates even though there are numerous publications discussing the connection between the chemicals and thyroid function adverse effects, many of which were publicly available before the 2005 decision. According to 21 U.S.C. 348(c)(5) and 21 CFR 170.3(i), both were obligated to consider the cumulative effect of pharmacologically-related substances in the diet when considering the safety of any new chemical or chemical use in food.

perchlorate levels, those fed exclusively cow-based formula or soy-based formula had cumulative levels, after adjusting for potency, in their urine to the class that was 43 to 48% greater than breast milk-fed babies.

Table A. Comparison of mean levels of three contaminants in urine based on the nutrition source for infants younger than one year old and cumulative levels after adjusting for potency.

Nutrition source for infant	Perchlorate	Nitrate	Adjusted Nitrate[1]	Thiocyanate	Adjusted Thiocyanate[2]	Cumulative Class[3]
Breast milk (n = 92)	4.97 ppb	18,350 ppb	76.46 ppb	189 ppb	12.60 ppb	94.03 ppb
Cow milk-based formula (n = 51)	2.89 ppb	29,330 ppb	122.21 ppb	151 ppb	10.07 ppb	135.17 ppb
Soy-based formula (n = 63)	1.07 ppb	32,070 ppb	133.83 ppb	70 ppb	4.67 ppb	139.57 ppb

Adapted from Table 1 of Valentin-Blasini, 2011.
[1] Adjusted by dividing nitrate level by 240 based on Tonacchara 2004.
[2] Adjusted by dividing thiocyanate level by 15 based on Tonacchara 2004.
[3] Sum of perchlorate, adjusted nitrate, and adjusted thiocyanate levels.

3. We used the same method Valentin-Blasini and colleagues[5] at the Centers for Disease Control and Prevention used in their article to convert these levels in urine to an estimated perchlorate dose in µg/kg bw/day for the infants.

Table B. Estimated cumulative dose for infants younger than one year old based on nutrition source to perchlorate, thiocyanate and nitrates after adjusting for potency.

Nutrition source for infant	Perchlorate levels in urine	Perchlorate dose alone (µg/kg-bw/day)	Adjusted cumulative levels in urine for class	Estimated cumulative dose to class (µg/kg-bw/day)[1]
Breast milk (n = 92)	4.97 ppb	0.420	94.03 ppb	7.95
Cow milk-based formula (n = 51)	2.89 ppb	0.208	135.17 ppb	9.73
Soy-based formula (n = 63)	1.07 ppb	0.065	139.57 ppb	8.48

Adapted from Table 2 of Valentin-Blasini, 2011.
[1] Estimated cumulative dose to class = Perchlorate dose alone * (adjusted cumulative levels in urine for class / perchlorate levels in urine).

[5] Valentin-Blasini L, Blount BC, Otero-Santos S, Cao Y, Bernbaum JC, and Rogan WJ. Perchlorate exposure and dose estimates in infants. Environ. Sci. Technol. 2011, 45: 4127–4132, dx.doi.org/10.1021/es103160j

According to our assessment, infants younger than one year old could be exposed to this class of chemicals, namely perchlorate, nitrates and thiocyanates, at doses ranging from 7.95 to 9.73 µg/kg-bw/day. These cumulative exposure levels are 11 to 13 times greater than Ciba's acceptable daily intake (ADI) of 0.7 µg/kg-bw/day. And as we explain later, new scientific developments indicate that the ADI should be much lower which will make the risk of harm to developing brains even greater.

Concern #4: "FAP 4B4808 asserts that new information identifies hypothyroxinemia as a more sensitive indicator of perchlorate health effects than indicators considered by FDA when TOR 2005-006 became effective or the listing for potassium perchlorate in 21 CFR 177.1210 was promulgated. However, no information is provided as to the level of exposure to perchlorate which would result in hypothyroxinemia, nor is information provided demonstrating that the effect level considered by FDA in its original review is not sufficiently conservative to capture this endpoint."

In section I.D.1 of the petition, we explained that FDA's researchers[6] estimated that the level of exposure to perchlorate that would result in hypothyroxinemia was 4.2 µg/kg-bw/day for pregnant women consuming 75 µg/day of iodine. As noted in Appendix 4 of the petition, 10% of pregnant woman have iodine intakes lower than 75 µg/day.

The 4.2 µg/kg-bw/day level is essentially the lowest observed adverse effect level (LOAEL). To calculate the ADI from the Lumen *et al*. estimated LOAEL, the following safety factors are needed:

- 10X: Because the level is a LOAEL not a No Observed Adverse Effect Level (NOAEL). FDA typically uses a 10-fold safety factor to convert from a LOAEL to NOAEL.
- 10X: Because the level is based on human studies, the typical 10-fold intra-species safety factor is necessary.

Therefore, applying a safety factor of 100 to 1, the estimated ADI based on the model developed by FDA's researchers should be 0.042 µg/kg-bw/day. Using the corrected, but still underestimated exposure to perchlorate from use approved by TOR 2005-006, of 0.36 µg/kg-bw/day (see Concern #1 above), the estimated exposure would be more than 8.5 times greater than the ADI (0.36 ug/kg-bw/day > 0.042 ug/kg-bw/day) without considering the effect of thiocyanate and nitrates.

As we noted in the petition, FDA's model considered only the third trimester of pregnancy. The fetus is more vulnerable in the first trimester when its thyroid gland is developing; during this time, the fetus is entirely dependent on its mother for T4 (thyroxine) thyroid hormone for the brain to properly develop.

[6] Lumen A, Mattie DR, and Fisher JW. Evaluation of Perturbations in Serum Thyroid Hormones During Human Pregnancy Due to Dietary Iodide and Perchlorate Exposure Using a Biologically Based Dose-Response Model. 2013. *Toxicological Sciences* 133(2): 320–341.

These are not the only problems with the FDA's model. We provide extensive detailed analysis of its shortcomings in the petition. If FDA's scientists were to correct these problems, the LOAEL would be lower than the estimated 4.2 μg/kg-bw/day.

Concern #5: "The petition also references limited new epidemiological studies which examine the effect of perchlorate levels, but the petition does not utilize this data to determine an exposure level for perchlorates which is unsafe, nor correlate such a level to the allowed uses for perchlorate.

We reference the 2014 epidemiological study[7] because it confirms the conclusion by the Environmental Protection Agency's Science Advisory Board that perchlorate exposure is associated with harm to a child's brain development.

[7] Taylor PN, Okosieme OE, Murphy R, Hales C, Chiusano E, Maina A, Joomun M, Bestwick JP, Smyth P, Paradice E, Channon S, Braveman LE, Dayan CM, Lazarus JH, Pearce EN. Maternal perchlorate levels in women with borderline thyroid function during pregnancy and the cognitive development of their offspring; Data from the Controlled Antenatal Thyroid Study. J Clin Endocrinol Metab. 2014. Jul 24:jc20141901.

Attachment 2
Response to FDA's Concerns Raised in its November 24, 2014 Letter with May 18, 2014 Draft Perchlorate Food Additive Petition (PNC No. 001447)

The bold text below represents selected text from FDA's letter that represents the concerns raised by the agency. The plain text that follows represents our responses to FDA's concerns.

Concern #1 regarding format: "PNC 1447 does not provide the necessary data to support these assertions of deficiency or to address these deficiencies in a manner that would support a final conclusion that the allowed uses of perchlorate are unsafe." "Although PNC 1447 provides some information on exposure to and toxicity of perchlorates, the submission does not constitute a risk assessment as per 21 CFR 171.130 – that is, PNC 1447 does not 1) evaluate available toxicity data to identify a level of exposure to perchlorates that is not safe; and 2) then apply that level to perchlorate exposure to support an assertion that the allowed uses are unsafe. As a general recommendation, PNC 1447 should be restructured in the format of a risk assessment. The risk assessment should be a cohesive document which clearly states the conclusions of the assessment and also clearly delineates the relationship of the information presented to those conclusions."

We disagree that 21 CFR 171.130 requires a risk assessment. Paragraph (b) states that:

> "Any such petition shall include an assertion of facts, supported by data, showing that new information exists with respect to the food additive or that new uses have been developed or old uses abandoned, that new data are available as to toxicity of the chemical, or that experience with the existing regulation or exemption may justify its amendment or repeal. New data shall be furnished in the form specified in §§171.1 and 171.100 for submitting petitions."

In FAP No. 4B4808, we demonstrate that new information exists with respect to the food additives and that new data are available as to the toxicity and exposure of the chemical. We provide that new information in the proper format for submitting petitions and explain that a ban on the perchlorate as a food additive is the only appropriate means for FDA to fulfill its legal obligation to ensure the uses meet the safety standard of reasonable certainty of no harm.

Despite the absence of a requirement for a risk assessment, and reserving our objection to FDA's assertion that such an assessment is required of petitioners seeking to revoke a regulation as insufficient to ensure a reasonable certainty of no harm, we provide that information in Attachment 1.

Regarding the endpoint selection to identify the most sensitive toxicological effect in the petition, we appreciate FDA's clarification that "[s]uch an "appropriate" endpoint need not be the most sensitive endpoint; as such a comprehensive evaluation of the total toxicological information on the additive may not be necessary to demonstrate that the regulated use of a food additive is unsafe." Therefore, in Attachment 1, we demonstrate that iodide uptake inhibition is an appropriate endpoint and that hypothyroxinemia is the most sensitive endpoint. For iodide uptake inhibition, we use the reference dose developed by the U.S. Environmental Protection

Agency (EPA) in 2005. For hypothyroxinemia, we use the dose estimated by FDA as likely to cause harm to a fetus and apply appropriate safety factors to identify the level that is reasonably certain to cause no harm during fetal brain development. For each estimated acceptable daily intakes (ADI), we demonstrate that the likely exposures from the use of perchlorate as a food additive exceed the ADI after considering probable consumption in the diet and cumulative effect of pharmacologically-related substances as required by 21 CFR 170.3(i)(1) and (2).

Concern #2 regarding approach: "FDA notes two different approaches which NRDC's [petition] could apply to a risk assessment which asserts that the allowed food contact uses for perchlorates are unsafe: 1) apply the reference dose (RfD) for perchlorates, set by the Environmental Protection Agency (EPA) and referenced in PNC 1447, to perchlorate exposure; or 2) conduct a comprehensive evaluation to support the assertion that the allowed food contact uses for perchlorates are unsafe based upon an adverse health effect not accounted for by EPA's RfD, and apply that evaluation to perchlorate exposure."

In Attachment 1, we use both approaches to demonstrate that there is no longer a reasonable certainty of no harm from the use of perchlorate as a food additive.

Concern #3 regarding specific considerations: "Recommendations on the specific information provided in PNC 1447 are provided below. These recommendations are given in the context of the general recommendation discussed above: that PNC 1447 be re-structured in a format that 1) determines an exposure level to perchlorates that is unsafe and cites the specific data utilized to determine this level; 2) determines actual exposure to perchlorates and cites the specific data utilized to determine this exposure; and 3) correlates actual perchlorate exposure to the exposure level which is unsafe to support an assertion that the allowed uses are unsafe."

In Attachment 1, we provide the information in the format requested by FDA.

Concern #4 regarding hypothyroxinemia: "Should NRDC intend to assert that the allowed food contact uses for perchlorates are unsafe based upon a health effect not accounted for by EPA's RfD, they must demonstrate that this endpoint is suitable for the purposes of risk assessment by providing a comprehensive evaluation of available studies which evaluate exposure to perchlorates in the context of that endpoint. This comprehensive evaluation should present critical analysis of the key studies relied upon to reach a safety decision, as well as the criteria utilized when determining which studies are suitable for inclusion. The comprehensive evaluation should allow quantitative risk assessment by citing effect levels for the identified critical endpoint while providing justification for both the selection of that endpoint for safety assessment, and the derived effect level."

We incorporated by reference the critical analysis conducted by EPA's Science Advisory Board (SAB) in 2013 of the agency's 2005 RfD and its determination that hypothyroxinemia is the more sensitive and appropriate endpoint to protect the developing brain of a fetus or infant. We

also provided a critical analysis to FDA's model that relied on hypothyroxinemia as an endpoint. Since all other studies we found supported and reinforced SAB's conclusion, we believe that the information we provide is sufficient.

In Attachment 1, we provide the information in the format requested by FDA.

Concern #5 regarding additional safety factors to protect children: "PNC 1447 asserts that, due to the disproportionate impact of perchlorate exposure on infant health, additional safety factors beyond the 100-fold safety factor recommended in 21 CFR 170.22 should be applied when evaluating this exposure. FDA notes that the safety factor discussed in §170.22 deals with the application of experimental animal data to man – EPA's RfD is derived from human data, so 21 CFR 170.22 does not apply. FDA also notes that, in addition to other conservatisms, EPA utilized a 10-fold safety factor when determining the RfD to account for pregnant women and fetuses. Should NRDC intend to apply additional safety factors to EPA's RfD, or should NRDC utilize additional safety factors when determining an unsafe exposure level for perchlorates based upon an endpoint not accounted for in EPA's RfD, the basis for those additional safety factors must be supported."

We agree that the EPA used a 10-fold safety factor to protect fetuses and children in a manner that is consistent with Executive Order No. 13045. We also agree that the use was appropriate.

The 100-fold safety factor adopted by FDA in 1971 is the combination of a 10-fold factor to convert from a no observed adverse effect level (NOAEL) in an animal study to humans and a 10-fold factor to account for intraspecies variations among humans. In their risk assessments, FDA and EPA typically add an additional 10-fold factor to convert from a lowest observed adverse effect (LOAEL) to a NOAEL. In the Food Quality Protection Act of 1996, Congress directed EPA, pursuant to the recommendations of the National Academy of Sciences, to generally add an additional 10-fold safety factor to risk assessments under that Act to take into account the potential for pre- and post-natal toxicity and the completeness of the toxicology and exposure databases.[8] Such an additional safety factor is appropriate here due to the lack of complete data on pre- and post-natal toxicity and exposure.

As explained in Attachment 1, we maintain that a 100-fold safety factor must be applied to the LOAEL of 4.2 µg/kg-bw/day for human fetuses for hypothyroxinemia that FDA developed in its 2013 publication cited in the petition. This safety factor consists of 10-fold factor to convert from the LOAEL to the NOAEL and 10-fold factor to account for intraspecies variation.

We raised the issue of the 1997 Executive Order in the petition because we have not seen FDA specifically address it in its guidance, policies or procedures. In the context of this petition, additional safety factors beyond the 100-fold are necessary to protect children's brains because:

1. a pregnant woman's short-term exposure to perchlorate can cause irreversible harm to the fetal brain if the woman has low iodine intake, and

[8] EPA, Determination of the Appropriate FQPA Safety Factor(s) in Tolerance Assessments, 2002. See http://www.epa.gov/oppfead1/trac/science/determ.pdf.

2. FDA's model of pregnant women on the third trimester (the least sensitive period) has a number of problems that makes it not sufficiently protective of pre-natal and post-natal exposure to perchlorate.

Concern #6 regarding expansion by FDA of the original TOR request: "The incoming request for TOR 2005-006 listed an intended use for perchlorate monohydrate of 4% in antistatic agents. The antistatic agent would be used in finished plastic at a level of 30%, and the finished plastic would be used in contact with non-fatty dry foods (i.e., Food Type VIII) only. This is the intended use that was reviewed by the TOR committee. This intended use was inadvertently expanded in the final letter for TOR 2005-006, and later to the Agency's weblisting for the TOR, to include the use of the food contact substance in all food packaging at a use level of 4% in the finished packaging, with the finished packaging used in contact with all dry foods (i.e., Food Types VII and IX). FDA acknowledges that this expansion was in error. FDA will take steps to correct this error and list the use as reviewed by the TOR committee."

We thank FDA for acknowledging the error that we raised in May 2014. As of November 27, 2014, the error remains on the website. We remain confused why such an obvious error has not yet been corrected six months after we first alerted the agency.

Concern #7 regarding consideration of perchlorate exposure from the use listed in 21 CFR 177.1210: "PNC 1447 asserts that TOR 2005-006 did not account for exposure to perchlorates from the listing of potassium perchlorate in 21 CFR 177.1210. FDA notes that, due to the low use level of potassium perchlorate (1%) and assumptions normally applied to closure sealing gasket applications, the exposure to potassium perchlorate was reported as virtually nil when its listing was promulgated. As an exposure of virtually nil would have a negligible impact on the exposure calculated for TOR 2005-006, it was not necessary for the TOR committee to account for this exposure in allowing the TOR exemption for sodium perchlorate monohydrate to become effective."

One percent is not a "low use level" as FDA asserts. It is equivalent to 10,000,000 µg/kg of gasket material. For a chemical that FDA acknowledged in 2005 has a reference dose of 0.7 µg/kg-bw/day, it is arbitrary and capricious that the agency can disregard the exposure, especially when the material may be used in contact with aqueous solutions in which perchlorate can readily dissolve.

We find it disconcerting that FDA would rely on a claim of "virtually nil" in a petition submitted in 1962. Our ability to detect perchlorate and our understanding of the risk it poses to children goes well beyond claims made four decades earlier: claims that the agency does not make publicly available (as explained in Attachment 1). In short, FDA is basing its assertion that exposure to perchlorate from use listed in 21 CFR 177.1210 "would have a negligible impact on the exposure calculated for TOR 2005-006" on "assumptions" that the agency does not disclose in its guidance.

Based on FDA's response to FOIA Request No. 2014-1324 (Appendix 3 of the petition), there is no evidence that FDA considered exposure from sealing gaskets allowed by 21 CFR 177.1210 when it approved TOR No. 2005-006. For FDA to now assert that it was not necessary despite the Congressional mandate to consider the probable total consumption of the substance in the diet is arbitrary and capricious.

Concern #8 regarding application of use level to migration assumptions for Food Type VIII: "PNC 1447 notes that TOR 2005-006 utilizes FDA's standard assumption of 50 ppb for migration from packaging into Food Type VIII. However, the PNC also asserts that the TOR then mistakenly applied the use level of the food contact substance (FCS – in this instance the sodium perchlorate monohydrate) to this migration assumption. FDA notes that the 50 ppb assumption is an assumption of total migration from packaging into Food Type VIII. In the absence of contradictory data, the contribution of any packaging component to that 50 ppb is assumed to be commensurate to the percentage of that component in the packaging. As such, it is appropriate to correlate the contribution of a FCS to the 50 ppb total migration assumption to the percentage of the FCS in the finished packaging (e.g., in the case of TOR 2005-006, to multiply 50 ppb by the percent of the sodium perchlorate monohydrate in the finished polymer: 1.2 percent)."

As described in the petition, FDA's guidance says that the 50 ppb migration value may be assumed for the food contact substance. According to 21 CFR 170.3(e)(3), "*A food contact substance* is any substance that is intended for use as a component of materials used in manufacturing, packing, packaging, transporting, or holding food if such use is not intended to have any technical effect in such food." Subparagraph (e)(2) states that the "[u]se of a substance in a food contact article (e.g. food-packaging or food processing equipment) whereby the substance migrates, or may reasonably be expected to migrate, into food at such levels that the use has been exempted from regulation as a food additive under §170.39, and food contact substances used in accordance with a notification submitted under section 409(h) of the act that is effective." This statement makes clear that a food contact substance is a component of a food contact article. FDA defines a food contact article as "the finished film, bottle, dough hook, tray, or whatever that is formed out of the FCM."[9]

Therefore, FDA clearly intended the 50 ppb assumption to apply to only the food contact substance and not the entire food contact article. At a minimum, FDA is obligated to justify its deviation from its own guidance. The fact that FDA has previously ignored or deviated from its published guidance without a clear rationale or explanation only raises questions about the agency's past determinations.

Regarding the assumption, FDA's own expert has stated that the 50 ppb assumption for dry food has been contradicted by evidence from European Union lab studies and has publicly acknowledged that the agency needs to bring its science into the 21st century. There is no scientific justification for taking an already arbitrary assumption dating back decades and then

[9] FDA, Food Ingredients and Packaging Terms, http://www.fda.gov/Food/IngredientsPackagingLabeling/Definitions/default.htm. Accessed November 27, 2014.

arbitrarily reducing it again by multiplying the 50 ppb by the concentration of the substance in the packaging.

We stand by the calculations made in the petition and Attachment 1.

Concern #9 regarding reconsideration of the 50 ppb total migration assumption for Food Type VIII: "PNC 1447 notes that FDA has previously stated that the basis for the 50 ppb total migration assumption for Food Type VIII should be reviewed for accuracy. However, PNC 1447 provides no data which demonstrates that this assumption is not appropriately conservative, nor does the PNC propose a new approach, supported by data, that would provide a more accurate exposure estimate."

"PNC 1447 further asserts that as the function of the FCS in packaging is to "chemically interact" with dry food it is more likely to migrate to dry foods than other additives. It is unclear how a technical function of conductivity enhancement would be expected to result in increased migration into food. To take such an interaction into account NRDC would need to provide information to support this assertion and also quantify its effect on migration."

"If NRDC intends to present an exposure to perchlorate using assumptions other than those specified in FDA's Chemistry Guidance document they should specify those assumptions and provide a basis for their use."

In 2011, FDA's own expert has stated that the 50 ppb assumption for dry food has been contradicted by evidence from European Union lab studies and has publicly acknowledged that he hopes "we'll be able to bring our science into the 21st century."[10] Unfortunately in the intervening three years, the agency has not published revised guidance or explained the shortcomings it admitted to several years ago. It seems ironic for FDA to expect the petitioners to present evidence that the agency has chosen not to make publicly available. We suggest the agency consult with its own expert.

Much of the chemical details were redacted from the FOIA so we have little choice but to read between the lines. We know that sodium perchlorate is highly soluble in water. At room temperature, it is six times more soluble than sodium chloride.[11] It is unlikely that is chemically bound inside the non-polar plastic polymer. Rather it is gathers on the plastic's surface where it would be most useful as an anti-static agent. As it moves away from the surface of the plastic, it is much less effective in interacting with the dry good to neutralize the charge because the Coulombic interaction declines as the square of the distance between the ions.

If the dry food is a hydrogen-bonded structure such as starch, the sodium perchlorate is likely to strongly interact with these hydrogen bonds, just as it does in water. When you combine a relatively weak interaction with the plastic packaging, the energy required to draw the perchlorate ions away from the surface would be small.

[10] Perchlorate Petition FAP No. 484808, p17.
[11] Wikipedia, Solubility Table, accessed December 4, 2014 at http://en.wikipedia.org/wiki/Solubility_table.

In essence, perchlorate is not a typical inert chemical in the plastic. Its function in the plastic is to interact with the food to neutralize the static charge that can build-up in a dry powder. According to FDA's response to FOIA Request No. 2014-1324, the purpose of the perchlorate in the plastic was to provide a "conductive network within the polymer matrix. This conductive network dissipates any acquired static charge. Sodium perchlorate monohydrate is used in the [redacted] formulation as a 'conductivity enhancer.'" [12] To conduct a static charge, the dry food particles with a positive charge must be close to or contact the perchlorate in the plastic to neutralize the charge. When this occurs, the perchlorate is drawn from the plastic into the dry food. Therefore, the 50 ppb assumption may be unrealistically low. Unfortunately, FDA apparently failed to consider this possibility when it approved TOR No. 2005-006.

Concern #10 regarding use in all antistatic agents: "PNC 1447 asserts that FDA expanded TOR 2005-006 beyond the specific antistatic agent and finished polymer discussed in the original incoming. FDA notes that the exposure calculations provided in TOR 2005-006, and considered by the TOR committee, are inclusive of the use of the FCS in all polymer resins at a level of 1.2 percent. It should also be noted that the assumptions underlying the exposure calculation accounts for the FCS capturing 100% of the market - that is, that the FCS will be added to all polymeric packaging for food type VIII. As such it is appropriate to allow the use of the FCS without limitation as to the specific antistatic agent or finished polymer – neither of these factors will affect the calculated exposure."

We understand. It is appropriate to allow uses of perchlorate without limitation if the consumption factors are appropriate. However, as we noted in the petition, the consumption factors are based on only final product packaging and not the raw material packaging.

Concern #11 regarding use in bulk packaging: "PNC 1447 asserts that FDA did not consider the use of the FCS in packaging for foods prior to final packaging for sale to the consumer. The PNC notes that 1) the limitation language for TOR 2005-006 allows the use of the FCS at any point in the production chain as well final packaging for sale to the consumer; and 2) the consumption factor utilized in the exposure calculation only accounts for the use of the FCS in packaging for sale to the consumer."

"FDA agrees that the term "finished article" or "finished polymer" does not delineate between food packaging pre- or post-sale to the consumer. Rather, "finished" refers to the article or polymer in the form in which it will contact food. As such, the use limitations for TOR 2005-006 allow the use of the FCS in contact with Food Type VIII at any point in the production chain as well final packaging for sale to the consumer."

"FDA also agrees that the consumption factors published in our Chemistry Guidance Document, and the specific consumption factor utilized in the exposure calculation for TOR 2005-006, are mainly based on data specific to packaging for sale to the consumer. However, FDA also notes that the surface to volume ratio of packaging in general is

[12] See page 42 of the petition.

significantly higher for packaging for sale to the consumer (FDA assumes that each in^2 of packaging for consumers is in contact with 10 grams of food) than packaging of bulk ingredients for use in food production processes. As migration is a diffusion based process, this difference in surface area to volume ratio means that the vast majority of consumer exposure to a FCS is expected to be a result of the use of the FCS in packaging for sale to the consumer."

"If NRDC intends to present an argument that the use of the sodium monohydrate in bulk packaging for Food Type VIII invalidates the use of the consumption factor utilized in the exposure calculations for TOR 2005-006, they would need to demonstrate with supporting data that the use of the FCS in packaging of bulk ingredients for use in food production processes would result in an appreciable increase in exposure than that accounted for by basing the exposure calculation on the use of the FCS in packaging for sale to the consumer."

There are three serious flaws in FDA's logic. First, as noted above, the migration of perchlorate into the dry food may not simply be a diffusion-based process since the charged dry food particles are attracted to the perchlorate where the charge can be dissipated.

Second, final packaging represents only a single, time-limited interaction. In contrast, the various dry ingredients are likely repeatedly contacting the perchlorate-laden packaging throughout the manufacturing process. While the contact between the food in bulk packaging and the package itself is less than in final product packaging, it may be more than offset by the repeated exposure of the ingredients to the perchlorate.

Third, the consumption factor is based only on the amount of final food products that consist of dry food. However, as we noted in the petition, ingredients are often stored and handled as dry food where they can be stored longer and shipped more efficiently than wet food. Therefore, FDA's consumption factor fails to consider the perchlorate migrating into food products that are not considered dry but were made from dry ingredients.

Concern #12 regarding repeat use: "PNC 1447 incorrectly assumes that the safety review for TOR 2005-006 did not consider repeat use applications, as the TOR did not present information consistent with FDA's recommendations for repeat use articles as presented in Appendix II, Section 4 of our Chemistry Guidance document. The PNC also infers that the presence of the FCS in repeat-use bulk packaging further increases the safety concern for that use. NRDC should be aware that the cited recommendations from FDA's Guidance document are specific to articles intended for repeat use applications only, and that FDA considers single use applications to be "worst-case" – that is, they encompass repeat use applications. The reasoning behind this is that most finished articles are assumed to have a finite reservoir of migratable material. For repeat use articles it is typically assumed that reservoir is depleted over the lifetime of the article – as such FDA's recommendations for additives to repeat use articles account assume that 100% of the additive will migrate into food and that this migration will occur over the total volume of food the article will see during its use lifetime. For single use articles it is assumed that all migration occurs in a

single use and the article is disposed of after every use and a new article takes its place, with a new reservoir of migratable material. As such, the exposure calculated for a single use article encompasses the exposure which would occur from a repeat use article under the same use conditions."

"In short, the use of the FCS in repeat use food packaging was considered in FDA's review of TOR 2005-006, and the listed limitations for that TOR exemption appropriately allow this use. In the opinion of FDA, the fact that some of the bulk packaging which contain the FCS may be used repeatedly further reduces the potential that these uses would contribute significantly to the cumulative exposure (as discussed in Section II .vi of this correspondence) to the FCS from its use in such packaging."

FDA appears to be assuming that perchlorate is chemically bound to the plastic. Given its structure, there is no reason to think it is chemically integrated into non-polar plastic such as polypropylene, polystyrene, or polyethylene. Like a plasticizer, it may be released as the plastic degrades or is flexed.

Concern #13 regarding use in packaging for infants: "PNC 1447 correctly states that the exposure calculation presented in TOR 2005-006 utilizes assumptions specific to adult consumers, and that the limitation language for the TOR allows the use of the FCS in packaging intended for infant food. At the time that TOR 2005-006 became effective, The Office of Food Additive Safety (OFAS) utilized a safety assessment paradigm which considered the safety of FCSs used in contact with infant food as part of a lifetime exposure/safety assessment. However, OFAS currently reviews the use of FCSs on a case-by-case basis to determine if an exposure/safety assessment specific to infants is necessary to support the intended use of a FCS. In PNC 1447, NRDC asserts that exposure to perchlorates has an inordinate effect on the health of infants. If NRDC contends that sodium monohydrate perchlorate is used in food packaging intended for infants as well as adults, NRDC could calculate exposure separately for these subpopulations and conduct a safety assessment for each exposure."

"Further information on the various assumptions recommended for calculation of adult and infant exposure is provided in Attachment 1 to this correspondence."

"Please note that, as the calculation provided in TOR 2005-006 was appropriate for FDA's guidelines at the time of consideration, any recommendations as a result of this calculation would need to be correlated to a safe level of exposure to perchlorate, rather than FDA's TOR requirement of 0.025 µg/kg bw/day."

We provide the calculation for infants in Attachment 1. In 2005, when FDA made its TOR decision, FDA apparently had information on perchlorate in infant formula.[13]

[13] FDA, http://www.fda.gov/Food/FoodborneIllnessContaminants/ChemicalContaminants/ucm077615.htm.

Concern #14 regarding exposure to perchlorates from the use listed in 21 CFR 177.1210: "The proposal in PNC 1447 to remove the allowances for perchlorate is based upon the assertion that the allowed food contact uses for perchlorates are unsafe. However, PNC 1447 does not provide information on exposure to potassium perchlorate as a result of its use in sealing gaskets for food containers in support of its assertion that the use listed in 21 CFR 177.1210 is unsafe. Rather, the PNC states that this information is in FDA's files and as such it is not necessary for such information to be provided. PNC 1447 also does not provide a risk assessment for this use of perchlorates, but rather includes only a statement that such use is "unnecessary" due to perchlorate's toxicity. As stated earlier in this correspondence, in the FAP process the onus of demonstrating safety is on the petitioner – to amend a regulation based upon safety concerns the petitioner must demonstrate that the exposure from the allowed use is unsafe. To not provide information on the exposure from the regulated use which the petition seeks to amend would only be acceptable under 21 CFR 170.130 if an accompanying risk assessment adequately demonstrated that any exposure from the regulated use is unsafe (for further information see the discussion in Section II.f of this correspondence)."

"As stated in Section II.a.ii. of this correspondence, FDA considered an exposure of virtually nil to potassium perchlorate from its use in sealing gasket applications when promulgating the listing in 21 CFR 177.1210. If NRDC intends to assert that the use for potassium perchlorate listed in 21 CFR 177.1210 is unsafe, they would need to either present an adequate risk assessment demonstrating that any exposure to perchlorates from this use is unsafe (see the discussion in Section II.f of this correspondence) or provide adequate information which supports a conclusion that FDA's assumption of virtually nil is incorrect, calculate a new exposure, and provide an adequate risk assessment demonstrating that this exposure is unsafe."

For our response, see Concern #2 in Attachment 1 and Concern #7 in this attachment.

Concern #15 regarding exposure to perchlorate from contamination of the food supply: "In the FAP process, the onus of demonstrating safety is on the petitioner. If NRDC intends to present a risk assessment based upon the 90th percentile range of exposure to perchlorates in the diet, NRDC should either support its generalization that the 90th percentile is expected to be twice the mean, or they should review available information to determine 90th percentile exposure to perchlorate in food. If NRDC intends to utilize the provided levels of perchlorates in infant formula they should provide an exposure calculation specific to infants based upon this information and correlate such exposure to a level which is unsafe as part of their risk assessment. As the assertion in PNC 1447 is that the allowed food contact uses for perchlorates are unsafe, it is recommended that NRDC quantify cumulative perchlorate exposure accounting for both contamination and that resulting from effective allowances for food contact use."

For our response, see Concern #3 in Attachment 1.

Concern #16 regarding exposure to pharmacologically-related substances: "PNC 1447 asserts that 21 U.S.C. 348(c)(5) and 21 CFR 170.3(i) also require FDA to consider the cumulative dietary exposure to pharmacologically related substances when evaluating food additive safety. The PNC notes that thiocyanate and nitrates share a common mechanism of toxicity with perchlorate, presents survey data for urine levels as evidence of infant exposure to these substances, and notes that there are multiple regulated food additive uses for nitrates. However, no attempt is made to quantify exposure to thiocyanates or nitrates in the diet (either from regulated food additive uses or contamination of the food supply), or the efficacy of these substances towards the common mechanism of toxicity. The PNC also does not determine a level of "perceived" exposure to perchlorate that is unsafe as a result of cumulative exposure to perchlorate, thiocyanates, and nitrates."

"It should be noted that FDA has not reached a conclusion on the applicability of exposure to nitrates and thiocyanates to the safety of allowed food contact uses for perchlorates. However, NRDC should specify if the discussion on thiocyanate and nitrates is intended to lend general support to conservatisms utilized in the estimation of a level of exposure to perchlorates that is unsafe, or to support an assertion that the allowed food contact uses of perchlroates is unsafe based on the "perceived" level of perchlorate in the diet as a result of cumulative exposure to perchlorate, thiocyanates, and nitrates. If the "perceived" level of perchlorate in the diet as a result of cumulative exposure to pharmacologically related substances is necessary to support an assertion that the allowed food contact uses for perchlorates are unsafe, further information on exposure, efficacy, and correlation of exposure of these proposed pharmacologically related substances to a "perceived" level of exposure to perchlorate that is unsafe should be provided. Such information should be presented in the form of a risk assessment."

For our response, see Concern #3 in Attachment 1.

Concern #17 regarding environmental requirements" "PNC 1447 cites a claim of categorical exclusion under 21 CFR 25.32(m) and states that no extraordinary circumstances exist which would require submission of an Environmental Assessment or Environmental Impact Statement. FDA notes that the prohibition of a FCS may result in the use of alternative substances. We request that NRDC expand on the statement of no extraordinary circumstances to include a discussion of the environmental impacts that may occur from the use of replacement products for the FCSs which NRDC is proposing to be removed from the CFR and from the list of effective TOR exemptions. This could be addressed by noting that such replacement products would be food additives and as such would require review by FDA: any submission to FDA for the use of such replacement products would require an evaluation of the environmental impacts of those replacement products as required under the National Environmental Policy Act (NEPA). Pursuant to 21 CFR 25.15(a) this evaluation would be required to be presented as either a either a claim of a categorical exclusion (i.e., 21 CFR Part 25.30 or 25.32) or an Environmental Assessment (i.e., as described under 21 CFR 25.40).

"PNC 1447 requests that FDA promulgate a new regulation in 21 CFR 189 Subpart D to

prohibit the use of perchlorate in antistatic agents for use in food contact articles. In general, a regulation to prohibit the food additive use of a substance is appropriate only if an adequate risk assessment demonstrates that any exposure to the substance from the specified food additive use is not safe (for example, if the substance is currently present in the food supply as a contaminant at levels which are unsafe, or if the substance is a carcinogen as defined in Section 409(c)(3)(A) of the Food, Drug and Cosmetic Act). It is recommended that NRDC provide information to this effect should they intend to request FDA to promulgate such a regulation."

We addressed this issue in FAP No. 4B4808 we submitted on October 15, 2014.

Concern #18 regarding proposal to promulgate a new regulation in 21 CFR 189 to prohibit the use of perchlorates: "PNC 1447 requests that FDA promulgate a new regulation in 21 CFR 189 Subpart D to prohibit the use of perchlorate in antistatic agents for use in food contact articles. In general, a regulation to prohibit the food additive use of a substance is appropriate only if an adequate risk assessment demonstrates that any exposure to the substance from the specified food additive use is not safe (for example, if the substance is currently present in the food supply as a contaminant at levels which are unsafe, or if the substance is a carcinogen as defined in Section 409(c)(3)(A) of the Food, Drug and Cosmetic Act). It is recommended that NRDC provide information to this effect should they intend to request FDA to promulgate such a regulation."

Based on the evidence we submitted in the petition and in these supplementary materials, we ask that FDA:

1. Revoke its 2005 approval of "threshold of regulation" (TOR) No. 2005-006 allowing as much as 1.2% sodium perchlorate monohydrate in dry food packaging;[55]
2. Promulgate a new 21 CFR § 189.301 prohibiting the use of perchlorate as a conductivity enhancer in the manufacture of antistatic agents to be used in food contact articles; and
3. Remove potassium perchlorate as an allowed additive in sealing gaskets for food containers in existing 21 CFR § 177.1210.

Exhibit C

Benjamin C. Blount et al.
Perchlorate Exposure of the U.S. Population, 2001-2002 (2007)

Journal of Exposure Science and Environmental Epidemiology (2007) 17, 400–407

www.nature.com/jes

Perchlorate Exposure of the US Population, 2001–2002

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Perchlorate is commonly found in the environment and can impair thyroid function at pharmacological doses. As a result of the potential for widespread human exposure to this biologically active chemical, we assessed perchlorate exposure in a nationally representative population of 2820 US residents, ages 6 years and older, during 2001 and 2002 as part of the National Health and Nutrition Examination Survey (NHANES). We found detectable levels of perchlorate ($>0.05\,\mu g/l$) in all 2820 urine samples tested, indicating widespread human exposure to perchlorate. Urinary perchlorate levels were distributed in a log normal fashion with a median of $3.6\,\mu g/l$ ($3.38\,\mu g/g$ creatinine) and a 95th percentile of $14\,\mu g/l$ ($12.7\,\mu g/g$ creatinine). When geometric means of urinary perchlorate levels were adjusted for age, fasting, sex and race-ethnicity, we found significantly higher levels of urinary perchlorate in children compared with adolescents and adults. We estimated total daily perchlorate dose for each adult (ages 20 years and older), based on urinary perchlorate, urinary creatinine concentration and physiological parameters predictive of creatinine excretion rate. The 95th percentile of the distribution of estimated daily perchlorate doses in the adult population was $0.234\,\mu g/kg$-day [CI 0.202–0.268 $\mu g/kg$-day] and is below the EPA reference dose ($0.7\,\mu g/kg$-day), a dose estimated to be without appreciable risk of adverse effects during a lifetime of exposure. These data provide the first population-based assessment of the magnitude and prevalence of perchlorate exposure in the US.
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Keywords: *perchlorate, human, urine, exposure assessment, biomonitoring, NHANES.*

Introduction

Perchlorate is an inorganic anion that is synthesized primarily as ammonium perchlorate for use as an oxidant in solid rocket propellant (Mendiratta et al., 1996). Perchlorate can also form naturally in the atmosphere (Dasgupta et al., 2005) leading to trace levels in precipitation and is concentrated geologically in some locations such as regions of west Texas (Dasgupta et al., 2005) and northern Chile (Urbansky et al., 2001). A combination of human activities and natural sources has led to the widespread presence of perchlorate in the environment. The US Environmental Protection Agency (EPA) included perchlorate on the Drinking Water Candidate Contaminant List and requires public water systems to monitor and report perchlorate in drinking water (EPA, 1998, 1999). As of November 2005, perchlorate was detected at least once in 4.1% of community drinking water systems from 26 different states and two territories, with levels ranging from the method detection limit of $4\,\mu g/l$ to a maximum at $420\,\mu g/l$ (EPA, 2005b). Perchlorate exposure from the diet is likely, due to the contamination of vegetable crops irrigated with perchlorate-containing water (Yu et al., 2004) or fertilized with Chilean nitrate (Urbansky et al., 2001). Milk can also contain perchlorate, possibly from perchlorate contamination of forage crops (Kirk et al., 2003; Capuco et al., 2005).

The prevalence of trace levels of perchlorate in the environment leads to human exposure. Environmental perchlorate exposure is of possible health concern because much larger doses of perchlorate have been shown to competitively inhibit iodide uptake by the thyroid gland (Wyngaarden et al., 1953; Greer et al., 2002); sustained inhibition of iodide uptake could potentially lead to hypothyroidism. The thyroid plays a crucial role in energy homeostasis and neurological development. Hypothyroidism can lead to metabolic problems in adults and abnormal development in children (Braverman and Utiger, 2000).

Useful human exposure data can be obtained by directly measuring levels of an environmental toxicant in the human body (i.e., biomonitoring) (Pirkle et al., 1995). Urinary perchlorate provides a reasonable measure of human exposure because 70–95% of a perchlorate dose is excreted unchanged in the urine with a half-life of ~ 8 h (Anbar et al., 1959; Lawrence et al., 2000; Greer et al., 2002). Sensitive and selective methods are needed to quantify perchlorate anion in urine in the presence of much higher levels of chloride, sulfate and phosphate anions. We recently developed a sensitive and

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[1]The findings and conclusions in this report are those of the authors and do not necessarily represent the views of the Centers for Disease Control and Prevention

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selective analytical method capable of quantifying perchlorate in human urine as low as 0.05 μg/l (Valentin-Blasini et al., 2005). In this paper, we have applied this method to measure perchlorate in urine samples collected from a representative sample of 2820 persons, aged 6 years and older, as part of the 2001–2002 National Health and Nutrition Examination Survey (NHANES).

Subjects and methods

Study Design

NHANES is conducted by the National Center for Health Statistics of the Centers for Disease Control and Prevention (CDC). This survey is designed to assess the health and nutrition status of the civilian, non-institutionalized US population (CDC, 2004). The sampling design for NHANES is based on a complex multistage probability design, which includes selection of primary sampling units (counties), household segments within the counties and finally sample persons from selected households. Data were collected through a household interview and a standardized physical examination, which was conducted in a mobile examination center. In NHANES 2001–2002, urine and serum specimens were collected from each participant, aged 6 years and older, during one of three daily scheduled examination periods (i.e., morning, afternoon and early evening). Sociodemographic information and medical histories of the survey participant and the family were collected during the household interview. NHANES 2001–2002 was conducted in 30 locations throughout the US (CDC, 2004), with a random one-third subsample consisting of 2892 NHANES study participants collectively representing the civilian, non-institutionalized US population, aged 6 years and older. Overall, the survey interview response rate was 83.9% and the exam response rate was 79.6%. Perchlorate measurements were conducted on the 2820 study participants with available urine specimen.

Demographic Variables

Sociodemographic data were self-reported by study participants. Age was grouped as children (6–11 years), adolescents (12–19 years) and adults (≥20 years), consistent with the *Third National Report on Human Exposure to Environmental Chemicals* (CDC, 2005). Similarly, a race/ethnicity variable was derived from self-reported questionnaire data, resulting in four categories of race/ethnicity: non-Hispanic white, non-Hispanic black, Mexican Americans and others. Non-Hispanic blacks and Mexican Americans were over-sampled as part of NHANES; urinary perchlorate data were weighted to adjust for this oversampling (CDC, 2004). Data are not presented separately for the 'other race/ethnic groups' because of the small number of individuals in this group; however, these individuals are included in the analyses of the overall population and age and sex population groups.

Table 1. Characteristics of the population with urinary perchlorate measured, US, NHANES[a] 2001–2002.

Category	(n)	(%)
Age		
6 years and over	2820	100.0
6–11 years	374	13.3
12–19 years	828	29.4
20 years and over	1618	57.4
Sex		
Female	1485	52.7
Male	1335	47.3
Race/ethnic groups		
Non-Hispanic White	1228	43.5
Non-Hispanic Black	681	24.1
Mexican American	708	25.1
Other race/ethnic groups	203	7.2

[a]National Health and Nutrition Examination Survey.

Table 1 provides the study population characteristics by age, sex and race-ethnicity.

Laboratory Methods

During the physical examinations, spot urine specimens were collected from participants, aliquoted, and stored cold (2–4°C) or frozen until shipment. Samples collected for perchlorate measurements were shipped on dry ice to the CDC's National Center for Environmental Health. Urine samples were stored frozen (−70°C) for 3–4 years. Experiments evaluating storage at −70°C for >2 years indicate no changes in urinary perchlorate levels under these storage conditions. Urinary perchlorate was analyzed using the method of Valentin-Blasini et al. (2005). Briefly, 0.5 ml of urine was spiked with an isotopically labeled internal standard and diluted 1:1 with deionized water. This solution was subsequently analyzed using ion chromatography–electrospray ionization–tandem mass spectrometry. Perchlorate was quantified based on the peak area ratio of analyte to stable isotope-labeled internal standard. Two quality control pools were analyzed in each analytical batch with unknown samples. Reported results met the accuracy and precision specifications of the quality control/quality assurance program of the Division of Laboratory Sciences, National Center for Environmental Health, CDC (similar to rules outlined by Westgard (Westgard et al., 1981)). During analysis of urine for perchlorate, we analyzed these two quality control pools multiple times ($n = 117$) with an interday precision of 2.8% relative SD at 71 ± 2.0 μg/l and 3.0% relative SD at 4.7 ± 0.14 μg/l. In addition, reproducibility of the assay was evaluated by re-analysis of 5% of the samples, yielding an average relative percent difference of 1.5% (95% confidence interval (CI) 1.1%–2.0%). Absolute assay accuracy was verified by the blind analysis of four

different perchlorate reference solutions (AccuStandard, New Haven, CT, USA) prepared in synthetic urine (CST Technologies, Great Neck, NY, USA). We assessed perchlorate contamination by lot screening all reagents and analyzing blanks with each batch of unknowns; no contamination problems were identified.

Urinary creatinine concentrations were determined using an automated colorimetric method on a Beckman Synchron AS/ASTRA clinical analyzer (Beckman Instruments Inc., Brea, CA, USA) at the Coulston Foundation (Alamogordo, NM, USA) in 2001 and Collaborative Laboratory Services (Ottumwa, IA, USA) in 2002 (CDC, 2004). Perchlorate concentrations were adjusted using creatinine concentrations to correct for variable water excretion rates in the spot urine samples.

Estimation of Total Daily Perchlorate Dose

We estimated total daily perchlorate dose based on measured spot urine perchlorate and creatinine concentrations, and estimated daily creatinine excretion rate (g/day) computed from each individual's measured weight, height, age and sex. Specifically, daily creatinine excretion was calculated for adults based on the Cockcroft–Gault equation (Cockcroft and Gault, 1976) as modified by Mage et al. (2004), where $k = 1.93$ for males and 1.64 for females:

$$\text{Adult } g\,\text{creatinine/day} = 10^{-6} * k * (140 - \text{age[yr]}) * \text{wt(kg)}^{1.5} * \text{ht(cm)}^{0.5}$$

Daily perchlorate dose was then estimated using the following formula:

$$\text{Perchlorate dose} = \mu\text{g perchlorate/g urinary creatinine} * \text{g creatinine/day} * 1/\text{wt(kg)}$$

Daily perchlorate dose is not presented for children and adolescents due to the limited validation of formulas for these age groups. Also, we assumed that 100% of perchlorate intake is absorbed and excreted unmetabolized in the urine (Anbar et al., 1959; Lawrence et al., 2000). This assumption leads to underestimation of perchlorate dose in lactating women because perchlorate is secreted in human milk (Capuco et al., 2005; Kirk et al., 2005) as well as urine. Based on questionnaire data, only 26 study participants were actively lactating during the study period.

Statistical Analysis

Univariate and regression analysis of perchlorate data used survey-specific sample weights to account for differential probabilities of selection and non-response. Geometric means and percentiles of urinary perchlorate were calculated using SUDAAN PROC DESCRIPT (SUDAAN v. 9.0.0, Research Triangle Institute, Research Triangle Park, NC, USA), with CI estimated based on the method of Korn and Graubard (1998). SUDAAN PROC REGRESS was used for analysis of covariance (ANCOVA) of perchlorate levels with predictor variables of age group, sex, race/ethnicity, fasting and urinary creatinine. The ANCOVA model used to calculate the adjusted geometric means included a continuous variable for urinary creatinine and categorical variables defining age (6–11, 12–19, 20+ years), fasting (<8 h since last meal or ≥8 h), sex and race/ethnicity groups. Separate adjusted means are provided for sex by race/ethnicity groups because of significant interaction between these two groups. Estimates of the CI were calculated using the Taylor series linearization method (SUDAAN Users Manual, 2001).

Table 2. Geometric means and selected percentiles of urinary perchlorate concentrations (μg/l) for the US population aged 6 years and older, NHANES[a] 2001–2002.

			Selected percentiles						
Category	N	GM[b]	5th	10th	25th	50th	75th	90th	95th
Total	2820	3.54 (3.29–3.81)[c]	0.78 (0.68–0.91)	1.1 (0.96–1.1)	2.0 (1.8–2.1)	3.6 (3.4–3.9)	6.2 (5.7–6.9)	10 (8.9–11)	14 (11–17)
Age: 6–11 years	374	4.93 (4.22–5.76)	1.1 (0.78–1.5)	1.6 (1.2–2.4)	3.1 (2.6–3.7)	5.2 (4.3–6.3)	8.1 (6.8–9.3)	11 (9–14)	19 (12–23)
Age: 12–19 years	828	3.80 (3.44–4.20)	0.76 (0.47–1.2)	1.1 (0.78–1.5)	2.4 (2.0–2.6)	4.4 (3.8–4.7)	6.8 (6.2–7.3)	10 (8.9–11)	12 (11–17)
Age: ≥20 years	1618	3.35 (3.08–3.65)	0.78 (0.69–0.87)	1.0 (0.97–1.1)	1.9 (1.7–2.0)	3.5 (3.2–3.7)	5.8 (5.2–6.5)	9.9 (8.6–11)	12 (11–16)
Males	1335	4.19 (3.93–4.46)	1.1 (0.88–1.2)	1.3 (1.2–1.6)	2.4 (2.3–2.6)	4.4 (4.2–4.5)	7.0 (6.3–7.8)	11 (9.4–12)	13 (11–17)
Females	1485	3.01 (2.74–3.31)	0.65 (0.54–0.82)	0.93 (0.82–1.0)	1.6 (1.3–1.7)	3.1 (2.7–3.4)	5.3 (4.9–5.9)	9.2 (8.2–11)	13 (11–16)
Non-Hispanic white	1228	3.51 (3.18–3.88)	0.78 (0.66–0.95)	1.0 (0.94–1.2)	1.9 (1.7–2.2)	3.6 (3.4–4.1)	6.2 (5.6–7)	10 (8.7–11)	14 (11–18)
Non-Hispanic black	681	3.51 (3.07–4.02)	0.76 (0.6–0.99)	1.1 (0.82–1.3)	2.0 (1.8–2.4)	3.6 (3.1–4.1)	5.8 (5.0–6.9)	9.1 (7.8–12)	14 (11–19)
Mexican American	708	4.02 (3.48–4.64)	1.0 (0.63–1.2)	1.4 (1.1–1.5)	2.3 (1.9–2.8)	4.4 (3.6–4.9)	7.1 (5.8–8.2)	11 (9.4–13)	14 (12–17)
Females, age 15–44	662	3.40 (3.00–3.85)	0.62 (0.37–0.83)	0.85 (0.62–1.2)	1.5 (1.2–1.9)	2.9 (2.4–3.4)	5.0 (4.0–6.4)	9.2 (7.2–12)	13 (9.1–17)

[a]National Health and Nutrition Examination Survey.
[b]Geometric mean.
[c]95% CI.

Results

We found perchlorate in all 2820 urine samples tested from NHANES 2001–2002, with levels ranging from 0.19 to 160 μg/l. Geometric means and selected percentiles of weighted perchlorate concentrations in the NHANES urine samples are shown in Table 2 (in μg/l) and Table 3 (in μg/g of creatinine). The geometric means and selected percentiles of the population are presented for the total population as well as population groups defined by age, sex and race-ethnicity.

Women of reproductive age (15–44 years) are also listed based on the recent classification of the pregnant woman/developing fetus as a potentially susceptible population (NAS, 2005). We found that women of reproductive age had urinary perchlorate levels with a median of 2.9 μg/l (CI 2.4–3.4 μg/l), 2.97 μg/g creatinine (CI 2.64–3.30 μg/g) and a 95th percentile of 13 μg/l (CI 9.1–17 μg/l), 12.1 μg/g creatinine (CI 8.15-18.1 μg/g). Of the 662 women of reproductive age, a subset ($n = 115$) were pregnant at the time of the study. The pregnant women in the study had median urinary perchlorate levels of 3.5 μg/l (CI 1.8–5.4 μg/l); 3.27 μg/g creatinine (CI 2.23–4.88 μg/g).

Children had higher median urinary perchlorate levels (5.2 μg/l; 5.79 μg/g creatinine) compared with adults (3.5 μg/l; 3.25 μg/g creatinine). We applied an ANCOVA model to further evaluate the higher levels of unadjusted urinary perchlorate observed in children compared with adolescents and adults. The adjusted geometric means for urinary perchlorate levels in each demographic group are shown in Table 4 and Figure 1. After adjustment for age, urinary creatinine, fasting, sex and race/ethnicity, urinary perchlorate levels were higher in children compared with adolescents ($P < 0.001$) or adults ($P < 0.001$). We found a significant interaction between sex and race/ethnicity and present the data for these demographic groups accordingly. Non-Hispanic white males had higher adjusted urinary perchlorate levels than non-Hispanic white females ($P = 0.01$) and non-Hispanic black males ($P < 0.001$). Fasting for 8 or more hours was associated with decreased urinary perchlorate ($P < 0.001$), likely due to a lack of dietary intake and the relatively short physiological half life of perchlorate in the human body (Anbar et al., 1959; Lawrence et al., 2000).

The geometric means and selected percentiles of estimated daily perchlorate doses for adults are shown in Table 5.

Discussion

We report the distribution of perchlorate levels in urine samples collected from a representative sample of 2820 US residents, aged 6 years and older. Based on these results, perchlorate exposure appears to be wide-spread in the US population. Human exposure to perchlorate may occur via several different routes. Perchlorate from both natural and

Table 3. Geometric means and selected percentiles of urinary perchlorate (μg/g creatinine) for the US population aged 6 years and older, NHANES[a] 2001–2002.

Category	N	GM[b]	Selected percentiles						
			5th	10th	25th	50th	75th	90th	95th
Total	2818	3.56 (3.34–3.80)[c]	1.10 (0.976–1.20)	1.40 (1.30–1.52)	2.17 (1.97–2.39)	3.38 (3.18–3.66)	5.61 (5.29–6.00)	9.35 (8.22–10.3)	12.7 (11.1–14.1)
Age: 6–11 years	374	5.71 (5.22–6.25)	1.91 (1.64–2.38)	2.50 (2.25–2.88)	3.64 (3.27–4.11)	5.79 (5.19–6.25)	8.33 (7.41–9.74)	13.0 (11.2–16.0)	17.4 (13.1–22.6)
Age: 12–19 years	827	2.95 (2.64–3.29)	0.922 (0.712–1.10)	1.17 (1.06–1.33)	1.88 (1.60–2.06)	2.89 (2.56–3.39)	4.48 (3.96–5.23)	7.12 (6.57–8.10)	9.87 (7.46–13.4)
Age: ≥20 years	1617	3.46 (3.20–3.73)	1.09 (0.932–1.21)	1.40 (1.27–1.54)	2.11 (1.93–2.36)	3.25 (3.04–3.59)	5.36 (4.93–5.92)	9.02 (7.61–10.2)	12.3 (10.2–14.4)
Males	1335	3.40 (3.20–3.60)	1.06 (0.891–1.16)	1.36 (1.24–1.52)	2.09 (1.94–2.27)	3.25 (3.04–3.47)	5.35 (4.93–5.86)	8.75 (7.52–9.87)	11.4 (10.1–12.7)
Females	1483	3.72 (3.39–4.09)	1.13 (1.01–1.25)	1.48 (1.30–1.60)	2.25 (1.96–2.58)	3.59 (3.20–4.10)	5.99 (5.33–6.67)	10.0 (8.15–12.1)	13.4 (11.4–16.0)
Non-Hispanic white	1227	3.76 (3.46–4.08)	1.24 (1.09–1.37)	1.54 (1.41–1.69)	2.32 (2.03–2.65)	3.54 (3.22–4.02)	5.82 (5.43–6.25)	9.42 (8.30–10.5)	12.7 (11.2–14.3)
Non-Hispanic black	680	2.53 (2.24–2.86)	0.656 (0.461–0.997)	1.00 (0.856–1.09)	1.49 (1.29–1.63)	2.54 (2.12–2.84)	4.07 (3.51–4.93)	6.87 (5.93–8.43)	10.0 (8.33–12.2)
Mexican American	708	3.77 (3.23–4.39)	1.20 (0.944–1.35)	1.52 (1.30–1.72)	2.20 (1.90–2.53)	3.51 (3.02–4.44)	6.05 (4.93–7.64)	10.4 (8.37–13.0)	14.4 (11.5–17.4)
Females, age 15–44	662	3.12 (2.72–3.57)	0.930 (0.645–1.10)	1.21 (1.05–1.39)	1.86 (1.61–2.05)	2.97 (2.64–3.30)	4.89 (3.91–6.25)	8.40 (6.32–11.7)	12.1 (8.15–18.1)

[a]National Health and Nutrition Examination Survey.
[b]Geometric mean.
[c]95% CI.

Table 4. Geometric means for urinary perchlorate (μg/l), adjusted by analysis of covariance for race/ethnicity, sex, age, fasting and urinary creatinine for ages 6 and older, NHANES 2001–2002.

Category	Adjusted geometric mean	95% confidence interval
6–11 years of age (children)	5.40[a]	(4.66–6.27)
12–19 years of age (adolescents)	3.30	(2.96–3.67)
≥20 years of age (adults)	3.41	(3.12–3.72)
Males: non-Hispanic whites	3.92[b]	(3.58–4.29)
Males: non-Hispanic blacks	2.61	(2.30–2.96)
Males: Mexican-Americans	3.94	(3.42–4.55)
Females: non-Hispanic whites	3.41[c]	(2.98–3.93)
Females: non-Hispanic blacks	3.03[d]	(2.66–3.47)
Females: Mexican-Americans	3.83	(3.12–4.70)
Fasting <8 h	3.89[e]	(3.56–4.25)
Fasting ≥8 h	3.37	(3.08–3.69)

[a]Higher than adolescents and adults ($P<0.001$).
[b]Higher than male non-Hispanic blacks ($P<0.001$).
[c]Lower than male non-Hispanic whites ($P=0.01$).
[d]Higher than male non-Hispanic blacks ($P=0.02$).
[e]Higher than fasting ≥8 h ($P<0.001$).

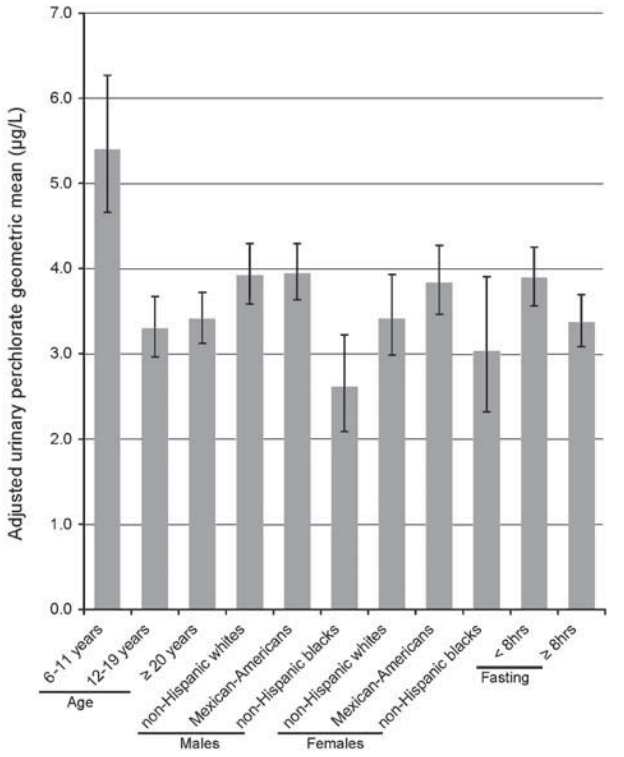

Figure 1. Geometric means and 95th percentile confidence intervals for urinary perchlorate (μg/l), adjusted by analysis of covariance for race/ethnicity, sex, age, fasting and urinary creatinine for ages 6 and older, NHANES 2001–2002.

anthropogenic sources can contaminate drinking water and food crops. Exposure can also result from inhalation of dust containing perchlorate, especially in occupational settings (Gibbs et al., 1998). Measuring perchlorate in human urine assesses the combined exposure from all sources.

The demographic group with the highest levels of urinary perchlorate was children, similar to previously published results for urinary iodine (Caldwell et al., 2005). Covariate-adjusted urinary perchlorate levels were statistically higher in children compared with both adolescents and adults, even after adjusting for urinary creatinine (Table 4). These age-associated differences in urinary perchlorate levels could represent differences in pharmacokinetics, the relationship of dose per body weight and/or exposure. For example, dietary habits such as the consumption of milk and green leafy vegetables vary across age and ethnicity groups. Samples of dairy milk and green-leafy vegetables have been reported to contain perchlorate (Hogue, 2003; Kirk et al., 2003; FDA, 2004; Capuco et al., 2005; Jackson et al., 2005). Therefore, increased consumption of these foods could increase perchlorate exposure (Blount et al., 2006).

Several small studies have also found measurable perchlorate levels in human urine or milk. For 61 adults living in Georgia, all urine samples contained measurable levels of perchlorate, with a median of 3.2 μg/l and a log–normal distribution (Valentin-Blasini et al., 2005). Similar background levels of perchlorate (median 5.5 μg/l) were detected in urine from 13 subjects in a Southern California study (Braverman et al., 2006). Kirk et al. (2005) reported measurable levels of perchlorate in all samples of breast milk collected from 36 women residing in 18 different states (mean 10.5 μg/l).

Other previously published studies did not report measurable background levels of perchlorate, likely due to inadequate analytical sensitivity (Lawrence et al., 2000; Greer et al., 2002; Gibbs et al., 2004; Braverman et al., 2005); therefore, application of these methods resulted in reported urinary background values of less than method detection limits of 500 μg/l (Lawrence et al., 2000), 20 μg/l (Greer et al., 2002; Merrill et al., 2005) and 5 μg/l (Gibbs et al., 2004; Braverman et al., 2005). Significantly higher levels of urinary perchlorate were found in populations in northern Chile consuming tap water with perchlorate levels as high as 114 μg/l (Tellez et al., 2005). As expected, urinary perchlorate levels in these highly exposed Chilean populations (median 35 μg/l) were significantly higher than the levels found in this study.

Occupational exposure to perchlorate can lead to levels and doses that are much higher than those observed for this sample of the US population (Gibbs et al., 1998; Lamm et al., 1999; Braverman et al., 2005). Occupational survey data indicate that less than 10,000 US workers actively handle perchlorate (CDC, 1995). This small number of workers should have a minimal impact on population estimates presented here.

Measurement of a single spot urine sample was used to assess individual exposure. Urinary perchlorate levels are

Table 5. Geometric mean and selected percentiles of estimated perchlorate dose (μg/kg-day) for the US population aged 20 years and older, NHANES[a] 2001–2002.

			Selected percentiles		
Category	N	GM[b]	5th	50th	95th
Total	1532	0.066 (0.060–0.071)[c]	0.020 (0.017–0.023)	0.064 (0.059–0.069)	0.234 (0.202–0.268)
Males	726	0.071 (0.066–0.077)	0.021 (0.019–0.027)	0.069 (0.063–0.074)	0.249 (0.208–0.292)
Females	806	0.061 (0.054–0.067)	0.018 (0.015–0.022)	0.059 (0.054–0.066)	0.215 (0.184–0.260)

[a]National Health and Nutrition Examination Survey.
[b]Geometric mean.
[c]95% CI.

presented both as micrograms per liter and as micrograms per gram of urinary creatinine to allow for comparisons between different demographic groups and adjustment for differences in urinary dilution (Barr et al., 2005). For a single person, more precise exposure estimates could be derived by averaging perchlorate levels from two or three spot urine samples. However, for population estimates such as geometric means and percentiles, results of multiple persons are averaged. For these point estimates, use of a single spot urine sample from each individual would constitute one source of random error, not bias. As a source of random error, this would lead to less statistical power to detect differences in perchlorate levels between groups of interest.

Urine is the principal route by which non-lactating humans excrete perchlorate (Anbar et al., 1959; Lawrence et al., 2000). During lactation human mammary tissue expresses the sodium iodide symporter (Wolff, 1998), and thus significant transfer of perchlorate into human milk is likely. The presence of micrograms per liter concentrations of perchlorate in milk collected from US women (Kirk et al., 2005) confirms lactation as a relevant perchlorate excretion path. Additional data from another lactating mammalian species (dairy cattle) confirm that a substantial portion of a perchlorate dose can be excreted in milk (Capuco et al., 2005). If lactating women are secreting perchlorate in milk, then urine-based estimates of total perchlorate exposure for these individuals are likely to be lower than actual. However, the overall impact of lactation on our population estimates of perchlorate exposure is likely to be minimal because only 26 of the 2820 participants in our study population reported that they were currently breastfeeding a child.

Our initial measurements indicate that perchlorate exposure is widespread. The toxicological impact of perchlorate exposure at these levels is an area of ongoing research. The EPA recently set the reference dose (RfD), a dose estimated to be without appreciable risk of adverse effects during a lifetime of exposure, for perchlorate at 0.7 μg/kg-day (EPA, 2005a). This RfD was recommended by the National Academy of Sciences expert panel in their perchlorate risk assessment (NAS, 2005). To compare our measured perchlorate concentrations in spot urine samples with this toxicological benchmark dose, we estimated daily dose based on physiological parameters and measured spot urine perchlorate and creatinine. Estimation of perchlorate dose in adults revealed a median of 0.066 μg/kg-day and a 95th percentile of 0.234 μg/kg-day. These estimated perchlorate dose levels are lower than the current EPA reference dose of 0.7 μg/kg-day. Only 11 adults had estimated perchlorate exposure in excess of the reference dose.

The NAS has specified pregnant women, fetuses and infants as populations who may be more sensitive to the potential health effects of perchlorate exposure (NAS, 2005). Mild hypothyroidism during pregnancy can be associated with subsequent cognitive deficits in children (Haddow et al., 1999; Klein et al., 2001). Additionally, active expression of the sodium iodide symporter in the placenta and lactating breast tissue allows perchlorate exposure of the mother to be distributed to the developing fetus and infant. Perchlorate measurement began at 6 years of age in our study, so we do not have exposure information for infants. Women of reproductive age can be used as a surrogate population for assessing fetal exposure. Women of reproductive age had a median estimated perchlorate dose of 0.057 μg/kg-day and a 95th percentile of 0.214 μg/kg-day. Daily perchlorate exposure doses were also estimated for the pregnant women in the study who had complete data sets for age, height and weight ($N = 110$). This population of pregnant women had an estimated median perchlorate dose of 0.066 μg/kg-day. These estimated perchlorate dose levels are lower than the current EPA reference dose of 0.7 μg/kg-day.

Conclusions

We assessed urinary perchlorate levels in a US reference population and present the data here stratified by age, sex and race/ethnicity. We found perchlorate in all human urine samples tested, indicating widespread trace-level perchlorate exposure in the general population. We estimated daily perchlorate dose and found that the 95th percentile of

estimated dose is less than the EPA RfD. The results provide information for risk modeling and provide a reference range for comparisons with results from other potentially exposed population groups. These data provide the first population-based assessment of the magnitude and prevalence of perchlorate exposure in the US.

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Exhibit D

U.S. Food and Drug Administration
Threshold of Regulation Exemption for Sodium Perchlorate Monohydrate

Threshold of Regulation (TOR) Exemptions

TOR No. 2005-006

Threshold of Regulation Exemptions are generally applicable and are effective for the food contact substance (FCS) for the listed intended use regardless of manufacturer or supplier.

Food Contact Substance:	Sodium perchlorate monohydrate (CAS Reg. No. 7791-07-3)
Use Limitations*:	As a conductivity enhancer in the manufacture of antistatic agents for use in polymeric food packaging. The food contact substance may be used at a level not to exceed 1.2 percent by weight of the finished polymer. The finished polymer may be used in contact with Food Type VIII only.
Requestor:	Ciba Specialty Chemical Corp.

*For references to food types and conditions of use, see Food Types & Conditions of Use for Food Contact Substances[5].

Links on this page:

1. http://www.addthis.com/bookmark.php?u508=true&v=152&username=fdamain
2. http://www.addthis.com/bookmark.php
3. http://www.fda.gov/default.htm
4. http://www.fda.gov/food/ingredientspackaginglabeling/ucm112642.htm
5. http://www.fda.gov/Food/IngredientsPackagingLabeling/PackagingFCS/FoodTypesConditionsofUse/default.htm

Page Last Updated: 03/04/2016

Note: If you need help accessing information in different file formats, see Instructions for Downloading Viewers and Players.

U.S. Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993
Ph. 1-888-INFO-FDA (1-888-463-6332)
Contact FDA

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ADD 117

3. http://www.fda.gov/default.htm
4. http://www.fda.gov/food/ingredientspackaginglabeling/ucm112642.htm
5. http://www.fda.gov/Food/IngredientsPackagingLabeling/PackagingFCS/FoodTypesConditionsofUse/default.htm

Exhibit E

U.S. Food and Drug Administration
Food Types & Conditions of Use for Food Contact Substances

U.S. Food and Drug Administration
Protecting and Promoting *Your* Health

Food Types & Conditions of Use for Food Contact Substances

CFSAN/Office of Food Additive Safety

These tables were created for easy reference for notifications relating to a food contact substance.

Table 1--Types of Raw and Processed Foods

I. Nonacid, aqueous products; may contain salt or sugar or both (pH above 5.0).

II. Acid, aqueous products; may contain salt or sugar or both, and including oil-in-water emulsions of low- or high-fat content.

III. Aqueous, acid or nonacid products containing free oil or fat; may contain salt, and including water-in-oil emulsions of low- or high-fat content.

IV. Dairy products and modifications:

- A. Water-in-oil emulsions, high- or low-fat.
- B. Oil-in-water emulsions, high- or low-fat.

V. Low-moisture fats and oil.

VI. Beverages:

- A. Containing up to 8 percent of alcohol.
- B. Nonalcoholic.
- C. Containing more than 8 percent alcohol.

VII. Bakery products other than those included under Types VIII or IX of this table:

- A. Moist bakery products with surface containing free fat or oil.
- B. Moist bakery products with surface containing no free fat or oil.

VIII. Dry solids with the surface containing no free fat or oil (no end test required).

IX. Dry solids with the surface containing free fat or oil.

Table 2--Condition of use

A. High temperature heat-sterilized (e.g., over 212 deg.F).

ADD 120

B. Boiling water sterilized.

C. Hot filled or pasteurized above 150 deg.F.

D. Hot filled or pasteurized below 150 deg.F.

E. Room temperature filled and stored (no thermal treatment in the container).

F. Refrigerated storage (no thermal treatment in the container).

G. Frozen storage (no thermal treatment in the container).

H. Frozen or refrigerated storage: Ready-prepared foods intended to be reheated in container at time of use:

1. Aqueous or oil-in-water emulsion of high- or low-fat.
2. Aqueous, high- or low-free oil or fat.

I. Irradiation

J. Cooking at temperatures exceeding 250 deg.F.

More in Food Types & Conditions of Use for FCS (/Food/IngredientsPackagingLabeling/PackagingFCS/FoodTypesConditionsofUse/default.htm)

Exhibit F

Clarence William Murray et al.
U.S. Food and Drug Administration's Total Diet Study: Dietary Intake of Perchlorate and Iodine
(2008)

Journal of Exposure Science and Environmental Epidemiology (2008) 18, 571–580

www.nature.com/jes

US Food and Drug Administration's Total Diet Study: Dietary intake of perchlorate and iodine

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The US Food and Drug Administration (FDA) has conducted the Total Diet Study (TDS) since 1961, which designed to monitor the US food supply for chemical contaminants, nutritional elements, and toxic elements. Recently, perchlorate was analyzed in TDS samples. Perchlorate is used as an oxidizing agent in rocket propellant, is found in other items (e.g., explosives, road flares, fireworks, and car airbags), occurs naturally in some fertilizers, and may be generated under certain climatic conditions. It has been detected in surface and groundwater and in food. Perchlorate at high (e.g., pharmacological) doses can interfere with iodide uptake into the thyroid gland, disrupting its function. The National Academy of Sciences (NAS) has identified that ''the fetuses of pregnant women who might have hypothyroidism or iodide deficiency as the most sensitive population.'' This study reports on intake estimates of perchlorate and iodine, a precursor to iodide, using the analytical results from the TDS. Estimated average perchlorate and iodine daily intakes as well as the contribution of specific food groups to total intakes were estimated for 14 age/sex subgroups of the US population. The estimated smallest lower bound to the largest upper bound average perchlorate intakes by the 14 age/sex groups range from 0.08 to 0.39 micrograms per kilogram body weight per day (μg/kg bw/day), compared with the US Environmental Protection Agency (EPA) reference dose (RfD) of 0.7 μg/kg bw/day. Infants and children demonstrated the highest estimated intakes of perchlorate on a body weight basis. The estimated average iodine intakes by the 14 age/sex groups reveal a lower bound (ND = 0) and upper bound (ND = LOD) range of average intakes from 138 to 353 μg/person/day. Estimated iodine intakes by infants 6–11 months exceed their adequate intake (AI), and intakes by children and adult age/sex groups exceed their relevant estimated average requirement (EAR).
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Keywords: *Total Diet Study, dietary intakes, nutritional element, iodine, perchlorate, monitoring.*

Introduction

For the last 46 years, the Total Diet Study (TDS) has been an important monitoring program that provides the US Food and Drug Administration (FDA) with baseline information on the levels of pesticide residues, chemical contaminants, radionuclides, nutrient elements, and toxic elements in the US food supply. The study involves retail purchases of foods representative of the ''total diet'' of the average US population, which includes baby food, beverages including bottled water, dairy, eggs, fat, oil, fruits, grains, legumes, mixtures, meat, poultry, fish, sweets, and vegetables. The study also includes the analysis of the foods for levels of specific analytes and estimation of dietary intake of those analytes by selected age/sex groups.

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FDA began the TDS mainly in response to public health concerns regarding the levels of radioactive contamination in foods from atmospheric nuclear testing. Initially, the study estimated dietary intakes of two radionuclides (strontium-90 and cesium-137), several organochlorine and organophosphate pesticides, and selected nutrients by 16- to 19-year old male subjects (Pennington and Gunderson, 1987). Since 1961, the TDS has undergone many changes and refinements — expansion of the sample collection sites and the number of foods analyzed, addition of many analytes, improvement of analytical methods, and addition of population subgroups for which intakes are estimated (Pennington and Gunderson, 1987; Pennington et al., 1996). For a complete listing of various TDS publications and a more in-depth description of the history, please go to the following website: http://www.cfsan.fda.gov/~comm/tds-toc.html.

The present assessment focuses on perchlorate and iodine, two of the many analytes studied in the TDS. In recent years, perchlorate and iodine have received a fair amount of attention in the scientific literature. Perchlorate is a chemical that is found to occur naturally in Chilean nitrate fertilizer, which has been used in the United States (Dasgupta et al., 2006). Perchlorate is also synthesized in the United States

and used as an oxidizing agent in solid rocket propellant and found in other items (e.g., explosives, road flares, fireworks, car airbags, herbicides, and so on). Since the mid 1990s, the US Environmental Protection Agency (EPA), along with other government agencies, has sought to understand and assess the potential health effects of perchlorate levels in soil, groundwater, and drinking water around the country. In 2002, EPA, along with other federal agencies asked the National Academy of Sciences (NAS) to review the relevant scientific literature and key findings underlying EPA's 2002 Toxicological Review (NAS, 2005). In 2005, the NAS (NAS, 2005) advised EPA that a reference dose (RfD) of 0.0007 milligram per kilogram body weight per day (mg/kg bw/day), based on a no-observed-effects level of 0.007 mg/kg bw/day from a study by Greer et al. (2002), with the application of an uncertainty factor of 10 would protect the most sensitive population — the fetuses of pregnant women who might have hypothyroidism or iodide deficiency. The EPA accepted the NAS recommendations for the RfD (http://www.epa.gov/iris/subst/1007.htm).

Perchlorate at high pharmacological doses (0.02, 0.1, and 0.5 mg/kg bw/day) interferes with iodide uptake into the thyroid gland and, if the inhibition is severe enough, can disrupt thyroid function. Disruption of iodine uptake may cause the thyroid to become enlarged (goiter), and, if the disruption continues, it may cause hypothyroidism. The NAS (2005) reviewed findings in regards to iodine intake and thyroid function, and the committee stated that, ''Generally, thyroid hormone production is normal even when iodide intake is quite low. Hypothyroidism occurs only if daily iodide intake is below about 10 to 20 μg (about one-fifth to one tenth of the average intake in the United States). However, for pregnant women, iodide deficiency of that severity can result in major neurodevelopmental deficits and goiter in their offspring. Lesser degrees of iodide deficiency may also cause important neurodevelopmental deficits in infants and children.''

Blount et al. (2007), focused on perchlorate exposure of 2820 US residents 6 years of age and older from the National Health and Nutrition Examination Survey (NHANES) during 2001–2002. All the participants were found to have detectable levels of perchlorate in their urine. From this work, Blount et al. were able to estimate a total daily perchlorate dose for adults 20 years of age and older. The total daily perchlorate dose was based on urinary perchlorate, urinary creatinine concentration, and physiological parameters predictive of creatinine excretion rates, which resulted in a median estimate of 0.064 μg/kg bw/day and 95th percentile of 0.234 μg/kg bw/day.

In another study, Blount et al. (2006) focused on urinary perchlorate and thyroid hormone levels in 2299 men and women participants who were 12 years of age and older from NHANES during 2001–2002. The investigators evaluated the potential relationship between urinary levels of perchlorate and serum levels of thyroid stimulating hormone (TSH) and total thyroxine (T4). The subjects were categorized and analyzed based on a cutoff point of 100 μg/l urinary iodine level. This value was based on the World Health Organization (WHO) definition of sufficient iodine intake in populations (WHO, 2004). Blount et al. observed that perchlorate was not a significant predictor of hormone levels for men. For women with urinary iodine levels <100 μg/l, perchlorate was a significant negative predictor for T4 and a positive predictor of TSH. For women with urinary iodine levels ≥ 100 μg/l, perchlorate was a significant positive predictor of TSH, but not T4. Blount concluded that the associations of perchlorate with T4 and TSH are coherent in direction and independent of other variables known to affect thyroid function, but are present at perchlorate exposure levels that were unanticipated based on previous studies. Finally, Blount et al. concluded that additional research is needed to affirm these findings.

The FDA recognizes the potential for perchlorate contamination in food through the use of some fertilizers, contaminated irrigation water, processing water, and source waters for bottle water. During 2004–2005, the FDA conducted exploratory surveys to monitor perchlorate levels in 28 types of foods and beverages consisting of bottled water, milk, fruits and fruit juices, vegetables, grain products, and seafood. The results of these exploratory surveys are found at FDA (2007), http://www.cfsan.fda.gov/~dms/clo4data.html. Since the results of these exploratory surveys focused on selected foods, the data do not provide information on the presence of perchlorate in the US food supply representing the total diet of the US population and are not included in this estimate. In 2005, FDA began testing all samples from the TDS to determine whether perchlorate is found in a broader range of foods. The TDS was determined to be an appropriate tool, since it includes all major components of the average American diet. In addition, because iodine has been analyzed in all TDS foods since late 2003, estimates of daily intakes of both perchlorate and iodine by the US population could be derived from the TDS results.

This study reports the estimated average dietary intakes of iodine based on analytical results from TDS samples collected between 2003 and 2004 and of perchlorate based on analytical results from TDS samples collected between 2005 and 2006. The total estimated daily intakes were calculated for 14 age/sex population groups from infants through adults. Also, the contributions of major food groups to total estimated intakes of iodine and perchlorate are reported.

Methods

Dietary intakes of perchlorate and iodine were estimated by combining analytical results from the TDS with food

consumption estimates developed specifically for estimating dietary exposure from TDS results (referred to as TDS diets).

Development of the TDS Food List and Diets

The following is a brief discussion of the methodology for developing both the TDS food list and diets; a more exhaustive explanation of the methodology is provided by Egan et al. (2007). The current TDS food list and diets were compiled in 2003 from the results of the US Department of Agriculture's 1994–1996, 1998 Continuing Survey of Food Intakes by Individuals (94–98 CSFII). For this survey, the data collection in 1994–1996 included individuals of all ages, and data collected in 1998 included children from birth through 9 years of age; the survey design allowed for all years of data to be combined for analysis. During the 94–98 CSFII, survey participants reported detailed consumption information on about 6000 different foods and beverages. For compiling the TDS food list, all 6000 survey foods were grouped (or aggregated) according to the similarity of their primary ingredients. Then average per capita (all individuals — eaters and noneaters alike) daily consumption amounts were calculated for each survey food, and, from each group of aggregated food codes, the food consumed in greatest was selected as the representative TDS food. In all, 285 foods and beverages were selected for the current TDS food list.

For compiling the TDS diets, the consumption amounts of all survey foods assigned to each TDS food were subtotaled to derive a TDS diet consumption amount for each TDS food. The complete set of TDS consumption amounts for each of the 14 age/sex groups is referred to collectively as the TDS diets. This approach to estimating dietary intakes assumes that the analytical profiles of the survey foods would be similar to those of the TDS foods to which they are assigned and that the TDS diets could, therefore, provide a reasonable estimate of total dietary exposure to the analytes from all foods in the diet — not from the TDS foods alone. The TDS diets do not account for consumption of water other than that used in the preparation of foods or beverages (i.e., the diets do not include drinking water from the tap although bottled water, consumed as a beverage, is included in calculations presented here). Additionally, the TDS diet for infants 6–11 months does not include consumption of breast milk, thus breastfed infants would have different exposure patterns from the estimates shown in Table 5.

TDS Sample Collection and Analyses

Total Diet Study samples are routinely collected four times a year, once in each of the four regions of the country (west, north central, south, and northeast). Each round of sample collections and analyses is referred to as a market basket. For each market basket, samples of each of the 285 foods are collected simultaneously in three cities within the region. The foods are purchased at retail from grocery stores and fast-food restaurants and are then shipped from the collecting locations to FDA's Kansas City District Laboratory in Lenexa (KS, USA). The foods are prepared table-ready prior to analyses, and salt is not added to any of TDS food prepared by the laboratory. Distilled water is used for all food preparation (e.g., washing, cooking, and beverage preparation). For each of the 285 foods, the products purchased in each of the three cities within the collection region are composited to form a single analytical sample for each regional market basket.

The estimated intakes reported in this study are based on analytical results for TDS samples collected between 2003 and 2006. Iodine was analyzed in all TDS foods from five market baskets conducted in late 2003 through 2004. For perchlorate, 54 of 57 baby foods were analyzed in four market baskets conducted in 2005; the remaining three baby foods were analyzed in only three market baskets because they were not available in the fourth market basket for 2005. The other 228 TDS foods were analyzed in 2006; of those, 128 were analyzed in four market baskets and 100 were analyzed in two market baskets. The dates and locations of each market basket are listed in Table 1.

Table 1. Dates and locations of sample collections for iodine and perchlorate results.

Market basket	Sample collection dates	Collection region and locations
2003-4	July 2003	North (Monmouth-Ocean City, NJ; Rochester, NY; Philadelphia, PA)
2004-1	October 2003	Central (Chicago, IL; Youngstown-Warren, OH; Detroit, MI)
2004-2	January 2004	West (Salt Lake City/Ogden, UT; Phoenix-Mesa, AZ; Las Vegas, NV)
2004-3	April 2004	South (Atlanta, GA; San Antonia, TX; Shreveport-Bossier City, LA)
2004-4	July 2004	North (Boston, MA; Syracuse, NY; Pittsburgh, PA)
2005-1	October 2004	Central (Kalamazoo-Battle Creek, MI; Omaha, NE; St. Cloud, MN)
2005-2	January 2005	West (Pueblo, CO; San Jose, CA; Boise City, ID)
2005-3	April 2005	South (Roanoke, VA; West Palm Beach-Boca Raton, FL; New Orleans, LA)
2005-4	July 2005	North (Hartford, CT; Bergen-Passaic, NJ; Binghamton, NY)
2006-1	October 2005	Central (Rockford, IL; Cincinnati, OH; Fargo-Moorhead, ND)
2006-2	January 2006	West (Los Angeles-Long Beach, CA; Santa Clara, CA; Seattle-Everett, WA)
2006-3	April 2006	South (Raleigh, NC; Norfolk-Virginia Beach, VA; Tulsa, OK)
2006-4	July 2006	North (Portland, ME; Nassau-Suffolk, NY; Scranton Wilkes-Barre, PA)

Table 2. FDA analytical techniques and limits for iodine and perchlorate.

Chemical name	Analytical technique	Nominal analytical limits	
		Limit of detection	Limit of quantitation
Iodine	UV-Vis	0.03 p.p.m.; for some up to 0.06 p.p.m.	0.3 p.p.m., for some up to 0.6 p.p.m.
Perchlorate	IC-TMS	1.00 p.p.b.	3.00 p.p.b.

IC-TMS, ion chromatography–tandem mass spectrometry; UV-Vis, ultraviolet–visible spectrometry.

Table 3. Description of food groups contributing to intakes.

Food groups	Includes
Baby food	All baby foods and infant formulas (excluding adult foods consumed by children). Infant formulas were samples of ready-to-eat products
Beverages	Beverages, including bottled water, except for fruit/vegetable juices
Dairy	All dairy products (e.g., butter, milk, cheese, and ice cream)
Eggs	Boiled egg, scrambled egg, omelet, and egg salad
Fat/oil	Vegetable fats and oils, and salad dressings
Fruits	Fruits and fruit juices
Grains	Items that are primarily grains, including cookies and pastries
Legumes	Legumes, nuts, and seeds
Mixtures	Primarily entrée items containing mixtures of meat/poultry/fish, grains, and vegetables (no predominant ingredient)
Meat, poultry, fish (MPF)	Items that are primarily meat, poultry, or fish (e.g., roasts, fried chicken, fish filets, and luncheon meats)
Sweets	Sugars, sweeteners, syrups, candy, jelly, and gelatin
Vegetables	Vegetables and vegetable juices

Iodine was measured by FDA's Kansas City District Laboratory using a method adapted from Fischer et al. (1986). The method consists of a ternary acid digestion with a determination of iodine by UV-VIS spectrophotometry through the catalysis of the $Ce+4/As+3$ reaction. The method for perchlorate was developed by FDA in a collaborative effort among the Center for Food Safety and Applied Nutrition, the Southeastern Regional Laboratory, and the Total Diet Research Center; the method was published by Krynitsky et al. (2006). Table 2 reports the analytical techniques, the nominal limit of detection (LOD), and limit of quantitation (LOQ). Cases in which perchlorate and iodine were found to be present in concentrations greater than or equal to the LOD but less than the LOQ were considered ''trace'' amounts. The LOD for perchlorate was 1.00 μg/kg, while the LOD for iodine ranged from 0.03 to 0.06 mg/kg.

Calculation of TDS Dietary Intakes

In calculating estimated intakes, the average iodine concentration per food was calculated from results of five market baskets. For perchlorate, the average concentration per food was calculated from results of either two or four market baskets, as mentioned above. To account for uncertainties associated with samples with no detectable concentrations of perchlorate or iodine (non-detects or NDs), three average concentrations were calculated for each TDS food assuming values of zero, half the LOD, and the LOD for non-detects. The three average concentrations in each food were then multiplied by the average daily consumption amount of the food for the given subpopulation group as compiled for the TDS diets to provide a range from lower bound (ND = 0) to upper bound (ND = LOD) estimated average intakes from each TDS food. Finally, estimated intakes from all TDS foods were summed to estimate the range of average total estimated daily intakes of iodine and perchlorate for each age/sex group. The estimated perchlorate intakes were compared with the EPA's RfD for perchlorate, and estimated iodine intakes were compared with the appropriate US Dietary Reference Intakes that represent average daily intake requirements (NAS, 2000). For the TDS age/sex groups other than infants, estimated iodine intakes were compared with the relevant estimated average requirements (EARs), which are defined by NAS as the nutrient intake levels estimated to meet the requirements of half the healthy individuals within a particular age/sex group. The estimated iodine intake by the TDS group of infants 6–11 months was compared with the adequate intake (AI) of 130 μg/person/day (NAS, 2000); an AI is set by NAS when there is insufficient scientific evidence to determine an EAR and is defined as the recommended average daily intake level of a nutrient that is assumed to be adequate for a group of apparently health individuals.

The contributions of major food groups to total estimated intakes of perchlorate and iodine were also calculated. TDS foods were assigned to 1 of 12 major food groups; descriptions of these food groups are provided in Table 3, and a further rationale for TDS food assignment into the 12 major food groups are explained by Egan et al. (2007). The contributions of food groups to total estimated intake were calculated from the intake estimates based on average concentrations assuming values of half the LOD for non-detects. Contributions by food groups were determined by summing the estimated intakes from all TDS foods in each of the 12 food groups, and calculating the percentage of total intake for each food group.

Results

Perchlorate

From the TDS analytical results, it is evident that perchlorate is found in a wide range of foods. Detectable levels of perchlorate were found in 625 of 1065 (59%) of the total samples analyzed and 440 of 1065 (41%) of the samples had no detectable levels of perchlorate. Of the 625 samples with detectable levels of perchlorate, 231 contained "trace" amounts (i.e., concentrations between the LOD and LOQ). As for findings in specific foods, detectable levels of perchlorate were found in at least one sample in 74% (211 of 285) of TDS foods. In contrast, perchlorate was not detected in any sample of 74 of 285 (26%) of TDS foods.

Estimated dietary intakes of perchlorate are reported in Tables 4 and 5. The percentage contributions to total estimated daily intake by food group are presented in Table 4. The majority (81%) of the estimated perchlorate intake by infants 6–11 months comes from baby foods, which includes infant formula, and dairy foods. Dairy foods contribute about half of the total estimated daily intake of perchlorate by children 2, 6, and 10 years of age. Vegetables and dairy foods combined account for between 46% and 59% of the total estimated intake of perchlorate by teenagers and adults.

Table 5 presents the lower and upper bound estimated average total daily intakes as well as intakes by food group on a per person basis. Total estimated daily intakes are also presented per kg of body weight to compare with EPA's RfD of 0.7 μg/kg bw/day. Average body weights for each

Table 4. Contribution (%) by food groups to total estimated daily intake of perchlorate for 2005–2006.

Food group	Intake (% of total)						
	Infants 6–11 months	Children 2 years	Children 6 years	Children 10 years	Teenage girls 14–16 years	Teenage boys 14–16 years	Women 25–30 years
Baby food	49	0	0	0	0	0	0
Beverage	1	3	3	4	7	7	12
Dairy	32	51	50	47	29	37	20
Egg	0	0	0	0	0	0	0
Fat/oil	0	0	0	0	0	0	0
Fruit	4	15	11	9	11	7	8
Grain	2	6	8	8	8	9	8
Legume	0	0	0	0	0	0	0
Mixture	6	8	9	10	14	12	14
MPF	1	4	6	5	7	7	11
Sweets	0	1	1	1	1	1	1
Vegetable	5	12	12	16	23	20	26
	Men 25–30 years	Women 40–45 years	Men 40–45 years	Women 60–65 years	Men 60–65 years	Women 70+ years	Men 70+ years
Baby food	0	0	0	0	0	0	0
Beverage	12	12	11	9	9	6	7
Dairy	20	17	21	17	19	23	22
Egg	0	0	0	0	0	0	0
Fat/oil	0	0	0	0	0	0	0
Fruit	5	11	8	12	9	12	12
Grain	8	8	9	8	8	8	9
Legume	0	0	0	0	0	0	0
Mixture	16	13	13	9	10	10	10
MPF	9	7	8	7	8	5	7
Sweets	0	1	1	0	0	0	0
Vegetable	30	31	29	38	37	36	33

MPF, meat, poultry, fish.

Table 5. Range of estimated lower and upper bound average perchlorate intakes for 2005–2006.

Food group	Intake (μg/person/day)						
	Infants 6–11 month	Children 2 years	Children 6 years	Children 10 years	Teenage girls 14–16 years	Teenage boys 14–16 years	Women 25–30 years
Baby food	1.1–1.3	0.0–0.0	0.0–0.0	0.0–0.0	0.0–0.0	0.0–0.0	0.0–0.0
Beverage	0.00–0.1	0.0–0.3	0.0–0.4	0.0–0.5	0.02–0.8	0.0–1.1	0.2–1.2
Dairy	0.8–0.8	2.6–2.6	2.9–2.9	3.1–3.1	1.6–1.6	3.1–3.1	1.2–1.2
Egg	0.0–0.0	0.0–0.0	0.0–0.0	0.0–0.0	0.0–0.0	0.0–0.0	0.0–0.0
Fat/oil	0.0–0.0	0.0–0.0	0.0–0.0	0.0–0.0	0.0–0.0	0.0–0.0	0.0–0.0
Fruit	0.1–0.1	0.7–0.9	0.6–0.7	0.5–0.6	0.6–0.7	0.5–0.6	0.5–0.6
Grain	0.0–0.1	0.3–0.3	0.4–0.5	0.5–0.5	0.4–0.5	0.7–0.8	0.4–0.5
Legume	0.0–0.0	0.0–0.0	0.0–0.0	0.0–0.0	0.0–0.0	0.0–0.0	0.0–0.0
Mixture	0.1–0.1	0.4–0.5	0.5–0.6	0.6–0.7	0.8–0.8	1.0–1.1	0.9–0.9
MPF	0.0–0.0	0.2–0.2	0.3–0.3	0.3–0.4	0.3–0.4	0.5–0.6	0.7–0.7
Sweets	0.0–0.0	0.0–0.0	0.0–0.1	0.0–0.1	0.0–0.1	0.0–0.1	0.0–0.1
Vegetable	0.1–0.1	0.6–0.6	0.7–0.7	1.0–1.0	1.2–1.3	1.7–1.7	1.5–1.5
Total intake	**2.4–2.7**	**4.9–5.5**	**5.4–6.1**	**6.1–6.9**	**5.1–6.1**	**7.7–9.1**	**5.4–6.8**
Total intake (μg/kg bw/day)	**0.26–0.29**	**0.35–0.39**	**0.25–0.28**	**0.17–0.20**	**0.09–0.11**	**0.12–0.14**	**0.09–0.11**
	Men 25–30 years	Women 40–45 years	Men 40–45 years	Women 60–65 years	Men 60–65 years	Women 70+ years	Men 70+ years
Baby food	0.0–0.0	0.0–0.0	0.0–0.0	0.0–0.0	0.0–0.0	0.0–0.0	0.0–0.0
Beverage	0.2–1.6	0.3–1.3	0.2–1.7	0.2–1.0	0.2–1.3	0.1–0.7	0.1–0.9
Dairy	1.5–1.5	1.1–1.1	1.8–1.8	1.1–1.1	1.5–1.5	1.4–1.4	1.7–1.7
Egg	0.0–0.0	0.0–0.0	0.0–0.0	0.0–0.0	0.0–0.0	0.0–0.0	0.0–0.0
Fat/oil	0.0–0.0	0.0–0.0	0.0–0.0	0.0–0.0	0.0–0.0	0.0–0.0	0.0–0.0
Fruit	0.3–0.4	0.7–0.8	0.6–0.7	0.7–0.8	0.6–0.8	0.7–0.8	0.8–1.0
Grain	0.6–0.7	0.5–0.6	0.7–0.8	0.5–0.5	0.6–0.7	0.5–0.6	0.6–0.7
Legume	0.0–0.0	0.0–0.0	0.0–0.0	0.0–0.0	0.0–0.0	0.0–0.0	0.0–0.0
Mixture	1.2–1.3	0.8–0.9	1.1–1.1	0.6–0.6	0.8–0.9	0.6–0.6	0.7–0.8
MPF	0.7–0.7	0.5–0.5	0.6–0.7	0.4–0.5	0.6–0.7	0.3–0.4	0.5–0.6
Sweets	0.0–0.0	0.0–0.0	0.1–0.1	0.0–0.0	0.0–0.0	0.0–0.0	0.0–0.0
Vegetable	2.2–2.2	1.9–2.0	2.4–2.4	2.4–2.4	2.8–2.9	2.2–2.2	2.5–2.5
Total intake	**6.7–8.6**	**5.9–7.3**	**7.4–9.4**	**5.9–7.1**	**7.2–8.8**	**5.8–6.9**	**7.1–8.3**
Total intake (μg/kg bw/day)	**0.08–0.11**	**0.09–0.11**	**0.09–0.11**	**0.09–0.10**	**0.09–0.11**	**0.09–0.11**	**0.11–0.12**

MPF, meat, poultry, fish.
The total intake for a specific age/sex group are provided in bold.

population group were based on self-reported body weights from respondents in the 94–98 CSFII (Egan et al., 2007). Estimated perchlorate intakes by all age/sex groups are below the RfD. Children 2 years of age, with estimated lower and upper bound average intakes ranging from 0.35 to 0.39 μg/kg bw/day, have the highest total perchlorate intake per kg body weight per day. Total lower- and upper bound average intake ranges for infants 6–11 months, and children 6–10 years of age are estimated to be 0.26 to 0.29 μg/kg bw/day, 0.25 to 0.28 μg/kg bw/day, and 0.17 to 0.20 μg/kg bw/day, respectively. The estimated smallest lower bound and the highest upper bound average intakes by the other age/sex groups ranged from 0.08 to 0.14 μg/kg bw/day.

Iodine

From the TDS analytical results, it is evident that iodine is found in more than half the foods in the TDS. Detectable levels of iodine were found in at least one sample of 169 of 285 (59%) of the TDS foods, while iodine was not detected in 116 of 285 or 41% of TDS foods.

The percentage contributions by food group to total estimated daily intake of iodine are reported in Table 6. As with perchlorate, baby foods and dairy products account for nearly all (90%) of the estimated iodine intake by infants. Dairy products account for 70% or more of total estimated daily intake of iodine by children 2, 6, and 10 years of age, and 63% of total estimated iodine intake by teenage boys. For all other age/sex groups, dairy foods contribute about 50% of total estimated iodine intake. For children 2, 6, and 10 years of age, grains account for 10%, 14%, and 15%, respectively, of the total estimated daily iodine intake. Grain products contribute between 16% and 23% of total estimated iodine intake for teenagers and adults.

Table 7 reports the lower bound (ND = 0) and upper bound (ND = LOD) estimates of average iodine intakes as well as intakes by food group on a per person basis.

Table 6. Contribution (%) by food group to total estimated daily intake of iodine for 2003–2004.

Food group	Intake (% of total)						
	Infants 6–11 months	Children 2 years	Children 6 years	Children 10 years	Girls 14–16 years	Boys 14–16 years	Women 25–30 years
Baby food	56	0	0	0	0	0	0
Beverage	1	2	2	3	6	5	9
Dairy	34	73	70	70	53	63	49
Egg	2	3	2	2	2	2	4
Fat/oil	0	0	0	0	0	0	0
Fruit	2	5	3	2	4	3	3
Grain	3	10	14	15	20	16	20
Legume	0	0	0	0	0	0	0
Mixture	1	4	5	5	8	7	8
MPF	0	1	2	1	3	2	3
Sweets	0	1	1	1	2	1	2
Vegetable	1	1	1	1	2	1	2
	Men 25–30 years	Women 40–45 years	Men 40–45 years	Women 60–65 years	Men 60–65 years	Women 70+ years	Men 70+ years
Baby food	0	0	0	0	0	0	0
Beverage	10	10	9	9	8	6	6
Dairy	45	47	51	48	48	57	57
Egg	4	3	3	4	5	4	4
Fat/oil	0	0	0	0	0	0	0
Fruit	3	3	2	4	3	4	3
Grain	21	23	21	21	21	18	18
Legume	0	0	0	0	0	0	0
Mixture	11	8	7	6	7	5	5
MPF	3	3	3	4	4	3	4
Sweets	1	1	2	1	1	1	1
Vegetable	2	2	2	3	3	2	2

MPF, meat, poultry, fish.

Estimated intakes are compared to the AI or EAR relevant to the TDS population group. The lower bound (ND = 0) total estimated iodine intake by infants of 144 μg/person/day exceeds their AI for iodine (130 μg/person/day). The lower bound (ND = 0) daily estimated intakes of iodine by children are as follows: 225 μg/person/day for children 2 years, 255 μg/person/day for children 6 years, and 276 μg/person/day for children 10 years. These estimated intakes exceed the relevant EARs of 65 μg/person/day for children 1 through 8 years of age and 73 μg/person/day for children 9 through 13 years of age.

For teenage boys and girls aged 14–16 years, dairy and grain provide the highest sources of dietary iodine. These two food groups contribute 73% of total estimated intake by teenage girls and 79% of total estimated intake by teenage boys (Table 6). Teenage boys have the highest total daily estimated intake of iodine (304 to 353 μg/person/day) in comparison with the all other age/sex groups in the TDS (Table 7). Their lower bound (ND = 0) estimated iodine intake is three times their EAR of 95 μg/person/day. Like the teenage boys, the teenage girls' estimated dietary intake of iodine of 178 to 214 μg/person/day exceeds their EAR, which is also 95 μg/person/day.

For adults, dairy and grain provided the most significant sources of dietary iodine for all groups of adults (Table 6). The total estimated lower and upper bound average intakes by women 25–30 years of age range from 148 to 196 μg/person/day; for women 40–45 years of age, estimated intakes range from 145 to 197 μg/person/day (Table 7). For adult men 25–30 and 40–45 years of age, estimated iodine intakes range from 203 μg/person/day at the lower bound to 284 μg/person/day at the upper bound.

Finally, for older (60–65 and 70+ years of age) women and men, their main sources of dietary iodine are dairy and grains (Table 6). These foods account for between 69% and 75% of their total estimated daily intake. Total estimated lower and upper bound average intakes by women 60–65 years of age range from 138 to 182 μg/person/day (Table 7). Women 70+ years of age have an estimated iodine intake ranging from 154 to 192 μg/person/day. Estimated lower and upper bound average iodine intakes by both groups of older men range from 192 to 249 μg/person/day for men

Table 7. Range of estimated lower and upper bound average iodine intakes for 2003–2004.

Food group	Intake (μg/person/day)						
	Infants 6–11 months	Children 2 years	Children 6 years	Children 10 years	Girls 14–16 years	Boys 14–16 years	Women 25–30 years
Baby food	82.8–88.3	1.1–1.2	0.0–0.0	0.0–0.0	0.0–0.0	0.0–0.0	0.0–0.0
Beverage	0.0–1.8	0.0–7.6	0.1–11.3	0.0–14.6	0.1–22.9	0.0–31.2	0.2–32.1
Dairy	50.8–50.8	173.9–173.9	187.9–188.0	202.5–202.6	106.0–106.0	207.9–207.9	83.2–83.2
Egg	2.5–2.5	7.1–7.1	5.1–5.1	5.5–5.5	4.4–4.4	5.9–5.9	6.0–6.0
Fat/oil	0.0–0.0	0.1–0.2	0.2–0.3	0.3–0.4	0.5–0.6	0.5–0.7	0.6–0.7
Fruit	1.6–3.1	7.9–13.8	5.8–9.7	5.4–8.7	6.3–9.3	7.1–10.1	4.2–7.4
Grain	3.6–4.1	21.5–23.5	37.1–39.5	41.6–43.9	37.5–39.7	49.6–52.6	32.3–34.8
Legume	0.0–0.1	0.1–0.4	0.2–0.5	0.2–0.5	0.1–0.6	0.2–0.6	0.2–0.6
Mixture	1.9–2.5	8.1–10.0	11.2–13.3	12.3–14.4	14.6–16.9	22.5–25.8	12.6–15.8
MPF	0.5–0.6	2.9–4.0	4.0–5.3	3.4–5.1	4.2–6.0	5.2–7.6	4.6–6.4
Sweets	0.0–0.1	1.6–2.0	2.7–3.4	3.1–4.0	2.7–3.3	2.7–3.5	2.8–3.2
Vegetable	0.6–1.1	1.0–3.1	1.2–3.9	1.3–4.6	1.2–4.7	2.3–7.1	1.4–5.8
Total intake	**144–155**	**225–247**	**255–280**	**276–304**	**178–214**	**304–353**	**148–196**
Estimated average requirement (EAR)[a]	**130 (AI)**	**65**	**65**	**73**	**95**	**95**	**95**
	Men 25–30 years	Women 40–45 years	Men 40–45 years	Women 60–65 years	Men 60–65 years	Women 70+ years	Men 70+ years
Baby food	0.0–0.0	0.0–0.0	0.0–0.0	0.0–0.0	0.0–0.0	0.0–0.0	0.0–0.0
Beverage	0.1–45.5	0.2–35.5	0.1–45.7	0.4–27.7	0.1–36.2	0.2–20.9	0.1–24.9
Dairy	105.2–105.3	79.1–79.2	125.0–125.1	76.9–77.0	105.7–105.7	96.9–97.0	123.7–123.8
Egg	9.9–9.9	5.5–5.5	8.2–8.2	7.1–7.1	11.4–11.4	6.7–6.7	8.6–8.6
Fat/oil	0.7–0.9	0.7–1.0	1.0–1.3	0.6–0.9	0.7–1.0	0.5–0.7	0.6–0.8
Fruit	6.6–9.2	2.9–6.3	4.0–7.5	3.6–7.7	3.9–8.1	4.5–9.0	4.5–9.8
Grain	47.2–50.2	36.2–38.6	50.9–54.0	33.3–35.5	45.2–48.2	29.9–32.4	37.6–40.8
Legume	0.4–1.1	0.2–0.6	0.3–0.9	0.1–0.5	0.3–0.9	0.1–0.5	0.2–0.8
Mixture	22.9–26.7	12.8–15.5	15.9–19.7	7.8–10.4	13.3–16.9	7.8–10.6	9.7–13.0
MPF	6.1–9.0	4.0–6.0	5.6–8.7	5.6–7.5	7.2–9.9	4.6–6.2	7.0–9.0
Sweets	1.9–2.2	2.0–2.5	3.7–4.3	0.9–1.5	1.6–2.2	0.9–1.4	1.4–2.0
Vegetable	2.0–8.0	1.4–6.3	2.3–8.5	1.6–6.6	2.4–8.7	1.8–6.6	2.2–7.9
Total intake	**203–268**	**145–197**	**217–284**	**138–182**	**192–249**	**154–192**	**196–241**
Estimated average requirement (EAR)[a]	**95**	**95**	**95**	**95**	**95**	**95**	**95**

AI, adequate intake; MPF, meat, poultry, fish.
[a]Taken from National Academy of Sciences, Dietary Reference Intake for Vitamin A, Vitamin K, Arsenic, Boron, Chromium, Copper, Iodine, Iron, Manganese, Molybdenum, Nickel, Silicon, Vanadium, and Zinc, National Academies Press, Washington, D.C., 2000.
The total intake for a specific age/sex group are provided in bold.

60–65 years of age and 196 to 241 μg/person/day for men 70+ years of age. Estimated lower bound (ND = 0) average intakes by all groups of men and women exceed the EAR for adults of 95 μg/person/day.

Discussion

This assessment provides information on major dietary sources and estimated average dietary intakes of perchlorate and iodine in the United States. Intakes estimated from the TDS diets are based on average per capita food consumption; that is, the TDS diets reflect the average amounts of foods consumed by all individuals (eater and noneaters alike) within each of the 14 age/sex groups. However, the TDS as currently designed does not allow for estimating intakes at the extremes (i.e., upper or lower percentiles of food consumption) or for population subgroups within the 14 age/sex groups that may have specific nutritional needs (e.g., the subgroups of pregnant or lactating women within the groups of women of childbearing age). Given the increased caloric needs of these two groups of women, their perchlorate and iodine intakes are likely to be somewhat higher than those of women of childbearing age as a whole as represented by the TDS population groups. We also note that children 2 years of age are estimated to consume iodine at levels that exceed the tolerable upper limit. Nevertheless, the results of this estimated dietary intake assessment of iodine and perchlorate provides a general estimation of the average iodine and perchlorate intakes by specific age/sex groups in the United States.

The perchlorate intake estimates reveal that infants and children (2, 6, and 10 years) have the highest estimated intake on a body weight basis in comparison to other TDS age/sex groups, because they consume more food per their body weight and they have different food consumption patterns. Children 2 years of age have the highest estimated average perchlorate intake ranging from 0.35 to 0.39 μg/kg bw/day, which is between 50% and 56% of the EPA RfD, with dairy foods providing about 51% of perchlorate in their diet. The estimated lower and upper bound average perchlorate intakes by infants 6–11 months and children 6 years of age range from 0.26 to 0.29 and 0.25 to 0.28 μg/kg bw/day, respectively. The infants' estimated perchlorate intake range is 37% to 41% of EPA's RfD of 0.7 μg/kg body weight per day, with dairy foods providing 32% of their total estimated intake of perchlorate. For children 6 years of age, the estimated average range of perchlorate intake is between 36% and 40% of the EPA's RfD. Children 10 years of age had estimated lower and upper bound average perchlorate intakes of 0.17 to 0.20 μg/kg bw/day, which is between 24% and 29% of the RfD.

For teenage girls 14–16 years, women 25–30 years of age, and women 40–45 years of age had the same estimated average perchlorate intake ranges of 0.09 to 0.11 μg/kg bw/day, respectively. For these three age groups (teenage girls 14–16 years of age, women 25–30 years of age, and women 40–45 years) had estimated average range of perchlorate intakes between 13% and 16% of the EPA's RfD.

The remaining seven age/sex groups displayed estimated perchlorate intakes from the smallest lower bound of 0.08 to the highest upper bound of 0.14 μg/kg bw/day, which is between 11% and 20% of the EPA's RfD. The lower bound (ND = 0) range of estimated average perchlorate intakes for eight age/sex group that consist of men and women over 20 years of age (0.08 to 0.11 μg/kg bw/day) show relative agreement with Blount et al. (2007) median estimated perchlorate dose of 0.064 μg/kg bw/day.

It could be assumed that perchlorate would be found mainly in foods with high moisture content (e.g., milk and vegetables) because of its affinity for water, but results of the TDS analyses appear to indicate that perchlorate is more widely distributed in the food supply. As noted, detectable levels of perchlorate were found in 74% of the 285 TDS food. Since this assessment is based on a small number of composite samples (two or four) per TDS food, FDA plans to continue analyzing the full range of TDS foods for perchlorate in the future to develop a more robust data set on perchlorate levels in foods.

Perchlorate and iodine levels in selected foods have been reported previously in the literature (Pearce et al., 2004; Jackson et al., 2005; Kirk et al., 2005; Sanchez et al., 2005a, b; Sanchez et al., 2006). In addition, FDA conducted exploratory surveys in 2004 and 2005 to determine perchlorate levels in selected foods. Table 8 compares the perchlorate concentrations in 10 commodities reported elsewhere with the levels found in similar TDS foods. Perchlorate results show fairly good agreement for 5 of the 10 commodities (milk, iceberg lettuce, green leaf lettuce, oranges, and grapefruit). For the other commodities (spinach, collards, cucumbers, tomatoes, and cantaloupe), perchlorate results varied considerably. Table 9 compares iodine concentrations for three foods as reported in the literature to findings in similar TDS foods. The iodine

Table 8. Perchlorate levels in selected foods.

Perchlorate levels		Concentration–wet weight (μg/kg)	
Commodity	*n* samples	Mean[a]	Source
Milk	47	2	Kirk et al. (2005)
	125	5.8	FDA exploratory samples
	8	7	FDA TDS
Lettuce, iceberg	63	7.4	Sanchez et al. (2005a)
	24	8	Sanchez et al. (2005b)
	43	8.1	FDA exploratory samples
	4	2.1	FDA TDS
Lettuce, green leaf	69	16.5	Sanchez et al. (2005a)
	24	33	Sanchez et al. (2005b)
	26	10.6	FDA exploratory samples
	2	4.4	FDA TDS
Spinach	10	85.1	Sanchez et al. (2005a)
	36	115	FDA exploratory samples
	4	40	FDA TDS
Collards	1	5	Sanchez et al. (2005a)
	13	95.1	FDA exploratory samples
	4	17.7	FDA TDS
Cucumbers	1	40	Jackson et al. (2005)
	1	770	Jackson et al. (2005)
	20	6.6	FDA exploratory samples
	4	19.1	FDA TDS
Tomatoes	1	42	Jackson et al. (2005)
	1	220	Jackson et al. (2005)
	73	13.6	FDA exploratory samples
	4	78	FDA TDS
Cantaloupe	1	1600	Jackson et al. (2005)
	48	28.6	FDA exploratory samples
	4	24.4	FDA TDS
Oranges	28	7.4	Sanchez et al. (2006)
	10	3.4	FDA exploratory samples
	4	2.7	FDA TDS
Grapefruit	15	3.3	Sanchez et al. (2006)
	4	0.5	FDA TDS

LOD, limit of detection; ND, non-detect.
[a]Mean for FDA samples are based on ND = 1/2LOD.

Table 9. Iodine levels in selected foods.

Iodine levels		Concentration–wet weight (μg/kg)	
Commodity	*n* samples	Mean	Source
Milk	47	89.2	Kirk et al. (2005)
	18	464	Pearce et al. (2004)
	20	417	FDA TDS
Infant formula	8	159	Pearce et al. (2004)
	15	136	FDA TDS
Bread	17	334	Pearce et al. (2004)
	25	312	FDA TDS

concentrations in milk reported by Kirk et al. (2005) were considerably lower than either the TDS samples or those reported by Pearce et al. (2004), but TDS iodine levels in infant formula and bread were consistent with those reported in the literature.

These TDS results increase substantially the available data for characterizing dietary exposure to perchlorate and provide a useful basis for the beginning to evaluate overall perchlorate and iodine estimated dietary intakes in the US population. The next major step is to analyze future TDS market baskets for perchlorate and iodine. More robust data sets will provide a clearer picture of estimated perchlorate and iodine intakes using not only the TDS approach to estimating intakes but also by using the analytical results from the TDS with detailed consumption data from the CSFII or NHANES surveys. Targeting the food consumption patterns based upon results from these surveys could provide an estimate of the distribution of iodine and perchlorate intakes by women of childbearing age who are pregnant and/or lactating. Data from these surveys could also be combined to develop an estimate of iodine and perchlorate intakes specifically for pregnant and lactating women, which could provide more information about the potential for perchlorate inhibition of iodide uptake by the thyroid to occur in this population subgroup.

Acknowledgements

The Total Diet Study is a collaborative effort of FDA's Center for Food Safety and Applied Nutrition (CFSAN) and FDA's district offices and laboratories. Finally, the authors of this work do not have any involvement, financial, or otherwise, that might potentially bias their work.

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Exhibit G

National Institutes of Health
MedlinePlus: Hypothyroidism

National Institutes of Health / U.S. National Library of Medicine

URL of this page: https://www.nlm.nih.gov/medlineplus/hypothyroidism.html

Hypothyroidism

Your thyroid [https://www.nlm.nih.gov/medlineplus/thyroiddiseases.html] is a butterfly-shaped gland in your neck, just above your collarbone. It is one of your endocrine glands, which make hormones. Thyroid hormones control the rate of many activities in your body. These include how fast you burn calories and how fast your heart beats. All of these activities are your body's metabolism. If your thyroid gland is not active enough, it does not make enough thyroid hormone to meet your body's needs. This condition is hypothyroidism.

Hypothyroidism is more common in women, people with other thyroid problems, and those over 60 years old. Hashimoto's disease, an autoimmune disorder, is the most common cause. Other causes include thyroid nodules, thyroiditis, congenital hypothyroidism, surgical removal of part or all of the thyroid, radiation treatment of the thyroid, and some medicines.

The symptoms can vary from person to person. They may include

- Fatigue
- Weight gain
- A puffy face
- Cold intolerance
- Joint and muscle pain
- Constipation
- Dry skin
- Dry, thinning hair
- Decreased sweating
- Heavy or irregular menstrual periods and fertility problems
- Depression
- Slowed heart rate

To diagnose hypothyroidism, your doctor will look at your symptoms and blood tests. Treatment is with synthetic thyroid hormone, taken every day.

NIH: National Institute of Diabetes and Digestive and Kidney Diseases

Start Here

- Hypothyroidism [http://familydoctor.org/familydoctor/en/diseases-conditions/hypothyroidism.printerview.all.html]

ADD 134

(American Academy of Family Physicians)
Available in Spanish [http://es.familydoctor.org/familydoctor/es/diseases-conditions/hypothyroidism.printerview.all.html]

- Hypothyroidism [http://www.thyroid.org/hypothyroidism/] (American Thyroid Association)
  Available in Spanish [http://www.thyroid.org/hipotiroidismo/]
- Hypothyroidism [http://www.niddk.nih.gov/health-information/health-topics/endocrine/hypothyroidism/Documents/Hypothyroidism_508.pdf] (National Institute of Diabetes and Digestive and Kidney Diseases) - **PDF**
- Hypothyroidism (Underactive Thyroid) [http://www.mayoclinic.org/diseases-conditions/hypothyroidism/home/ovc-20155291?p=1] (Mayo Foundation for Medical Education and Research)

Latest News

- Overactive Thyroid Linked to Breast Cancer Risk [https://www.nlm.nih.gov/medlineplus/news/fullstory_157203.html] (02/11/2016, HealthDay)

Diagnosis and Tests

- Free T4 (Thyroxine) Test [https://labtestsonline.org/understanding/analytes/t4/tab/test]
  (American Association for Clinical Chemistry)
- T3 (Triiodothyronine) Test [https://labtestsonline.org/understanding/analytes/t3/tab/test]
  (American Association for Clinical Chemistry)
- Thyroid Function Tests [http://www.thyroid.org/thyroid-function-tests/] (American Thyroid Association)
- Thyroid Scan and Uptake [http://www.radiologyinfo.org/en/info.cfm?PG=thyroiduptake]
  (Radiological Society of North America, American College of Radiology)
  Available in Spanish [http://www.radiologyinfo.org/sp/info.cfm?pg=thyroiduptake]
- Thyroid Tests [http://www.niddk.nih.gov/health-information/health-topics/diagnostic-tests/thyroid-tests/Pages/default.aspx] (National Institute of Diabetes and Digestive and Kidney Diseases)
- TSH (Thyroid-Stimulating Hormone) Test [https://labtestsonline.org/understanding/analytes/tsh/tab/test]
  (American Association for Clinical Chemistry)

Treatments and Therapies

- Medicines for Hypothyroidism [http://www.hormone.org/~/media/Hormone/Files/Questions%20and%20Answers/Thyroid/MedicinesforHypothyroidismEnglishWEB.pdf] (Hormone Health Network) - **PDF**
  Available in Spanish [http://www.hormone.org/audiences/pacientes-y-cuidadores/preguntas-y-respuestas/2012/medicines-for-hypothyroidism]
- Thyroid Hormone Treatment [http://www.thyroid.org/thyroid-hormone-treatment/] (American Thyroid Association)

Related Issues

- Endocrinologist: What Is an Endocrinologist? [http://www.hormone.org/contact-a-health-professional/what-is-an-endocrinologist] (Hormone Health Network)
- Hypothyroidism and Heart Disease [http://www.hormone.org/questions-and-answers/2013/hypothyroidism-and-heart-disease] (Hormone Health Network)
  Available in Spanish [http://www.hormone.org/~/media/hormone/files/questions-and-answers/thyroid

ADD 135

/fs_td_hypothyroidism_heart_sp-116.pdf]

- Hypothyroidism: Can It Cause Peripheral Neuropathy? [http://www.mayoclinic.org/diseases-conditions/peripheral-neuropathy/expert-answers/hypothyroidism/FAQ-20058489?p=1] (Mayo Foundation for Medical Education and Research)
- Hypothyroidism: Does It Cause Joint Pain? [http://www.mayoclinic.org/diseases-conditions/hypothyroidism/expert-answers/hypothyroidism/FAQ-20057789?p=1] (Mayo Foundation for Medical Education and Research)
- Iodine Deficiency [http://www.thyroid.org/iodine-deficiency/] (American Thyroid Association)
  Available in Spanish [http://www.thyroid.org/deficiencia-de-yodo/]
- Myth vs. Fact: Wilson's Temperature Syndrome [http://www.hormone.org/sitecore%20modules/web/~/media/Hormone/Files/Myth%20vs%20Fact/MFSWilsonsSyndrome%20524.pdf] (Hormone Health Network) - **PDF**
- Thyroid and Weight [http://www.thyroid.org/thyroid-and-weight/] (American Thyroid Association)

Specifics

- Goiter [http://www.mayoclinic.org/diseases-conditions/goiter/basics/definition/CON-20021266?p=1] (Mayo Foundation for Medical Education and Research)
- Hashimoto's Disease [http://www.mayoclinic.org/diseases-conditions/hashimotos-disease/basics/definition/CON-20030293?p=1] (Mayo Foundation for Medical Education and Research)
- Hashimoto's Disease [http://www.niddk.nih.gov/health-information/health-topics/endocrine/hashimotos-disease/Documents/hashimoto_508.pdf] NIH (National Institute of Diabetes and Digestive and Kidney Diseases) - **PDF**

Genetics

- Genetics Home Reference: Congenital hypothyroidism [https://ghr.nlm.nih.gov/condition/congenital-hypothyroidism] NIH (National Library of Medicine)
- Genetics Home Reference: Hashimoto thyroiditis [https://ghr.nlm.nih.gov/condition/hashimoto-thyroiditis] NIH (National Library of Medicine)

Clinical Trials

- ClinicalTrials.gov: Hypothyroidism [https://clinicaltrials.gov/search/open/condition=%22Hypothyroidism%22] NIH (National Institutes of Health)
- ClinicalTrials.gov: Thyroiditis, Autoimmune [https://clinicaltrials.gov/search/open/condition=%22Thyroiditis,+Autoimmune%22] NIH (National Institutes of Health)

Journal Articles

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- Article: Subclinical Hypothyroidism Overdiagnosis in Pregnant Women. [http://www.ncbi.nlm.nih.gov/pubmed/26524757?tool=MedlinePlus]
- Article: Drugs for hypothyroidism. [http://www.ncbi.nlm.nih.gov/pubmed/26488425?tool=MedlinePlus]

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- Hypothyroidism -- see more articles [http://www.ncbi.nlm.nih.gov/pubmed?term=hypothyroidism[majr]+AND+english[la]+AND+humans[mh]+AND+(guideline[pt]+OR+clinical+trial[pt]+OR+jsubsetk[text]+OR+jsubsetaim[text]+OR+jsubsetn[text]+OR+patient+education+handout[pt])+NOT+(letter[pt]+OR+editorial[pt]+OR+case+reports[pt])+AND+%22last+2+Years%22[edat]&tool=MedlinePlus]

Reference Desk

- Thyroid Disease Definitions [http://kidshealth.org/en/teens/thyroid-definitions.html] (Nemours Foundation)
- What Does the Thyroid Gland Do? [http://www.hormone.org/hormones-and-health/what-do-hormones-do/what-does-the-thyroid-gland-do] (Hormone Health Network)

Find an Expert

- American Thyroid Association [http://www.thyroid.org/]
- Find an Endocrinologist [http://www.hormone.org/contact-a-health-professional/find-an-endocrinologist] (Hormone Health Network)
- Find an Endocrinology - Thyroid Specialist [http://www.thyroid.org/patient-thyroid-information/endocrinology-thyroid-doctor/] (American Thyroid Association)
- Hormone Health Network [http://www.hormone.org/]
- National Institute of Diabetes and Digestive and Kidney Diseases [http://www.niddk.nih.gov/Pages/default.aspx] NIH

Children

- Congenital Hypothyroidism [http://www.hormone.org/questions-and-answers/2012/congenital-hypothyroidism] (Hormone Health Network)
  Available in Spanish [http://www.hormone.org/audiences/pacientes-y-cuidadores/preguntas-y-respuestas/2012/hipotiroidismo-congenito]

Women

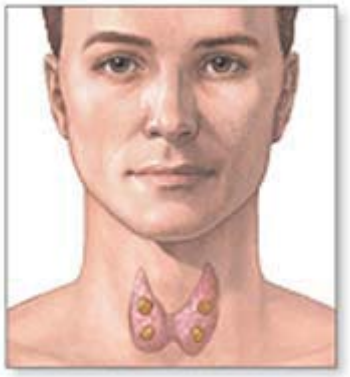
- Hashimoto's Disease [http://womenshealth.gov/publications/our-publications/fact-sheet/hashimoto-disease.html] (Department of Health and Human Services, Office on Women's Health)
- Patient's Guide to Detecting and Treating Hypothyroidism Before, During, and After Pregnancy [http://www.hormone.org/sitecore%20modules/web/~/media/Hormone/Files/Patient%20Guides/Womens%20Health/PGMaternalHypothyroidism%20523.pdf] (Hormone Health Network) - **PDF**

Patient Handouts

- Chronic thyroiditis (Hashimoto's disease) [https://www.nlm.nih.gov/medlineplus/ency/article/000371.htm]
  Available in Spanish [https://www.nlm.nih.gov/medlineplus/spanish/ency/article/000371.htm]
- Factitious hyperthyroidism [https://www.nlm.nih.gov/medlineplus/ency/article/000309.htm]
  Available in Spanish [https://www.nlm.nih.gov/medlineplus/spanish/ency/article/000309.htm]
- Hashimoto's Disease [http://www.niddk.nih.gov/health-information/health-topics/endocrine/hashimotos-disease/Documents/hashimoto_508.pdf] NIH (National Institute of Diabetes and Digestive and Kidney Diseases) - **PDF**

ADD 137

- Hypothyroidism [https://www.nlm.nih.gov/medlineplus/ency/article/000353.htm]
  Available in Spanish [https://www.nlm.nih.gov/medlineplus/spanish/ency/article/000353.htm]
- Neonatal hypothyroidism [https://www.nlm.nih.gov/medlineplus/ency/article/001193.htm]
  Available in Spanish [https://www.nlm.nih.gov/medlineplus/spanish/ency/article/001193.htm]
- Silent thyroiditis [https://www.nlm.nih.gov/medlineplus/ency/article/000388.htm]
  Available in Spanish [https://www.nlm.nih.gov/medlineplus/spanish/ency/article/000388.htm]
- Subacute thyroiditis [https://www.nlm.nih.gov/medlineplus/ency/article/000375.htm]
  Available in Spanish [https://www.nlm.nih.gov/medlineplus/spanish/ency/article/000375.htm]
- T4 test [https://www.nlm.nih.gov/medlineplus/ency/article/003517.htm]
  Available in Spanish [https://www.nlm.nih.gov/medlineplus/spanish/ency/article/003517.htm]
- Thyroid Tests [http://www.niddk.nih.gov/health-information/health-topics/diagnostic-tests/thyroid-tests/Pages/default.aspx] NIH (National Institute of Diabetes and Digestive and Kidney Diseases)
- TSH test [https://www.nlm.nih.gov/medlineplus/ency/article/003684.htm]
  Available in Spanish [https://www.nlm.nih.gov/medlineplus/spanish/ency/article/003684.htm]



MEDICAL ENCYCLOPEDIA

Chronic thyroiditis (Hashimoto's disease) [https://www.nlm.nih.gov/medlineplus/ency/article/000371.htm]

Factitious hyperthyroidism [https://www.nlm.nih.gov/medlineplus/ency/article/000309.htm]

Hypothyroidism [https://www.nlm.nih.gov/medlineplus/ency/article/000353.htm]

Neonatal hypothyroidism [https://www.nlm.nih.gov/medlineplus/ency/article/001193.htm]

Silent thyroiditis [https://www.nlm.nih.gov/medlineplus/ency/article/000388.htm]

Subacute thyroiditis [https://www.nlm.nih.gov/medlineplus/ency/article/000375.htm]

T4 test [https://www.nlm.nih.gov/medlineplus/ency/article/003517.htm]

Thyroid scan [https://www.nlm.nih.gov/medlineplus/ency/article/003829.htm]

TSH test [https://www.nlm.nih.gov/medlineplus/ency/article/003684.htm]

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Related Health Topics

Hyperthyroidism [https://www.nlm.nih.gov/medlineplus/hyperthyroidism.html]

Thyroid Cancer [https://www.nlm.nih.gov/medlineplus/thyroidcancer.html]

Thyroid Diseases [https://www.nlm.nih.gov/medlineplus/thyroiddiseases.html]

National Institutes of Health

The primary NIH organization for research on *Hypothyroidism* is the National Institute of Diabetes and Digestive and Kidney Diseases [http://www.niddk.nih.gov/]

NIH MedlinePlus Magazine

Hypothyroidism: Symptoms, Diagnosis & Treatment [https://www.nlm.nih.gov/medlineplus/magazine/issues/spring12/articles/spring12pg24-25.html]

MedlinePlus links to health information from the National Institutes of Health and other federal government agencies. MedlinePlus also links to health information from non-government Web sites. See our disclaimer [https://www.nlm.nih.gov/medlineplus/disclaimers.html] about external links and our quality guidelines [https://www.nlm.nih.gov/medlineplus/criteria.html] .

Page last updated on 12 February 2016

Topic last reviewed: 9 May 2014

ADD 139

Exhibit H

Charles W. Husum and Jack M. Wheaton
Closure Sealing Gaskets, U.S. Patent No. 2,689,840 (filed Aug. 26, 1952)

Patented Sept. 21, 1954

2,689,840

UNITED STATES PATENT OFFICE

2,689,840

CLOSURE SEALING GASKETS

Charles W. Husum and Jack M. Wheaton, Toledo, Ohio, assignors to Owens-Illinois Glass Company, a corporation of Ohio

No Drawing. Application August 26, 1952, Serial No. 306,499

6 Claims. (Cl. 260—41.5)

1

The present invention relates to improvements in sealing gaskets which are utilized in conjunction with metal closures in hermetically closing containers, particularly glass containers, for perishable foods.

An object of this invention is the provision of a sealing gasket of such composition as will completely prevent, or in any event reduce to a point at which any deleterious effect is negligible, both corrosion of the metal closure and discoloration of the packaged product.

Both corrosion and discoloration have posed extremely serious problems and resulted in substantial annual loss to the packers, aggregating hundreds of thousands of dollars. With respect particularly to discoloration, many foods, such as beets, squash, carrots, peaches, sweet potatoes, etc., the discoloration (darkening) is quite pronounced, but with practically all products there is some appreciable and objectionable discoloration. Whereas foods sealed with an ordinary standard metal closure become seriously discolored within g aiven period of time, identical foods sealed with closures incorporating our improved sealing gasket, for the same period of time and under like conditions, show absolutely no discoloration.

It has been quite conclusively determined that entrance of oxygen into the packages is the primary, if not the sole cause of such discoloration. Permeability of conventional sealing gasket compounds to oxygen is the controlling factor with relation to discoloration. We have, as a consequence of the foregoing, determined "GRA," which is butadiene-acryonitrile rubber, to be most effective in retarding the passage of oxygen into the sealed containers. Butyl rubber has also been found to be satisfactory from permeability standpoint, but is not suitable for use as a gasket because of its lack of resilience.

With respect to corrosion, such occurs in the tin plated closures as a result of very small exposed parts of the iron base material and the creation in effect of an electrolytic cell. Such is due to the existence of an electric circuit through the packed product (which functions as an electrolyte), the sealing gasket, and iron base material beneath the tin coating of the closure.

Our experiments have shown that the part of the carbon filler that has a chain-like structure acts as the cathode and the iron in the closure provides the anode.

Closures of the general type involved are shown in Hoge Patent #2,441,918 and Hohl et al. Patent #2,443,506. Obviously, other types of closures may be used. The tin coating almost invariably contains small pinholes, which actually expose the base metal. Organic coatings applied to the plate have weak spots (low dielectric) through which a current will flow. Such conditions, together with the electrical conductivity characteristics of conventional sealing gasket compositions, contributes to the creation of the aforementioned electrolytic cell, and consequent corrosion. As a result there is serious pitting and corrosion of the underside of the closure "panel" or top portion and frequent pinholing. Consequently, food spoilage occurs.

2

We have discovered, as suggested in our copending application, S. N. 237,118, filed July 17, 1951, entitled Method and Means for Inhibiting Corrosion of Metal Closures, that such corrosion can be eliminated by utilizing a gasket formulation, or composition, which limits the percentage of carbon black present with chain-like or electric current conducting structure, as observed under an electron microscope. To this end we have formulated a composition possessing the two-fold function of (1) effectively preventing transfer of oxygen through the gasket to the interior of the container, and (2) preventing an electro-chemical effect. Thus, in a single composition we have provided a structure which eliminates both discoloration and corrosion.

In the sealing gasket which has been found to be most effective, the components, in parts by weight, are about as follows:

GRA-butadiene-acrylonitrile rubber	100
Sulphur	3
Zinc oxide	5
Plasticizer	20
Stearic acid	1
Accelerator	1
Thermax (isolated globule type carbon black particles)	130
Philblack A (chain-type carbon black)	20
	280

Thermax is a product of Thermatomic Carbon Company and Philblack A, a product of Phillips Chemical Company, Akron, Ohio. The components indicated may be increased, or decreased, slightly, as determined by the physical characteristics desired in the gasket. We have ascertained that "Thermax" which is a carbon black of generally isolated, large globular, or particle structure apparently of about 274 millimicrons

diameter, may comprise from about 125 to 140 parts by weight in a composition of 280 parts. In such carbon black, when compounded into rubber, the globules are sufficiently discrete and isolated from each other to be ineffective in conducting electric current. Such material serves as an excellent filler, but contributes little to the resiliency or hardness of the compound. Any carbon black having the characteristics indicated may be utilized.

With respect to "Philblack A" which is a chain-type carbon black, apparently having a mean particle diameter of about 51 millimicrons, we have determined that it should comprise no more than about 12% by weight of the total composition. This is based upon the discovery that if used in excess, Philblack A, or its equivalent, definitely causes corrosion. This chain-type carbon is a filler which functions to impart smoothness for extrusion purposes, as well as the necessary degree of resilience and hardness. In lieu of Philblack A, we may use in the same amounts any of the following carbon blacks: Statex K, or Statex M., which are furnace blacks produced by Columbian Carbon Company, of New York city; Sterling 30, a product of Cabot, Inc., Boston, Massachusetts; or Dixie 50, or Kosmos 50, which are products of United Carbon Company, Inc., Charleston, W. Va.

We have also discovered that satisfactory results, or in any event, results incomparably superior to those obtained with conventional gaskets, may be obtained where 125 or 140 parts by weight of "Thermax" are used together with 25 or 10 parts by weight of Philblack A, respectively.

As being indicative of the asserted criticalness of the particular carbon content and proportions, we show below three formulations in which the amounts of the two carbons have been varied.

	A	B	C
GRA	100	100	100
Sulphur	3	3	3
Zinc oxide	5	5	5
Plasticizer	20	20	20
Stearic Acid	1	1	1
Accelerator	1	1	1
Thermax	110	125	140
Philblack A	40	25	10

Applicant's several years of experience in the actual testing of processed food closures for resistance to corrosion, or pitting, has developed the fact that the absence of significant pitting, at the end of three months' storage at 125° F., is a reliable index of the performance of closures for one year at room temperature. Quite frequently sheets of tinplate, as received from the tin mill, contain slight pits of from .001 to .003 of an inch in depth. It has also been our observation that a slight etching of the tinplate often occurs, which does not continue after a depth of .001 or .002 of an inch has been reached.

Because of the foregoing we are not concerned with pits of from .001 to .003 of an inch in depth. However, we have discovered that when a pit is in excess of .003 of an inch in depth, after a period of three (3) months' storage at 125° F., that is .004, .005, etc., there is serious danger that corrosion will continue, cause perforation and probable food spoilage.

In the following tables, we have indicated the comparative results of using the three gasket compositions above described. The importance of controlling the carbon black content is readily apparent.

3 MONTHS—100° F.

Product	Gasket Formula	Caps Examined	Caps with Pits over .003" in Depth
Beets	A	20	3
Do	B	46	0
Do	C	46	0
Carrots	A	20	7
Do	B	44	0
Do	C	44	0
Liver Soup	A	20	2
Do	B	46	0
Do	C	46	0

3 MONTHS—125° F.

Beets	A	28	6
Do	B	66	0
Do	C	67	0
Carrots	A	28	4
Do	B	65	0
Do	C	65	0
Liver Soup	A	20	3
Do	B	45	0
Do	C	45	0

In all instances, the product color was excellent, thus indicating the impermeability of the selected type of rubber to atmospheric oxygen and that discoloration is caused by entry of oxygen into the container. Corrosion, however, was excessive in formulation A. By contrast, the modification of the carbon content in formulations A and B, wherein Thermax was increased and Philblack A decreased, there was no ultimate corrosion deeper than .003 of an inch.

It has been determined that the best results, as regards non-corrosive action, are obtained where the ratio of Philblack A to Thermax is less than about 4 to 11.

Thus, it is apparent that we have discovered that corrosion and discoloration are not interrelated as regards cause, in that either can be present without the other. Also, that permeability of the gasket material to oxygen determines the extent and rapidity of discoloration and that the carbon black content and type, determine whether corrosion will, or will not develop, quite apart from the discoloration aspects. It is possible to concurrently have severe corrosion of the closure and good color retention, such being due to the use of the proper type of rubber, but improper carbon blacks and in the wrong proportions. Moreover, both corrosion resistance and poor color retention may result, if the rubber component is incorrect. In our gasket composition both of the foregoing problems have been completely solved.

Inasmuch as some foods are much less subject to discoloration than others and in such instances only corrosion prevention requires special attention, we contemplate the use of known types of rubber which may be less effective than GRA as a barrier to oxygen passage. However, the use of Termax or equivalent carbon blacks such as "Shell 53," is essential in corrosion prevention. Hence in such circumstances we utilize these two carbon blacks in about the proportions stated heretofore, it being understood that Philblack A serves to improve workability, extrusion, etc., of the composition, as explained above.

Modifications may be resorted to within the spirit and scope of the appended claims.

We claim:

1. A sealing gasket composition for sheet metal caps used in closing bottles and jars, which comprises about 100 parts butadiene acrylonitrile rubber; about 3 parts sulphur; about 5 parts zinc oxide; about 20 parts plasticizer; about 1 part stearic acid; about 1 part accelerator; about 130 parts of carbon black composed largely of discrete isolated particles and about 20 parts of a chain-like carbon black.

2. The composition recited in claim 1, wherein furnace type carbon black is the chain-like carbon black.

3. The composition recited in claim 1, wherein the chain-type carbon black constitutes a maximum of about 12% by weight of the total composition.

4. A sealing gasket composition for sheet metal caps used in closing bottles and jars comprising 100 parts by weight of butadiene-acrylonitrile rubber, from about 25 to about 10 parts by weight of a carbon black of chain-like structure and from about 125 to about 140 parts by weight of a carbon black composed of isolated globular particles.

5. A sealing gasket composition for sheet metal caps used in closing bottles and jars comprising butadiene acrylonitrile rubber and a filler consisting of a carbon black which is composed largely of substantially discrete, relatively isolated particles and a carbon black having a chain-like structure, the ratio of the second named carbon black to the first named carbon black being less than 4 to 11 and the carbon black of chain-like structure comprising less than about 12% by weight of the total composition.

6. A sealing gasket composition for sheet metal caps used in closing bottles and jars comprising butadiene acrylonitrile rubber, a carbon black of chain-like particle structure, and a carbon black consisting largely of substantially discrete relatively isolated globular particles whose diameter is approximately 274 millimicrons, the ratio of the carbon black of chain-like particle structure to the second named carbon black being less than 4 to 11 and the carbon black of chain-like structure comprising less than about 12% by weight of the total composition.

References Cited in the file of this patent

UNITED STATES PATENTS

Number	Name	Date
2,594,165	Helms	Apr. 22, 1952

Exhibit I

Paul Honigfort
Memorandum of Meeting with the Society of the Plastics Industry and BASF Corporation Regarding the Allowed Use of Perchlorates in Food Contact Applications (July 10, 2015)

Memorandum

Date: July 10, 2015

From: Paul Honigfort, Ph.D.
To: Administrative File: FAP 4B4808

MEMORANDUM OF MEETING

RE: Meeting with the Society of the Plastics Industry (SPI) and BASF Corporation regarding the allowed use of perchlorates in food contact applications

MEETING DATE: May 18, 2015

TIME: 2:00 PM – 3:00 PM

LOCATION: 4300 River Road, College Park, MD 20740, Rm 2013

ATTENDEES:

Food and Drug Administration (FDA): Michael Adams (OFAS Deputy Office Director), Francis Lin (DFCN Division Director), Jason Peckenpaugh (Attorney, Office of Chief Council), Ralph Simmons (Policy Advisor), Kirk Arvidson (Supervisory Chemist), Jason Aungst (Supervisory Toxicologist), Edward Machuga (Supervisory Consumer Safety Officer), Suzanne Hill (Supervisory Environmental Reviewer), Geoff Patton (Toxicologist), Jessica Cooper (Chemist), Roseann Costantino (Chemist), Paul Honigfort (Consumer Safety Officer)

Society of the Plastics Industry (SPI): Kyra Mumbauer (Senior Director, Global Regulatory Affairs – SPI), Devon Hill (Legal Counsel – Keller and Heckman, LLP), Daniel Rubenstein (Legal Counsel – Keller and Heckman, LLP), Lester Borodinsky (Staff Scientist- Keller and Heckman, LLP)

BASF Corporation (BASF): Henry Su (Senior Product Regulations Specialist - BASF Corporation), John Hand (Staff Scientist – BASF Corporation), David Horst (Product Stewardship – BASF Corporation)

SUMMARY: Keller and Heckman, on behalf of both SPI and BASF, requested this meeting to discuss the currently allowed uses of perchlorates in food contact applications. At the meeting SPI noted that domestic and foreign producers of perchlorates may not currently manufacture perchlorate for use in closure sealing gaskets for food containers. BASF indicated that the use of sodium perchlorate monohydrate as a conductivity enhancer as per Threshold of Regulation (TOR) exemption 2005-006 does not result in migration of perchlorate to food.

During the meeting it was noted that the food contact uses of under discussion are the subject of a separate food additive petition (FAP 4B4808) currently under review by the Agency. FAP 4B4808 was submitted by the Natural Resources Defense Council and other petitioners and seeks to revoke the allowed uses of perchlorates based upon safety.

Paul S. Honigfort -S

Digitally signed by Paul S. Honigfort -S
DN: c=US, o=U.S. Government, ou=HHS, ou=FDA, ou=People, 0.9.2342.19200300.100.1.1=1300198120, cn=Paul S. Honigfort -S
Date: 2015.07.10 12:10:21 -04'00'

Paul Honigfort, Ph.D.

Exhibit J

Avram Levi
Inner Device for Neutralization of Electrostatic Charges from Material in Contact, U.S. Patent Application No. 2004/0004804 A1 (filed Dec. 23, 2002)

US 20040004804A1

(19) **United States**

(12) **Patent Application Publication** (10) **Pub. No.: US 2004/0004804 A1**

Levi (43) **Pub. Date: Jan. 8, 2004**

(54) **INNER DEVICE FOR NEUTRALIZATION OF ELECTROSTATIC CHARGES FROM MATERIAL IN CONTACT**

(76) Inventor: **Avram Levi**, Istanbul (TR)

Correspondence Address:
COLLEN IP
THE HOLYOKE MANHATTAN BUILDING
80 SOUTH HIGHLAND AVENUE
OSSINING, NY 10562 (US)

(21) Appl. No.: **10/328,110**

(22) Filed: **Dec. 23, 2002**

(30) **Foreign Application Priority Data**

Jul. 5, 2002 (TR)..... TR 2002/01757

Publication Classification

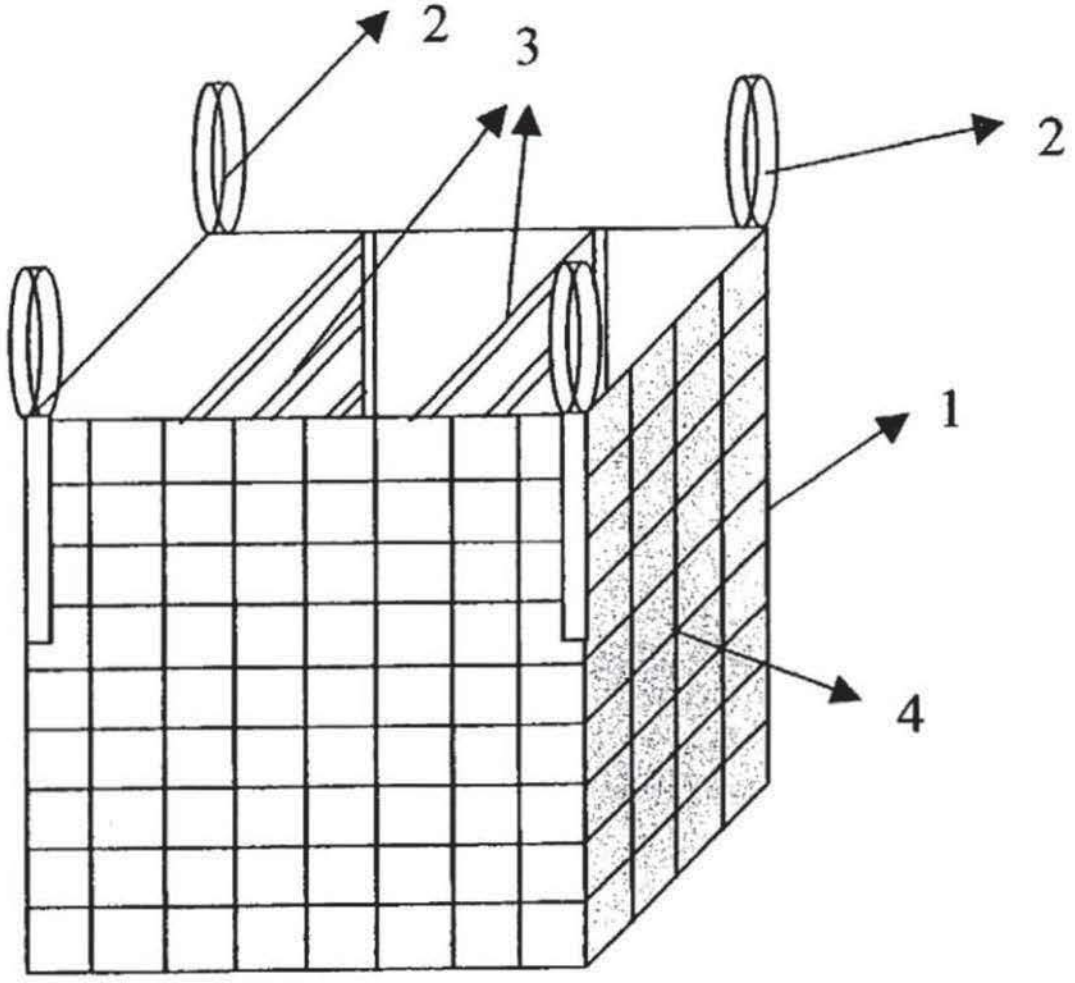
(51) **Int. Cl.**[7] **H02H 1/00**

(52) **U.S. Cl.** **361/220**

(57) **ABSTRACT**

The present invention is about a mechanism in the a container such as a FIBC, which enables the immediate neutralization of the electrostatic charges generated during filling, emptying or transporting of the containers. FIBCs are used to carry bulk solid powders, such as sugar, flour, starch and chemical substances.

The FIBC, which enables neutralization of the electrostatic charge generated within the material in the bag, developed with this invention, is characterized by inner devices knitted preferably with multi-filaments or mono-filaments and tapes, made of polymers in the form of a web or net with a special antistatic additive, established to an appropriate place in the FIBC so as to have maximum contact with the bulk solid powders in the FIBC in order to neutralize the electrostatic charge at distant points of the FIBC's wall.



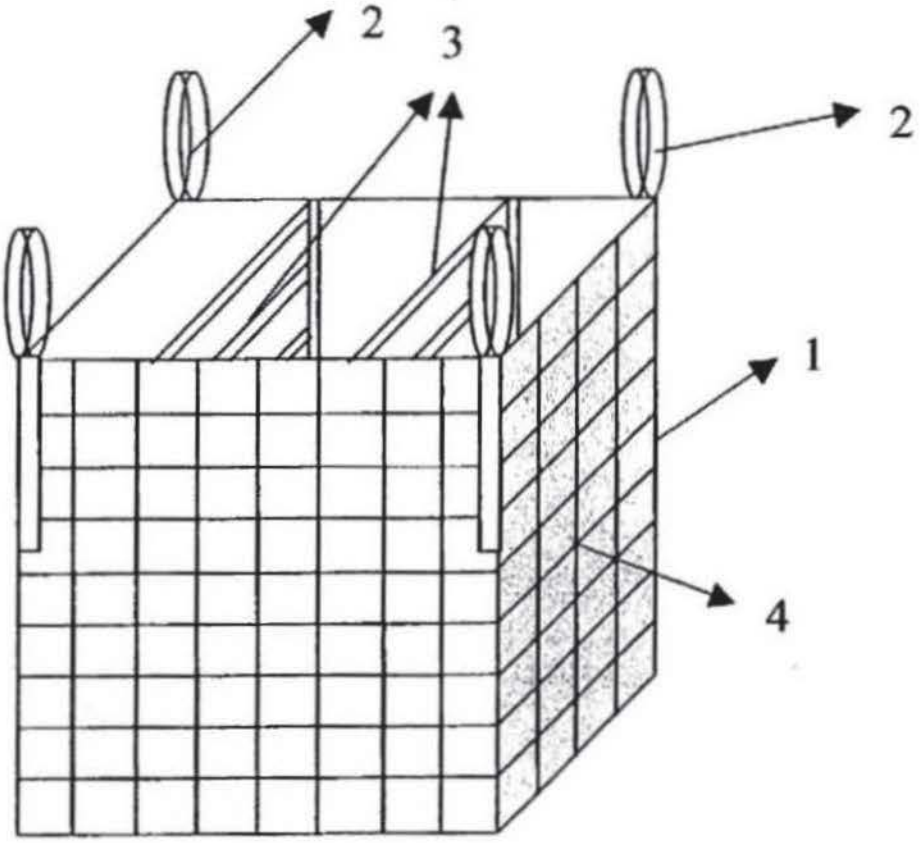


Figure -1

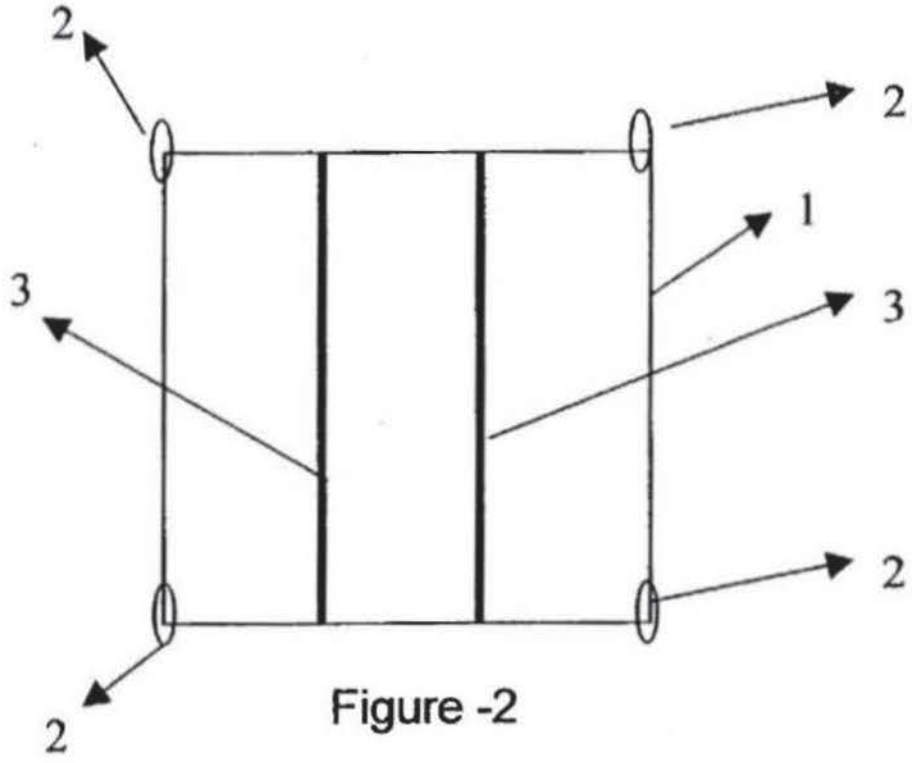


Figure -2

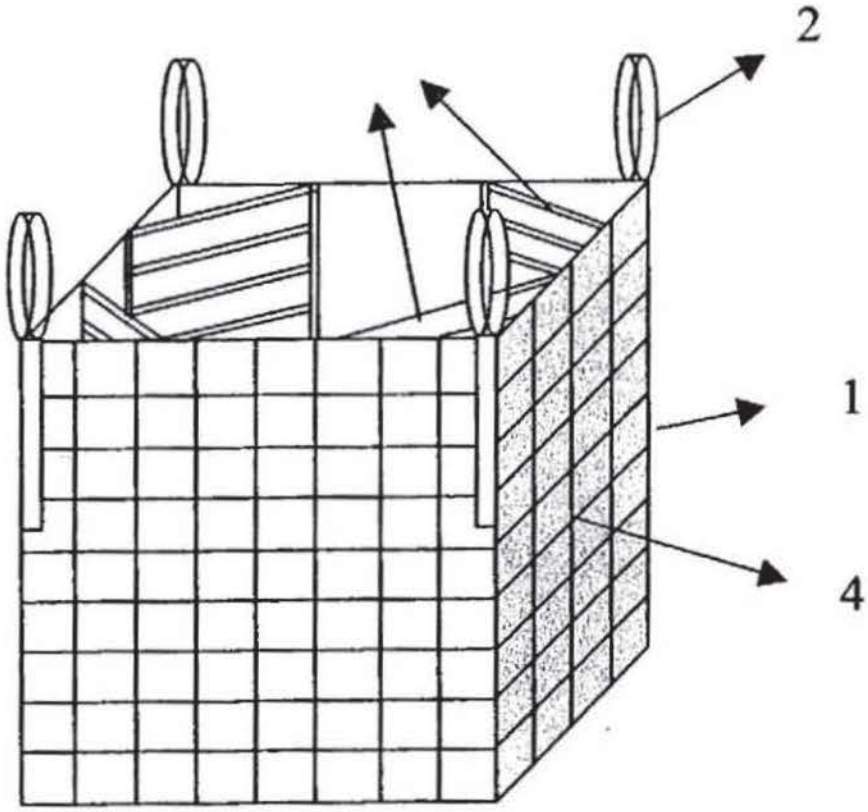


Figure -3

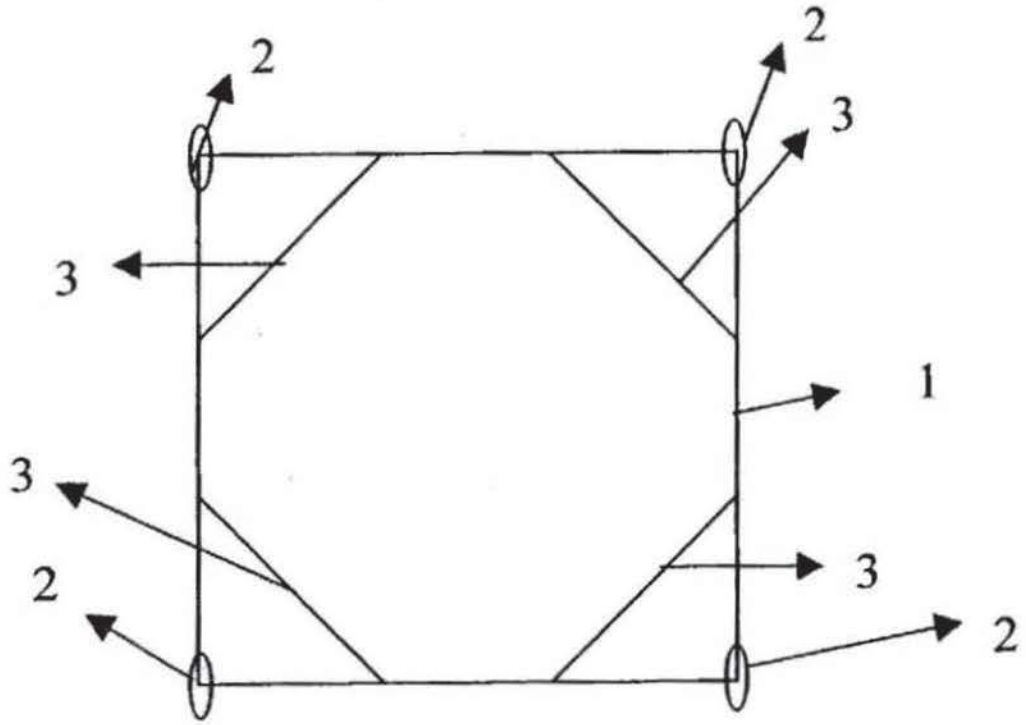


Figure -4

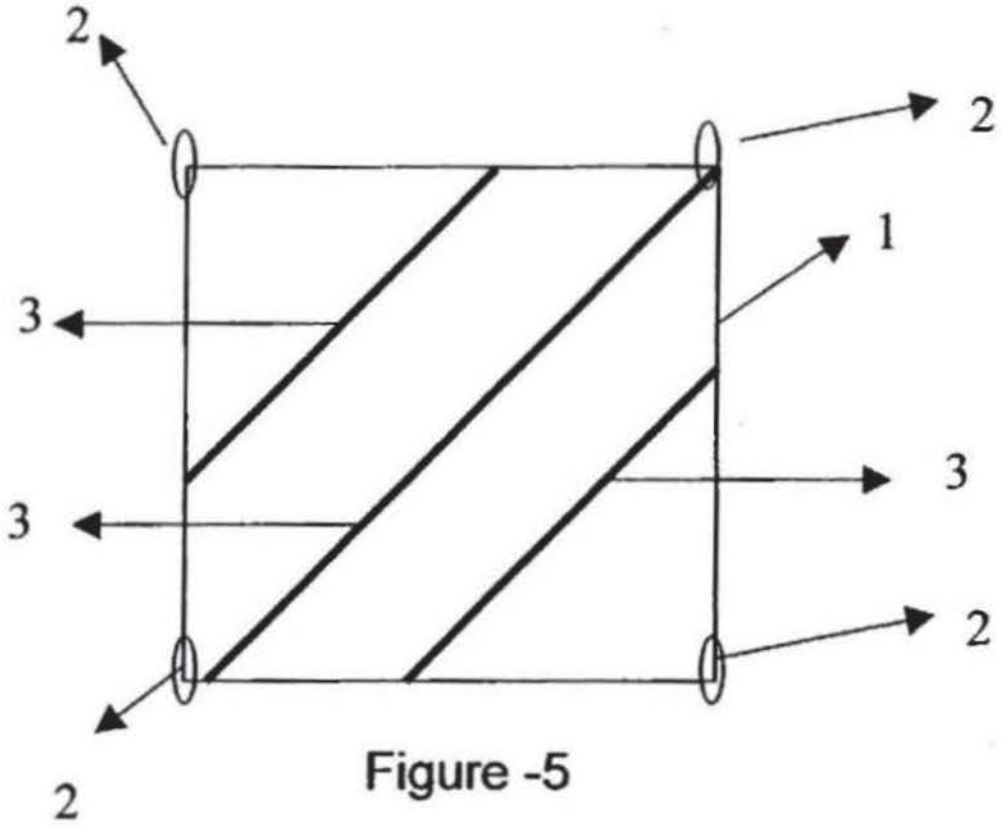


Figure -5

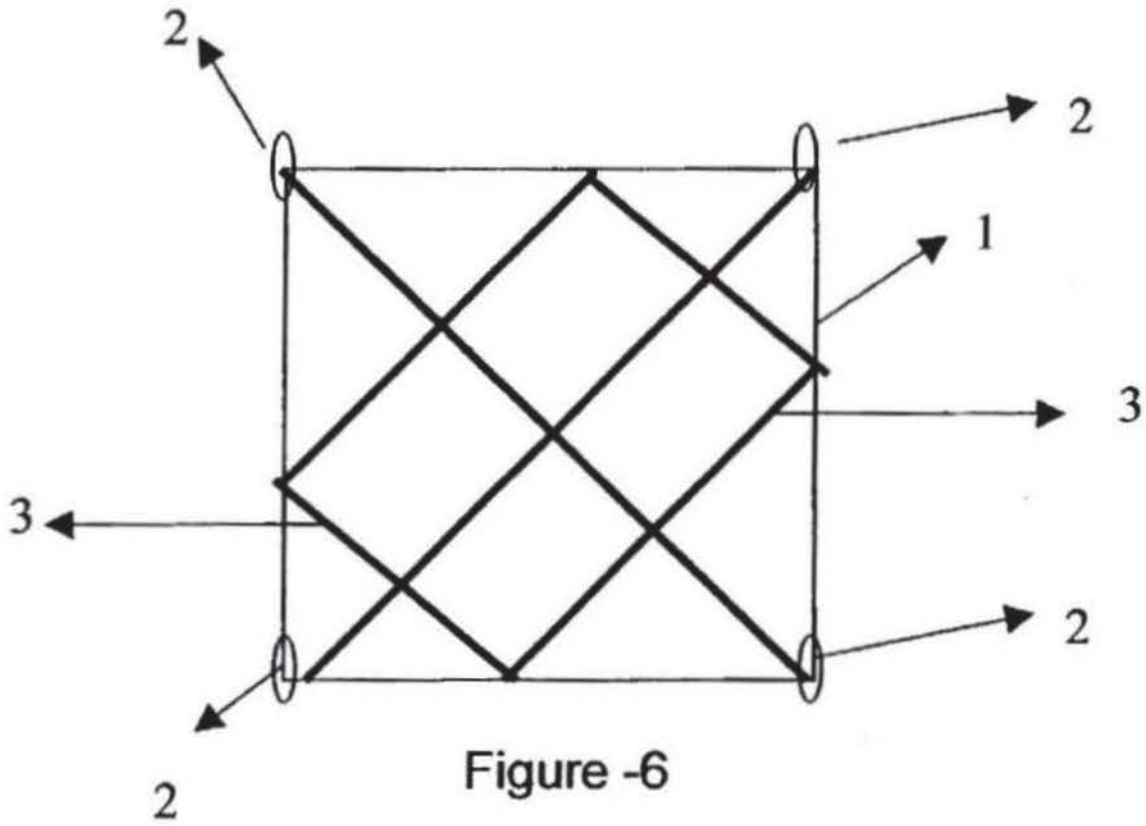


Figure -6

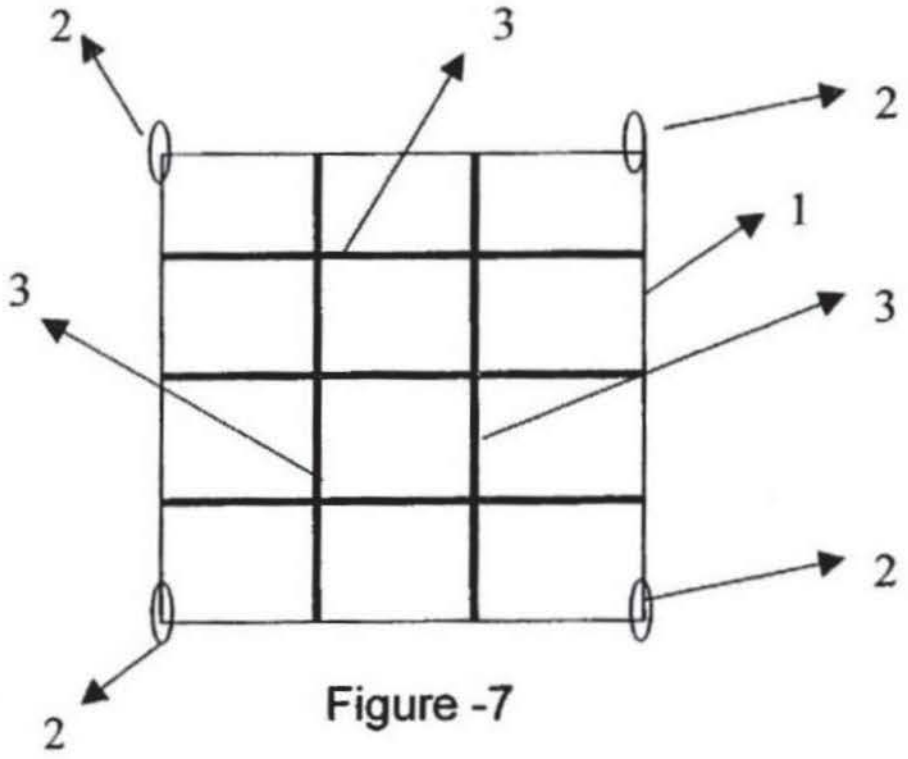


Figure -7

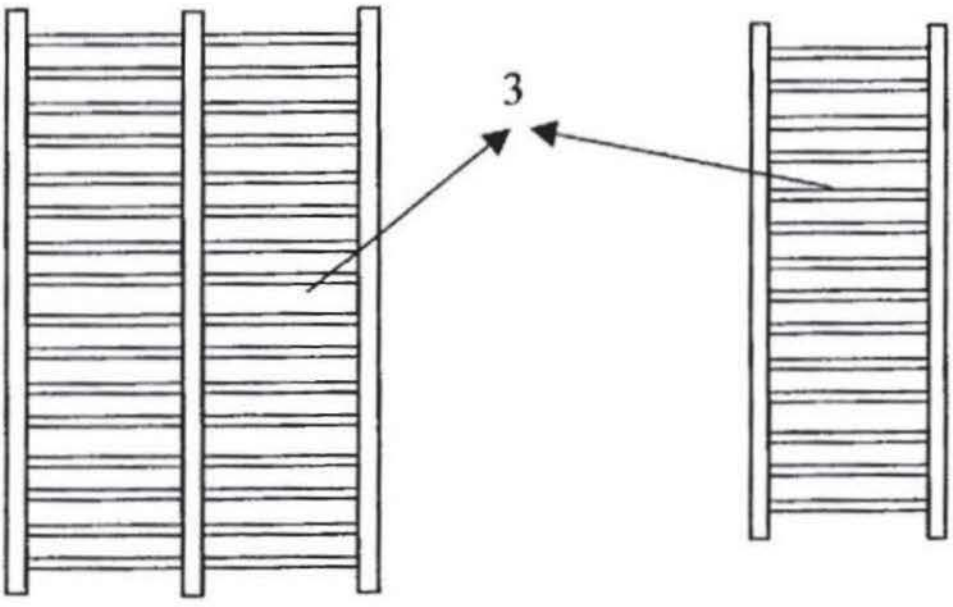


Figure -8

Figure -9

INNER DEVICE FOR NEUTRALIZATION OF ELECTROSTATIC CHARGES FROM MATERIAL IN CONTACT

BACKGROUND

[0001] The present invention addresses a mechanism for use in a Flexible Intermediate Bulk Container (FIBC), which enables the immediate neutralization of the electrostatic charges generated during filling, emptying or transporting of the FIBC. FIBC's are used to carry bulk solids powders, such as sugar, flour, starch and chemical substances.

[0002] During the filling and emptying of FIBC's which are typically made of polymer-based fabric such as polypropylene, HDPE, LLDPE etc., electrical charges can accumulate on the FIBC and inside the FIBC. Electrostatic charges may cause electrostatic discharges and ignition risks in the presence of flammable atmosphere.

[0003] In relation to this issue, there is a patent application TR2001/03444, filed on Nov. 28, 2001 at Turkish Patent Institute, titled "Flexible intermediate bulk container with multiple conductive fibers having permanent antistatic effect". It is explained that the electrostatic charge accumulated on the FIBC is discharged to the surrounding atmosphere by permanent anti-static-treated multi-filaments fibers in the FIBC. With the defined practice in this application the electrostatic charge generated during filling and emptying on the FIBC is neutralized. The static charge generated at a distance from the walls of the FIBC, however, cannot be neutralized immediately.

BRIEF SUMMARY OF THE INVENTION

[0004] An object of the present invention is to neutralize any electrostatic charges generated within the material in the FIBC bag during filling, emptying and transporting the FIBC, to avoid ignition risks in the presence of a flammable atmosphere.

[0005] The electrostatic changes generated in the material within the FIBC are neutralized in this invention by contact with inner devices which conduct the charge to the atmosphere. These inner devices consist of anti-static fibers configured within the material in the FIBC.

[0006] Although the present invention is described and depicted primarily in reference to its use inside FIBC's the principles of the inner devices can be readily adapted by one skilled in the art to other applications such as containers of all sizes including rail cars, trucks, silo's and any other enclosure used for storage/transport of bulk solid powders.

BRIEF DESCRIPTION FIGURES

[0007] The figures attached for further explanation of the FIBC and inner devices, which enables neutralization of the electrostatic charges within the material in the FIBC, are as follows:

[0008] **FIG. 1**—Perspective view of an example of a FIBC with inner devices for neutralizing electrostatic charge arranged in parallel with side

[0009] **FIG. 2**—Top view of an example of a FIBC with inner devices for neutralizing electrostatic charge arranged in parallel with one side

[0010] **FIG. 3**—Perspective view of an example of a FIBC with inner devices for neutralizing electrostatic charge arranged across to the corners

[0011] **FIG. 4**—Top view of an example of a FIBC with inner devices for neutralizing electrostatic charge arranged across to the corners

[0012] **FIG. 5**—Top view of an example of a FIBC with inner devices for neutralizing electrostatic charge arranged in parallel diagonally across the FIBC.

[0013] **FIG. 6**—Top view of an example of a FIBC with inner devices for neutralizing electrostatic charge arranged in parallel crisscrossing diagonally across the FIBC.

[0014] **FIG. 7**—Top view of an example of a FIBC with inner devices for neutralizing electrostatic charge arranged in parallel and perpendicular to opposing sides of the FIBC.

[0015] **FIG. 8**—Front view of an example of an inner device for a FIBC, in the shape of a ladder (double column)

[0016] **FIG. 9**—Front of an example of an inner device for a FIBC, in the shape of a ladder or web (single column)

DETAILED DESCRIPTION OF INVENTION

[0017] The FIBC **(1)**, which enables neutralization of the electrostatic charge generated within the material in the bag, developed with this invention, is characterized by inner devices **(3)** knitted preferably with multi-filaments or mono-filaments and configured in the various forms including ladder, web, or net, with a special antistatic additive. The FIBC inner devices are arranged in an appropriate configuration within the FIBC so as to have maximum contact with the bulk solids powders in the FIBC in order to neutralize the electrostatic charge at a distance from the FIBC's walls. There can be any number of internal devices as warranted to adequately neutralize the material within the bag. Sample configurations of these internal devices are depicted in FIGS. **1-7**. These inner devices **(3)** are configured in various geometrical forms and configurations to enable the neutralization of the electrostatic charge generated during filling, emptying and transporting and are preferably made of the same material as the sides. The inner devices are comprised of mono-filament or multi-filament fibers. These fibers for neutralizing the electrostatic charges preferably include permanent antistatic additives such as IRGASTAT P18 or IRGASTAT P22 manufactured by Ciba Geigy® at a ratio of %6-%20 preferably. The said inner devices **(3)** are produced from materials which can conduct electricity at each point. These antistatic agents are polyamide/polyether block amides which are incorporated as melt additives.

[0018] The resistance of the inner devices **(3)** of the FIBC **(1)**, which enables neutralization of the electrostatic charge generated within the material in the (FIBC), is 10^7 and 10^{12} ohms/square.

[0019] The fibers added to the inner devices **(3)** of the FIBC **(1)**, consist of polyamide and fiber conductive material with diameters of approximately 0.2 to 15 μm (micron) and are constructed in the inner devices so as to form a web, net or ladder configuration Handles **(2)** are preferably provided to facilitate transport.

[0020] The inner devices **(3)** are configured in any appropriate arrangement or shape in a manner to maximize

contact with the bulk material with which the FIBC is filled. This includes, but is not limited to, inner devices configured in parallel, diagonally or centrally within the FIBC in reference to the side and bottom walls.

[0021] The inner devices (3) are preferably made of materials which readily conduct electricity to the FIBC outer walls by direct contact with the lateral devices (4).

1. An inner device comprising:

anti-static fibers

the anti-static fibers configured to maximize contact with a material to be neutralized

the antistatic fibers connected at the outer limits of the material to conduct electrostatic charges to atmosphere via contact with an outer container which is configured to contain the inner device.

2. An inner device according to claim 1 in which the anti-static fibers are mono-filament.

3. An inner device according to claim 1 in which the anti-static fibers are multi-filament.

4. An inner device according to claim 1 in which the fibers comprising the inner device are configured in a interconnected manner.

5. An inner device according to claim 1 in which the diameter of the fibers ranges from 0.2 to 15 μm (micron).

6. An inner device according to claim 1 in which the inner device is characterized by a resistance ranging from 10^7 to 10^{12} ohms/square.

7. An inner device according to claim 1 in which the inner device is made of materials which conduct electricity.

8. An inner devise according to claim 1 in which the container is made of the same material as the inner device.

9. A plurality of inner devices according to claim 1 which are configured within the container in an arrangement that facilitates maximum contact with the material within the container.

10. An inner device according to claim 1 in which the container is a Flexible Intermediate Bulk Container (FIBC).

11. An inner device according to claim 1 in which the anti-static fibers include anti-static additives of polyamide and fiber conductive material.

12. An inner device according to claim 11 in which the additive is a permanent antistatic agent preferably IRGASTAT P18 or IRGASTAT P 22.

13. A FIBC according to claim 11 in which the IRGASTAT P18 or IRGASTAT P22 additive is in the range of 6-20%.

14. A method of neutralizing the electrostatic charge generated by material consisting of:

configuring an inner device of anti-static fibers.

configuring the anti-static fibers comprising the inner device in a manner to maximize contact with material to be neutralized.

connecting the anti-static fibers to the outer limits of the material to conduct static electricity to atmosphere via contact with an outer container which is configured to contain the inner device and material.

15. A method according to claim 14 in which the anti-static fibers include antistatic additives of polyamide and fiber conductive material, preferably IRGASTATE 18 or IRGASTAT 22.

16. A method according to claim 14 in which a plurality of inner devices are configured within the container.

17. A method according to claim 14 in which the container is made of the same material as the inner device.

18. A method according to claim 14 in which the container is a FIBC.

19. A method according to claim 14 in which the diameter of the fibers ranges from 0.2 to 15 μm (micron).

20. An inner device according to claim 14 in which the inner device is made of materials which conduct electricity.

* * * * *

Exhibit K

Paul S. Honigfort
Letter to Erik D. Olson Regarding Filing of Food Additive Petition (Dec. 31, 2014)

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
College Park, MD 20740

December 31, 2014

Erik D. Olson
Senior Strategic Director for Health and Food
Natural Resources Defense Council
1152 15th Street, N.W.
Suite 300
Washington, DC 20005

RE: Food Additive Petition (FAP) No. 4B4808

Dear Mr. Olson:

This is in reference to your petition, FAP 4B4808, proposing that 1) 21 CFR 177.1210 be amended to no longer provide for the use of potassium perchlorate as an additive in closure-sealing gaskets for food containers; 2) that Threshold Of Regulation exemption (TOR) No. 2005-006 be revoked to no longer exempt the use of sodium perchlorate monohydrate as a conductivity enhancer in the manufacture of antistatic agents for use in finished articles in contact with dry foods from regulation under the food additive provisions of the Federal Food, Drug and Cosmetic Act; and 3) to promulgate a new regulation in 21 CFR 189 Subpart D to prohibit the use of perchlorate in antistatic agents for use in food contact articles. This petition is based upon the assertion that such use is not safe due to the toxicity of perchlorate.

The petition has been filed. The date of this letter is the filing date of your petition. If we are not able to complete the scientific review within 90 days of the date of this letter, we will inform you by letter and extend the review for an additional 90 days.

Sincerely,

Paul S. Honigfort -A

Digitally signed by Paul S. Honigfort -A
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Date: 2014.12.31 09:50:07 -05'00'

Paul Honigfort, Ph.D.
Consumer Safety Officer
Division of Food Contact Notifications, HFS-275
Office of Food Additive Safety
Center for Food Safety
and Applied Nutrition

cc: HFS-275 FAP4B4808
FileName: FAP4B4808.FL.docx
R/D: P. Honigfort: HFS-275: 12/30/2014
INIT: E. Machuga: HFS-275: 12/30/2014
F/T:HFS-275:PHonigfort: 12/31/2014

Exhibit L

Francis Lin
Letter to Erik D. Olson Extending Scientific Review of Food Additive Petition (Mar. 31, 2015)

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
College Park, MD 20740

March 31, 2015

Erik D. Olson
Senior Strategic Director for Health and Food
Natural Resources Defense Council
1152 15th Street, N.W.
Suite 300
Washington, DC 20005

RE: Food Additive Petition (FAP) No. 4B4808

Dear Mr. Olson:

This letter is to inform you that we have extended the scientific review of the subject food additive petition for an additional 90 days in accordance with section 409(c)(2) of the Federal Food, Drug, and Cosmetic Act.

Sincerely,

Francis Lin, Ph.D.
Director
Division of Food Contact Notifications, HFS-275
Office of Food Additive Safety
Center for Food Safety
and Applied Nutrition

No. _____

UNITED STATES COURT OF APPEALS FOR THE NINTH CIRCUIT

IN RE BREAST CANCER FUND, CENTER FOR ENVIRONMENTAL HEALTH, CENTER FOR FOOD SAFETY, CENTER FOR SCIENCE IN THE PUBLIC INTEREST, ENVIRONMENTAL WORKING GROUP, and NATURAL RESOURCES DEFENSE COUNCIL, *Petitioners*,

v.

U.S. FOOD AND DRUG ADMINISTRATION and ROBERT M. CALIFF, COMMISSIONER OF THE U.S. FOOD AND DRUG ADMINISTRATION, *Respondents*.

DECLARATION OF RACHEL AZZOLINI

I, RACHEL AZZOLINI, do hereby affirm and state:

1. I am currently a member of the Center for Science in the Public Interest (CSPI), and have been for about 8 years.

2. I am deeply concerned about our environment and the impacts of environmental degradation, including the proliferation of chemical contaminants, on human health. The Center for Science in the Public Interest undertakes work to safeguard our environment and public health, and has long represented my interests.

3. I currently live in Santa Rosa Beach, Florida.

4. I am a new, 42-year-old mother to a six-month-old baby girl. I struggled with infertility for many years before becoming pregnant with my daughter. As a mother to an only child, I am especially concerned about my daughter's exposure to perchlorate.

5. I am aware that perchlorate is a chemical used in plastic packaging for dry foods. I understand that perchlorate disrupts thyroid gland function, decreasing the production of thyroid hormones, which people need for normal functioning. I am also aware that having sufficient thyroid hormones is especially important to children's cognitive development.

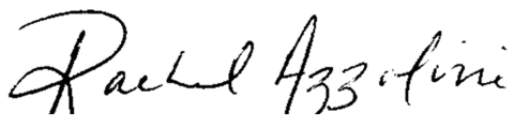
6. I consider myself a very health-conscious person. I worked as a personal trainer for 15 years, and am conscientious about my diet and the food my family eats. We eat a mostly organic diet rich in whole foods, including organic fruits and vegetables, and lean proteins. Still, despite my best efforts, perchlorate is almost certainly in both my and my daughter's diets. Due to poor milk supply, I have to formula-feed my child. Powdered baby formula comes in plastic packaging, and I am worried that there is perchlorate in that packaging, which gets into my daughter's food and then into her body. Furthermore, I am starting now to introduce small amounts of cereal and grains into my daughter's diet, which are likely contaminated with perchlorate through packaging as well. Even if the foods I and my daughter eat are not stored in plastic when I purchase them, they might

have been stored in plastic at some point in the production and distribution chain. It would therefore be impossible to eliminate foods that may have been contaminated with perchlorate from my and my daughter's diets. I worry that, despite my attempts to reduce our dietary exposure to perchlorate, I am unknowingly endangering our health.

7. Additionally, I am concerned that while I was pregnant with my daughter, perchlorate may have inhibited my thyroid's uptake of iodine, impairing the production of hormones critical to fetal brain development. I am aware that the fetus' thyroid is not yet fully functioning during the first two trimesters of pregnancy, so that the fetus depends entirely on maternal thyroid hormones.

8. I understand that, in 2014, CSPI petitioned the United States Food and Drug Administration (FDA) to prohibit uses of perchlorate in food packaging. I also understand that FDA has not yet responded to that petition, and that CSPI is suing to compel FDA to do so. CSPI has my full support in these matters.

I declare under penalty of perjury that the foregoing is true and correct.



_____ _____3/28/2016_____

Rachel Azzolini Date

No. _____

UNITED STATES COURT OF APPEALS FOR THE NINTH CIRCUIT

IN RE BREAST CANCER FUND, CENTER FOR ENVIRONMENTAL HEALTH, CENTER FOR FOOD SAFETY, CENTER FOR SCIENCE IN THE PUBLIC INTEREST, ENVIRONMENTAL WORKING GROUP, and NATURAL RESOURCES DEFENSE COUNCIL, *Petitioners*,

v.

U.S. FOOD AND DRUG ADMINISTRATION and ROBERT M. CALIFF, COMMISSIONER OF THE U.S. FOOD AND DRUG ADMINISTRATION, *Respondents*.

DECLARATION OF STEPHANIE COHEN

I, STEPHANIE COHEN, do hereby affirm and state:

1. I am a member of Center for Food Safety, and have been since 2015.

2. I currently live in San Francisco, California, and have lived here for the past 12 years.

3. I am a mother to two sons, aged 4 and 21 months. Both were fed a combination of breastmilk and formula.

4. I am aware that perchlorate is a constituent in plastic packaging for dry foods, and that it is used as an antistatic agent for food contact articles. I believe that perchlorate can transfer from packaging to the foods it contains, and that I may be consuming perchlorate when I eat foods held in packaging containing perchlorate.

5. I am aware that perchlorate is a chemical known to interfere with the thyroid gland's ability to uptake iodine, which is fundamental to hormone production. Thyroid hormones are essential for brain development in infants and fetuses, especially in the first two trimesters when the fetus's thyroid is not fully functioning. I understand that even transient exposures to perchlorate may result in permanent deficits in a child's cognitive ability.

6. I understand that perchlorate can be passed to children through breast milk, and that infant formula can also contain perchlorate. I am aware that children between six months and six years old have the greatest average exposures to perchlorate, which can inhibit their neurological development. This concerns me greatly because my children are in this age range.

7. I take care to avoid unnecessarily exposing my children to chemical contaminants, because their health is my priority. As a result, I spend time and energy to avoid serving them foods sold in packaging that contains harmful chemicals, and I also spend time, energy, and money to seek out chemical-free food storage containers to use in my home.

8. I regularly purchase and eat dry packaged foods, including rice, bread, tortillas, flour, sugar, pasta, chips, crackers, and cookies. My children also eat these products. I am aware that these dry packaged foods might be held in packaging containing perchlorate, and might therefore be contaminated

with perchlorate. I would like to avoid such packaging, but because it is not labeled, doing so is prohibitively difficult.

9. I also purchase and eat bulk dry foods, including oats, flour, granola, dried mango, apricots, other fruits, roasted and raw nuts, beans, and lentils. I choose bulk foods because they have less packaging and can be more economical. I have no way of knowing whether these bulk foods were contaminated with perchlorate due to being stored in plastic packaging containing perchlorate at some point in their production and distribution. As a result, it is impossible for me to avoid potential perchlorate exposure when purchasing these goods.

10. I understand that perchlorate is found in drinking water in California. I regularly consume tap water. My children also primarily drink tap water.

11. I am concerned about cumulative exposure to perchlorate from drinking water, food storage containers, and other sources that together may result in harmful levels of perchlorate in myself and my young children.

12. I am aware that CFS and others petitioned the United States Food and Drug Administration (FDA) in 2014 to ban uses of perchlorate in food packaging. I am aware that FDA has not yet responded to the petition, and that CFS is now suing FDA to compel FDA to do so.

13. FDA's continued failure to respond to the petition harms me and my children by allowing our exposure to perchlorate to continue at unsafe levels. FDA's

failure also impedes my ability to purchase dry foods with confidence that my family will not be exposed to perchlorate through those products.

14. This harm would be significantly lessened if FDA were to grant CFS's petition and therefore ban uses of perchlorate in food packaging. My family would be free from exposure to perchlorate from dry foods packaging, our cumulative exposure would be reduced, and our health would be protected. I would feel confident purchasing and eating dry packaged foods without fear of perchlorate exposure, and would feel relieved to know that my children and I would be exposed to perchlorate through one less source.

15. If FDA were to deny the petition, my injuries would still be reduced because I understand that even a denial would give CFS the means to independently assess whether FDA's decision not to ban uses of perchlorate in food packaging was justified. I trust CFS to conduct this assessment and to hold FDA accountable for protecting my health. If CFS were to conclude that FDA did not act appropriately to protect the public health, then it could take further action to challenge FDA's decision, which would protect my health.

I declare under penalty of perjury that the foregoing is true and correct.

3/25/16

Stephanie Cohen

Date

No. _____

UNITED STATES COURT OF APPEALS FOR THE NINTH CIRCUIT

IN RE BREAST CANCER FUND, CENTER FOR ENVIRONMENTAL HEALTH, CENTER FOR FOOD SAFETY, CENTER FOR SCIENCE IN THE PUBLIC INTEREST, ENVIRONMENTAL WORKING GROUP, and NATURAL RESOURCES DEFENSE COUNCIL, *Petitioners*,

v.

U.S. FOOD AND DRUG ADMINISTRATION and ROBERT M. CALIFF, COMMISSIONER OF THE U.S. FOOD AND DRUG ADMINISTRATION, *Respondents*.

DECLARATION OF CHRISTOPHER DAVIS

I, CHRISTOPHER DAVIS, do hereby affirm and state:

1. I am a member of Center for Food Safety, and have been since October 2, 2014.

2. I currently live in Moss Beach, California.

3. I currently work as a senior environmental program and project chemist for a major environmental consulting firm, for which I oversee sampling and analysis activities for remedial investigations and feasibility studies. I hold a B.S. in Marine Chemistry and a Certificate in Hazardous Materials Management, and have been an environmental chemist for 24 years. Prior to working for my current consulting firm, I worked for the Environmental Services Assistance Team (ESAT) for U.S.

Environmental Protection Agency (EPA) Region 9 for four years (a dedicated contract, not as an EPA employee).

4. Throughout my tenure as a program chemist, I have worked extensively with perchlorate analyses due to widespread contamination at Department of Defense (DoD) facilities, stemming from its use as rocket fuel, and am a recognized expert on analytic methods related to perchlorate. Perchlorate requires specialty analysis because of the requirements for low detection levels in order to protect human health.

5. I am hypothyroid, a condition known to be related to perchlorate exposure, which may have been due to possible perchlorate exposure in 2000 and 2002 when I worked on an analytical method to conduct field studies using ion-specific electrodes for EPA and the Army Corps of Engineers.

6. As a result of my work with and for the government, I am very aware of the government's failure to adequately regulate this chemical and to protect the public from perchlorate exposure. Although California and other states have enacted state maximum contamination levels (MCLs) between 1 and 6 parts per billion (ppb), EPA has dragged its feet and has failed to enact a federal MCL, although it enacted an MCL Goal (MCLG) of 15 ppb after a highly biased government sponsored study that was repudiated by most health scientists, all of whom believe that a responsible MCL would be less than 1 ppb. Regardless of the levels, they are all at

the low ppb level in an effort to protect human health, and even tiny direct exposures to perchlorate (such as in food packaging) exceed the ppb level.

7. I am also very aware of what perchlorate can do and that it may have affected my life significantly. In 2002 I was diagnosed with hypothyroidism. I experienced very low energy levels that affected my ability to work and prevented me from partaking in activities that I enjoy, such as surfing and mountain bike riding. My symptoms coincided with my possible direct exposure to perchlorate during the perchlorate field method studies that I performed. At the time I was also under a great deal of stress due to long work weeks, so I cannot say for sure that perchlorate exposure caused my hypothyroidism, but I do suspect it as a cause. I now take two pills each day to regulate my symptoms, and am able to live a normal life. However, these medications now cost me upwards of $360 per year, even with insurance. I know from experience that hypothyroidism is a very real condition and a serious issue.

8. Hypothyroidism is one of the confirmed adverse health effects caused by exposure to perchlorate. I believe that hypothyroidism is one of the largest undiagnosed health epidemics in the United States. Lots of people are unknowingly exposed to perchlorate, yet Western medicine has set tolerance levels for blood tests that are too high to appropriately diagnose hypothyroidism. Many people experience low energy levels and do not realize that it could be connected

to unknown exposure to perchlorate, or that their thyroid could be what is causing it. And almost no one is aware that the Food and Drug Administration (FDA) allows perchlorate to be used in food packaging.

9. I am aware, and EPA is aware, that perchlorate is a serious environmental contaminant. Perchlorate has been discovered in over 350 of 6,400 public water supply wells tested in California. Contamination of groundwater and of the Colorado River affects important drinking water and irrigation water supplies. There may be over 30 sites with perchlorate in California alone. Due to the serious nature of perchlorate contamination, perchlorate sites are the focus of a cooperative and innovative site assessment process by EPA and California. The discovery of perchlorate at sites where cleanups were already underway has both delayed those cleanups and added substantial costs over initial projections. It is very hard to remove perchlorate from water; it requires filtering through very expensive specialized resin beds or treatment by an oxidation reduction process which is expensive, and average water filters will not remove perchlorate. Nevertheless, EPA, DoD, and state agencies are actively pursuing characterization and remediation of perchlorate contamination in order to protect human health.

10. Hay and alfalfa supplies in the United States, especially in parts of California, are also contaminated with perchlorate, which affects livestock including horses and cows. This is especially alarming because children and

consumers can be exposed to perchlorate through cow's milk. I understand that children under the age of six are most affected by low concentration exposure to perchlorate, and are especially susceptible to the effects of perchlorate because it inhibits hormone production that is essential for brain development.

11. Perchlorate is a highly soluble inorganic salt, and dissolves readily upon contact with even small amounts of water or materials containing water, allowing it to contaminate water or food materials very rapidly. In addition, a person does not have to ingest it directly; even handling it creates exposure. It is especially inappropriate to allow it in any type of packaging, especially food packaging, because consumers and workers don't even have to eat it, just touch it, to begin the process of exposure to this chemical. Chronic exposure is not required to suffer the effects on health, such as hypothyroidism. Any exposure can cause this condition, which is not reversible. No one should be exposed to perchlorate under any circumstances if at all possible.

12. When handling perchlorate during my analytical studies for a field method to analyze for perchlorate, I was fastidious about not touching it. I wore gloves and took care to avoid direct contact. I did so because I know that perchlorate is absorbed through the skin and affects the thyroid very rapidly, causing the thyroid to essentially shut down. With perchlorate being allowed in food packaging, everyone should wear gloves to protect themselves from perchlorate exposure,

which is a preposterous idea. Alternatively, perchlorate should be banned from use in food packaging to protect human health.

13. I worry about others who cannot avoid exposures, including anyone who handles perchlorate-containing plastics. And I am also concerned about pregnant women who are exposed to perchlorate; fetuses whose mothers are affected by hypothyroidism can be born with hypothyroidism, which is an unfair and miserable life for a child. There are so many hidden exposures that people have no idea about, having such a dangerous chemical lurking in food packaging with the approval of the FDA is ludicrous.

14. I was shocked to learn that FDA approved the use of perchlorate in food packaging in 2005, despite the fact that it was widely recognized, including by EPA, to have serious adverse health effects at very low concentration exposure levels. It is stunning that FDA would allow a dangerous poison to be used intentionally in food packaging. It doesn't make any sense to allow food or any type of packaging to contain perchlorate when EPA and other health agencies are so actively pursuing ways to remove perchlorate from sources of drinking water. This is a complete conflict, and is intolerable.

15. I am a consumer who is very aware of environmental perchlorate exposure, and yet I do not expect to be exposed to perchlorate in my daily life. I drink local groundwater that I do not believe is contaminated with perchlorate. Accordingly, a

primary source of perchlorate exposure for me would be through dry food packaging. I regularly purchase and eat dry packaged foods, including rice, bread, tortillas, quinoa, flour, sugar, pasta, chips, crackers, seaweed, and cookies. I am now aware that these dry packaged foods might be held in packaging containing perchlorate, and might therefore be contaminated with perchlorate. I also purchase and eat bulk dry foods, including oats, flour, granola, dried mango, apricots, other fruits, roasted and raw nuts, beans, and lentils. I have no way of knowing whether these bulk foods were contaminated with perchlorate due to being stored in plastic packaging containing perchlorate at some point in their production and distribution.

16. Since becoming aware of perchlorate's presence in food production, I have committed to avoiding it. I very much want to avoid plastic packaging and want to know what products might contain perchlorate from their packaging so that I can avoid such products. If I did know what products contain it, I would avoid them. However, the lack of labeling makes it nearly impossible to avoid this source of perchlorate exposure because I have no real way of knowing what packaging and products, by extension, are exposing me and others to perchlorate.

17. As a person who really understands the harms and pervasiveness of perchlorate, I believe very strongly that it should be banned for any uses aside from what it was designed for: rocket fuel and explosives. Average people and

consumers should not be exposed to it. It must not be allowed to be added or used in anything to do with any product that can be ingested or handled. The simplest way to avoid exposure is to ban it. It would be illegal to knowingly contaminate drinking water to perchlorate in order to protect human health, so it is only logical that it should not be allowed in food packaging.

18. I am very disappointed, though not surprised, to learn that FDA is dragging its feet and rubber-stamping the requests of big business at the expense of consumers. FDA should be at the top of the list of entities that protect our health. FDA should immediately ban the use of perchlorate in any form of packaging for food, drugs, or anything else.

19. I am aware that CFS and others petitioned the United States Food and Drug Administration (FDA) in 2014 to ban uses of perchlorate in food packaging. I am aware that FDA has not yet responded to the petition, and that CFS is now suing FDA to compel FDA to do so.

20. FDA's continued failure to respond to the petition harms me by increasing the risks to my health from food contaminated with perchlorate, and curtails my ability to purchase dry foods with any confidence that they are free of perchlorate.

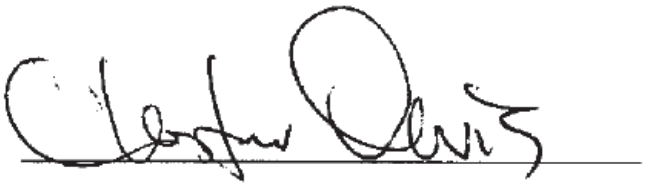
21. My injury would be significantly lessened if FDA were to grant CFS's petition and therefore ban uses of perchlorate in food packaging. I would be free from exposure to perchlorate from dry foods packaging, which is potentially a

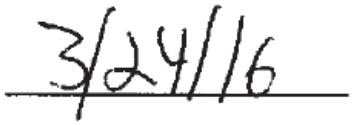
primary source of exposure for me. My cumulative exposure would also be reduced, and my health protected. I would feel confident purchasing and eating dry packaged foods without fear of perchlorate exposure. Further, I would gain confidence that FDA could take appropriate steps to protect Americans from exposure to this chemical that is widely known to be harmful.

22. If FDA were to deny the petition, my injuries would still be reduced because I understand that even a denial would give CFS the means to independently assess whether FDA's decision not to ban uses of perchlorate in food packaging was justified. I trust CFS to conduct this assessment and to hold FDA accountable for protecting my health. If CFS were to conclude that FDA did not act appropriately to protect the public health, then it could take further action to challenge FDA's decision, which would protect my health.

23. Simply put, FDA should ban perchlorate. Continuing to allow it to be *intentionally* added to food packaging, and therefore food, makes no sense, especially when you consider that EPA and state health agencies are so actively pursuing ways to reduce perchlorate exposure through drinking water and irrigation water sources. I do not want perchlorate to be in food packaging, especially if people have no way of knowing whether it's in their food.

I declare under penalty of perjury that the foregoing is true and correct.





Christopher Davis Date

No. _____

UNITED STATES COURT OF APPEALS FOR THE NINTH CIRCUIT

IN RE BREAST CANCER FUND, CENTER FOR ENVIRONMENTAL HEALTH, CENTER FOR FOOD SAFETY, CENTER FOR SCIENCE IN THE PUBLIC INTEREST, ENVIRONMENTAL WORKING GROUP, and NATURAL RESOURCES DEFENSE COUNCIL, *Petitioners*,

v.

U.S. FOOD AND DRUG ADMINISTRATION and ROBERT M. CALIFF, COMMISSIONER OF THE U.S. FOOD AND DRUG ADMINISTRATION, *Respondents*.

DECLARATION OF ELIZABETH ESPY

I, ELIZABETH ESPY, do hereby affirm and state:

1. I am a member of the Natural Resources Defense Council (NRDC), and have been for about thirteen years.

2. I currently live in San Luis Obispo, California.

3. I do not feel that our government does a good enough job of protecting us or the environment from corporate interests. I feel that if we do not stand up and do something about that, then we will be an even sicker nation than we already are, and have even less to leave to our children. I do not think that is right. I think we have a responsibility to be stewards of this planet for future generations, and to leave enough for others.

4. I am particularly concerned with the stewardship of our food system. Food is what we need to sustain us, and provide us with health. Yet, right now, I do not feel I can trust the federal government to test whether the many chemicals that enter our food are safe.

5. I have become particularly concerned with environmental issues, and food safety in particular, since having my two children, who are now seven and eleven years old. I have a fierce sense of protection for my children, and all children. They need the cleanest possible water and the cleanest possible food so that they have the best chance to be healthy as adults.

6. I support NRDC because it advocates effectively for the good stewardship of the environment, the protection of our food system, and the health of children like mine.

7. At home, my children and I regularly consume dry foods in plastic packaging, including bread, rice cakes, cereal, pretzels, crackers, tortillas, and pasta. In addition, we sometimes consume rice, flour, and sugar held in plastic packaging as well. We also go out to eat at restaurants once or twice each week, and consume dishes containing dry packaged ingredients.

8. I am aware that plastic packaging for dry foods may contain perchlorate, a chemical known to inhibit thyroid functioning in humans. I understand that perchlorate can be transferred from packaging to food.

9. Some of the rice, flour, and sugar that I purchase for my family does not come in plastic packaging; rather these foods are sometimes held in large, bulk-sized plastic bins at the store. Nonetheless, I understand that these dry foods may have been stored in plastic packaging containing perchlorate at some point in their production and distribution. I would have no way of knowing whether these foods were contaminated with perchlorate from such packaging.

10. I understand that the proper functioning of the thyroid is essential for the cognitive and physical development of children, and that exposure to perchlorate can therefore pose a significant health risk to children.

11. My children have a family history of thyroid problems: my father has hypothyroidism, and my mother-in-law has thyroid cancer. Because of this history, I am worried that my children might be hereditarily predisposed to have thyroid problems. I am also keenly aware of the importance of the thyroid to overall health.

12. I am also worried about my children's thyroid health because we live within ten miles of the Diablo Canyon Power Plant, a nuclear power plant. I understand that the Diablo Canyon Power Plant periodically releases bursts of radiation, to which my family is exposed. I fear this radiation might impede my children's thyroid functioning, rendering them more vulnerable to the adverse effects of perchlorate from dry food packaging.

13. It is my understanding that adults often develop health problems that may be caused by exposure to harmful chemicals earlier in life, even if those problems cannot be traced to particular exposures. I am afraid that my children will develop thyroid problems in this way, by unwittingly eating food contaminated with perchlorate.

14. In my view, because children develop so rapidly, anything that disrupts their development, including impaired thyroid function due to ingesting perchlorate, can be very detrimental to their health.

15. I am proactive in protecting my children's health. I take care not to buy my children food sold in packaging containing harmful chemicals, such as BPA. I am able to do this because labels on food packaging sometimes indicate that the packaging is BPA-free.

16. I have never seen a label on food packaging indicating that the packaging contains perchlorate. Because of this, I am unable to make fully informed decisions about what to feed my children, and do not feel confident that the food I provide them is not endangering their health.

17. I am aware that, in 2014, NRDC petitioned the United States Food and Drug Administration (FDA) to ban uses of perchlorate in food packaging. I am aware that FDA has not yet responded to NRDC's petition, and that NRDC is suing FDA to compel FDA to do so.

18. In my view, FDA has failed in its obligation to protect the country from dangerous chemicals that may enter our food supply. I worry that its decision has been influenced more by corporate interests than by what is healthy and right for Americans.

19. I believe that if a chemical is dangerous, as perchlorate is, it should not be in our food. I therefore want FDA to ban uses of perchlorate in food packaging.

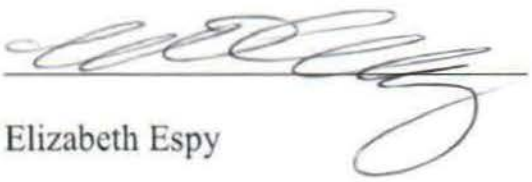
20. If FDA were to grant NRDC's petition and ban uses of perchlorate in food packaging, I would feel much more secure about the health of my children. I would not have to worry that I was buying food for them that might harm their health, and would not have to research how to protect my children from perchlorate in food packaging, as I currently plan to do. Given that there are so many threats to their health in our food and water supply, I would feel glad to have one fewer concern. Moreover, because stress itself is detrimental to human health, my physical wellbeing would likely be improved by the peace of mind a ban would give me.

21. If FDA were to deny NRDC's petition, I would remain skeptical of the healthfulness of dry packaged foods. However, I would also feel that FDA had taken an important first step simply by responding to NRDC's claims, and assessing the available scientific evaluations of the health effects of perchlorate in food packaging.

22. If FDA were to deny NRDC's petition, this would also give NRDC and the public an opportunity to assess whether FDA had done its job properly, and to assess whether FDA had proven beyond a shadow of a doubt that perchlorate is safe for use in food packaging. This would allow NRDC to undertake more effective public advocacy to improve the health of our food supply, which I would support. It would also allow me to make more informed choices about which foods I buy for my family.

23. For all the reasons stated above, I fully support NRDC in this matter.

I declare under penalty of perjury that the foregoing is true and correct.



Elizabeth Espy

3/22/16

Date

No. _____

UNITED STATES COURT OF APPEALS FOR THE NINTH CIRCUIT

IN RE BREAST CANCER FUND, CENTER FOR ENVIRONMENTAL HEALTH, CENTER FOR FOOD SAFETY, CENTER FOR SCIENCE IN THE PUBLIC INTEREST, ENVIRONMENTAL WORKING GROUP, and NATURAL RESOURCES DEFENSE COUNCIL, *Petitioners*,

v.

U.S. FOOD AND DRUG ADMINISTRATION and ROBERT M. CALIFF, COMMISSIONER OF THE U.S. FOOD AND DRUG ADMINISTRATION, *Respondents*.

DECLARATION OF TERESA HALE

I, TERESA HALE, do hereby affirm and state:

1. I am currently a member of the Center for Science in the Public Interest (CSPI), and have been for about 15 years.

2. Environmental issues are of great importance to me, and I am particularly concerned about chemicals in the environment that harm human health. The Center for Science in the Public Interest undertakes advocacy to protect human health and the environment, and has long represented my interests.

3. I currently live in Kansas City, Missouri.

4. I was diagnosed with Hypothyroidism in the 1990s. Having been a very energetic woman with a high metabolism, active in sports like softball, my adult

weight varied from 120-125. That changed when I began feeling incredibly tired, weak, cold all the time, and depressed. Among other frustrating symptoms, I began suffering from insomnia, developed memory lapses, noticed small cuts took an unusually long time to heal, and started having excessively dry hair and skin. My primary physician referred me to an Endocrinologist who diagnosed me as having Hypothyroidism and prescribed Synthroid.

5. My Synthroid dosages have been monitored ever since with blood tests every six months. I began at the lowest dose, but my doses have since fluctuated, and I now take 150 micrograms per dose.

6. I continue to experience many of the uncomfortable, unwelcome symptoms mentioned above, despite the close monitoring of my condition.

7. I try to eat organic, whole foods – especially those known to have minimal exposure to pesticides and other chemicals. Nonetheless, I still have incredibly low energy, skin issues, memory loss, insomnia, hair loss, and anxiety.

8. At present, three of my four sisters have also been diagnosed with Hypothyroidism. One of them has always been extremely health-conscious.

9. I have learned that the chemical perchlorate is used in plastic packaging for dry food products. I understand that perchlorate disrupts thyroid functioning, dampening the production of important thyroid hormones. In addition, I am aware

that exposure to perchlorate can be especially problematic for individuals with hypothyroidism, who already have an inadequate level of thyroid hormones.

10. I've tried to limit my dietary exposure to chemicals in plastics by buying food in bulk and eliminating as many packaged foods as possible. However, even many "healthy foods" come in plastic packaging, like spices, nuts, cereals, and other food products that I purchase regularly.

11. Because of my medical history, I am deeply concerned about exposure to perchlorate. Despite expensive, time-consuming treatment, I don't feel well.

12. Although I try to avoid eating food found in plastic packaging, I am worried that the ingredients in those foods might have been packaged in plastic before those foods ultimately ended up in the grocery store. There is simply no way for me to know one way or the other. Despite my best efforts, I feel powerless to ensure that I am not consuming food that has been contaminated with perchlorate from plastic packaging.

13. I worry that, despite the precautions I have taken to limit my dietary exposure to chemicals such as perchlorate, I am unwittingly endangering my own health due to circumstances far outside my control. It seems like there is no end in sight.

14. I am aware that CSPI petitioned the United States Food and Drug Administration (FDA), in 2014, to ban uses of perchlorate in food packaging. I

fully support this petition, CSPI's lawsuit to compel FDA to respond to the petition, and the fight to eliminate perchlorate from our food supply.

15. I've done a great deal of research since my diagnosis so long ago and I've made dietary changes in an effort to alleviate some of the symptoms of Hypothyroidism. I'm disheartened that FDA, an agency whose mission involves "protecting the public health," should exhibit such indifference for public health when severe, legitimate health concerns are documented and brought to its attention.

I declare under penalty of perjury that the foregoing is true and correct.

3/24/16

Teresa Hale Date

No. _____

UNITED STATES COURT OF APPEALS FOR THE NINTH CIRCUIT

IN RE BREAST CANCER FUND, CENTER FOR ENVIRONMENTAL HEALTH, CENTER FOR FOOD SAFETY, CENTER FOR SCIENCE IN THE PUBLIC INTEREST, ENVIRONMENTAL WORKING GROUP, and NATURAL RESOURCES DEFENSE COUNCIL, *Petitioners*,

v.

U.S. FOOD AND DRUG ADMINISTRATION and ROBERT M. CALIFF, COMMISSIONER OF THE U.S. FOOD AND DRUG ADMINISTRATION, *Respondents*.

DECLARATION OF THOMAS HAWKINS

I, THOMAS HAWKINS, do hereby affirm and state:

1. I am currently a member of the Natural Resources Defense Council (NRDC), and have been for about twenty-two years.

2. I follow environmental issues closely, and try to do my part to support environmental advocacy by signing petitions and making contributions for various causes, particularly those related to human health. Among the many environmental organizations, NRDC best represents my interests.

3. I currently live in Glendale, California.

4. About twenty-five years ago, I had a wonderful career teaching writing at the University of California, Berkeley. In 1990, however, I was diagnosed with

chronic fatigue immune dysfunction syndrome (CFIDS). I consulted with a doctor who was among the leading experts in treating CFIDS. He told me that my condition was probably environmentally caused, and that I was highly chemically sensitive. This doctor told me my health was likely being adversely affected by chemicals in the food I eat, the air I breathe, and the water I drink.

5. My CFIDS remained debilitating, and in 1993, I was forced to take early retirement.

6. In 1995, a different physician diagnosed me with hypothyroidism. This diagnosis was separate from, and additional to, my prior diagnosis of CFIDS. In 2010, I was prescribed medication for my hypothyroidism, which I have been taking ever since.

7. The symptoms of my hypothyroidism included exhaustion, muddled thinking, low body temperature, low blood pressure, and tremors.

8. Despite taking the prescribed medication, as well as various nutritional supplements, I continue to suffer from low energy and fatigue, as a result of both my CFIDS and my hypothyroidism.

9. Since my diagnosis with CFIDS in 1990, I have tried to limit my dietary exposure to chemicals to which I am sensitive, including those found in plastics. I therefore generally try not to eat foods stored in plastic containers. Nonetheless, I frequently consume grains, such as millet, oats, quinoa, teff, rice and buckwheat, as

well as powdered flavorings, such as cacao, stevia, and cinnamon, all of which are sold in plastic packaging.

10. I am aware that perchlorate is a chemical used in plastic packaging for dry foods. I understand that perchlorate is known to interfere with the proper function of the thyroid in humans, and that exposure to perchlorate can cause health problems for people with hypothyroidism.

11. Because of my medical history, I am deeply concerned about being exposed to perchlorate.

12. I understand that, even if the foods I eat are not stored in plastic when I purchase them, they might have been stored in plastic at some point in their production and distribution, without my knowledge. It would therefore be very difficult—indeed, probably impossible—for me to eliminate completely dry packaged foods from my diet.

13. I read the labels on all the food that I purchase, and if I see a harmful chemical listed as present in the food, I do not purchase it. For example, I take care to purchase only water bottles labeled as BPA-free. As far as I can recall, however, I have not seen labels indicating the presence or absence of other chemicals in food packaging, including perchlorate. I therefore cannot be sure whether the dry packaged foods I buy might be contaminated with perchlorate.

14. I worry that, despite the precautions I have taken to limit my dietary exposure to chemicals such as perchlorate, I am unwittingly endangering my own health. I am concerned that my thyroid medication is less effective than it would otherwise be, because I am ingesting perchlorate from food packaging. I fear that my medical conditions, which I am constantly managing, and which to this day can be crippling, are worse than they would otherwise be, because I am exposed to perchlorate through my diet.

15. I understand that, in 2014, NRDC petitioned the United States Food and Drug Administration (FDA) to ban uses of perchlorate in food packaging. I further understand that FDA has not yet responded to that petition, and that NRDC is suing to compel FDA to do so.

16. I believe FDA should enforce the highest standards of safety in food packaging. Since perchlorate is known to be dangerous to the health of people like me, I would support FDA banning uses of perchlorate in food packaging.

17. If FDA were to grant NRDC's petition, and ban uses of perchlorate in food packaging, I would feel more confident eating grains, powdered flavorings, and other dry foods stored in packaging that may today contain perchlorate. I would be glad to rid my mind of another cause for concern about my health. I would also feel that banning perchlorate was a very important first step by FDA towards

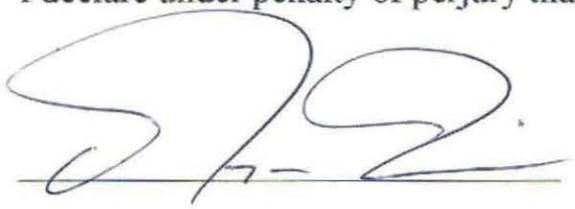
acknowledging the tremendous damage done to the health of the American people by under-regulating dangerous chemicals in our food.

18. If FDA were to deny NRDC's petition, I would be very disappointed. I would want NRDC to continue fighting to eliminate perchlorate from food packaging. I would also look a lot more closely at what chemicals FDA has allowed in our food, and consider ways of avoiding those that I believe should be regulated more strongly.

19. At a minimum, I feel strongly that FDA should respond to NRDC's petition. For FDA to ignore the petition indicates to me that FDA is too willing to accept the arguments of the food-packaging industry. FDA's failure to respond to NRDC's petition makes me doubt that the federal government is doing everything it should to protect my health.

20. For all the reasons stated above, I fully support NRDC in this matter.

I declare under penalty of perjury that the foregoing is true and correct.



3/14/16

Thomas Hawkins

Date

No. _____

UNITED STATES COURT OF APPEALS FOR THE NINTH CIRCUIT

IN RE BREAST CANCER FUND, CENTER FOR ENVIRONMENTAL HEALTH, CENTER FOR FOOD SAFETY, CENTER FOR SCIENCE IN THE PUBLIC INTEREST, ENVIRONMENTAL WORKING GROUP, and NATURAL RESOURCES DEFENSE COUNCIL, *Petitioners*,

v.

U.S. FOOD AND DRUG ADMINISTRATION and ROBERT M. CALIFF, COMMISSIONER OF THE U.S FOOD AND DRUG ADMINISTRATION, *Respondents*.

DECLARATION OF MICHAEL F. JACOBSON

I, MICHAEL F. JACOBSON, do hereby affirm and state:

1. I am the President and a Co-founder of the Center for Science in the Public Interest (CSPI). I have served in this position since 1971.

2. My duties include providing direction for the organization, including supervising the preparation of materials that CSPI distributes to members and prospective members. Those materials describe CSPI and identify its mission.

3. CSPI is a membership organization incorporated under the laws of the District of Columbia. It is recognized as a not-for-profit corporation under section 501(c)(3) of the United States Internal Revenue Code.

4. CSPI's U.S. office is located in Washington, D.C.

5. CSPI currently has approximately 600,000 members in the United States. There are CSPI members residing in each of the fifty United States and in the District of Columbia.

6. CSPI's mission statement declares that the organization is "a consumer advocacy organization whose twin missions are to conduct innovative research and advocacy programs in health and nutrition, and to provide consumers with current, useful information about their health and well-being." In addition, the mission statement includes three main goals, which are: 1) To provide useful, objective information to the public and policymakers and to conduct research on food, alcohol, health, the environment, and other issues related to science and technology; 2) To represent the citizen's interests before regulatory, judicial and legislative bodies on food, alcohol, health, the environment, and other issues; and 3) To ensure that science and technology are used for the public good and to encourage scientists to engage in public-interest activities. Protecting the consuming public from harmful chemicals in the food supply has been part of CSPI's work since its inception as an organization.

7. Protecting human health from the adverse effects of perchlorate in food packaging exemplifies CSPI's work. CSPI has sought for years to understand the risks of additives and packaging in the food supply, and has undertaken both public advocacy and litigation aimed at limiting human exposure to such harm.

I declare under penalty of perjury that the foregoing is true and correct.

Michael F. Jacobson

March 18, 2016

Michael F. Jacobson

Date

No. _____

UNITED STATES COURT OF APPEALS FOR THE NINTH CIRCUIT

IN RE BREAST CANCER FUND, CENTER FOR ENVIRONMENTAL HEALTH, CENTER FOR FOOD SAFETY, CENTER FOR SCIENCE IN THE PUBLIC INTEREST, ENVIRONMENTAL WORKING GROUP, and NATURAL RESOURCES DEFENSE COUNCIL, *Petitioners*,

v.

U.S. FOOD AND DRUG ADMINISTRATION and ROBERT M. CALIFF, COMMISSIONER OF THE U.S. FOOD AND DRUG ADMINISTRATION, *Respondents*.

DECLARATION OF ANDREW KIMBRELL

I, ANDREW KIMBRELL, do hereby affirm and state:

1. I am the Executive Director and Founder of Center for Food Safety (CFS).

2. CFS is a 501(c)(3) nonprofit membership organization incorporated under the laws of the District of Columbia. CFS has offices in the District of Columbia; San Francisco, California; Los Angeles, California; Portland, Oregon; and Honolulu, Hawai‘i. CFS has over 750,000 members, who reside in each of the fifty states and the District of Columbia.

3. CFS was founded to ameliorate the adverse impacts of industrial farming and food production systems on human health, animal welfare, and the environment. CFS's mission is to protect human health and the environment by

curbing the use of harmful food production technologies, including unsafe food additives, and promoting sustainable alternatives. CFS was created to protect the interests of its staff and its members in having access to sustainably-produced, safe food.

4. CFS provides oversight of governmental activities surrounding the safety of our foods. CFS develops and disseminates a wide array of educational and informational materials that address the potential health impacts of food production technologies and agricultural products to CFS members; policymakers; local, state and federal government personnel; international governmental officials; nonprofit organizations; and interested members of the general public. These educational and informational materials include, but are not limited to, in-depth scientific and legal reports, news articles, policy reports, white papers, legal briefs, press releases, newsletters, product guides, "action alerts," and fact sheets. Through these materials, CFS seeks to provide its members with a means of identifying potentially unsafe food products on the market and to encourage full public participation in food safety issues presented by our current regulatory framework.

5. CFS attempts to change the federal regulatory scheme in a way that protects its members and consumers by submitting rulemaking petitions to the U.S. Food and Drug Administration (FDA) related to food additives. In addition to the petition at issue in this litigation, CFS is a petitioner on Food Additive Petition No.

5A4810, seeking to prohibit the use of seven synthetic flavors that have been found by the National Toxicology Program to induce cancer; and a recently submitted petition to ban ortho-phthalates in food contact articles. CFS was also a petitioner on Food Additive Petition No. 4B4809, which successfully led FDA to ban the use of unsafe long-chain perfluorinated compounds in food contact substances.

6. When necessary, CFS also engages in public interest litigation to compel FDA to perform its statutory duties and protect the public and CFS members from the negative impacts of unsafe foods. Most recently, CFS filed suit against FDA for its failure to finalize its proposed rule governing the use of food additives that are "generally recognized as safe" (GRAS) under the Federal, Food, Drug, and Cosmetic Act (Food Act). That litigation resulted in a consent decree requiring FDA to issue a final rule governing GRAS food additives by August 31, 2016. *See* Consent Decree, *Ctr. for Food Safety v. Burwell*, No. 1:14-cv-267-RC (D.D.C. Oct. 20, 2014), ECF No. 15. CFS also successfully sued FDA in 2012 for failing to timely promulgate regulations under the Food Safety Modernization Act, which resulted in a consent decree requiring FDA to issue final regulations by dates certain. *See Ctr. for Food Safety v. Hamburg*, 954 F. Supp. 2d 965 (N.D. Cal. 2013).

7. The petition at issue in the instant litigation seeks action by FDA that will make our food system safer. FDA's failure to respond to the petition has injured,

and will continue to injure, CFS members by continuing to expose them to harmful levels of perchlorate from food packaging without any means of avoiding it, interfering with their ability to purchase and consume food free of perchlorate, and diminishing their sense of security and confidence in our nation's food supply. CFS members have an interest in and a right to consume safe foods that do not put them at increased risk of negative health effects, without having to take extreme precautionary measures; FDA's failure to respond to the petition harms these interests. Providing a response to the petition would help protect CFS members and millions of Americans from the risk of harm due to exposure to perchlorate, either by banning perchlorate or providing an opportunity for CFS to challenge FDA's failure to ban it.

8. CFS's organizational interests are being, and will be, adversely affected by FDA's actions as alleged in this lawsuit. FDA's failure to respond to the petition injures CFS's mission of protecting consumers from unsafe food production methods and technologies. FDA's failure has, and will continue to, injure CFS's organizational interests in addressing the food safety concerns raised by the current regulatory framework and the negative environmental, human health, and public safety harms of unsafe foods and production methods. CFS has an interest in informing its members of ways to avoid harmful foods and choose sustainable, safe products, which is impeded by FDA's actions. CFS has also diverted resources

away from its other litigation priorities to bring this suit to enforce the mandates of the Food Act in the public interest. Finally, CFS's procedural interests are being harmed by FDA's failure to comply with the clear response requirements mandated by the Food Act.

I declare under penalty of perjury that the foregoing is true and correct.

Andrew Kimbrell

3/24/2016

Date

No. _____

UNITED STATES COURT OF APPEALS FOR THE NINTH CIRCUIT

IN RE BREAST CANCER FUND, CENTER FOR ENVIRONMENTAL HEALTH, CENTER FOR FOOD SAFETY, CENTER FOR SCIENCE IN THE PUBLIC INTEREST, ENVIRONMENTAL WORKING GROUP, and NATURAL RESOURCES DEFENSE COUNCIL, *Petitioners*,

v.

U.S. FOOD AND DRUG ADMINISTRATION and ROBERT M. CALIFF, COMMISSIONER OF THE U.S. FOOD AND DRUG ADMINISTRATION, *Respondents*.

DECLARATION OF KIRSTEN KRANE

I, KIRSTEN KRANE, do hereby affirm and state:

1. I am currently a member of the Center for Science in the Public Interest (CSPI), and have been for about 8 years.

2. I am very concerned about environmental issues, and make an effort to support environmental advocacy. For example, I sign petitions and make donations to further various causes, particularly those related to human health. The Center for Science in the Public Interest has long represented my interests.

3. I currently live in East Glacier Park, Montana.

4. As a new mother to a seventeen-month-old baby girl, I am deeply concerned about exposure to perchlorate, primarily because my daughter was born with congenital hypothyroidism (CH).

5. My daughter has taken levothyroxine every single day since she was discovered to have CH at 10 days old. Before she ate solid foods, we crushed pills daily and fed them to her via oral syringe. She has to have blood drawn routinely every 2 – 3 months, which is difficult and upsetting. We also live 2.5 hours from the pediatrician, so it has resulted in a lot of additional time off of work for my husband and me.

6. I am aware that perchlorate is a chemical that manufacturers use in plastic packaging for dry foods. I understand that perchlorate interferes with normal thyroid functioning in humans, and that exposure to perchlorate can cause health problems for people, especially for fetuses, infants, young children, and those who already have hypothyroidism.

7. I am concerned that while I was pregnant with my daughter, perchlorate may have inhibited my thyroid's uptake of iodine, which impairs hormone production and is essential to fetal brain development. I understand that during the first two trimesters of pregnancy, the fetus' thyroid is not yet fully functioning, so the fetus depends completely on its mother for thyroid hormones.

8. My family regularly consumes dry foods contained in plastic packaging. In addition, I understand that, even if some of the foods my family consumes are not directly packaged in plastic, the ingredients in those foods might have been stored in plastic at some earlier point. It would therefore be virtually impossible for me to eliminate perchlorate-contaminated foods from my daughter's diet. I worry that, despite the precautions I have taken to limit my daughter's exposure to chemicals such as perchlorate, I am unwittingly endangering her health.

9. Furthermore, I am concerned that perchlorate is making my daughter's thyroid medication less effective, by countering the beneficial effects of that medication.

10. I understand that, in 2014, CSPI petitioned the United States Food and Drug Administration (FDA) to ban uses of perchlorate in food packaging. I strongly support CSPI's petition to FDA, as well as CSPI's lawsuit to compel FDA to answer the petition. I believe that CSPI's efforts are important steps toward protecting my daughter from the health risks posed by eating perchlorate-contaminated foods.

I declare under penalty of perjury that the foregoing is true and correct.

Kirsten Krane

March 25, 2015

Date

No. _____

UNITED STATES COURT OF APPEALS FOR THE NINTH CIRCUIT

IN RE BREAST CANCER FUND, CENTER FOR ENVIRONMENTAL HEALTH, CENTER FOR FOOD SAFETY, CENTER FOR SCIENCE IN THE PUBLIC INTEREST, ENVIRONMENTAL WORKING GROUP, and NATURAL RESOURCES DEFENSE COUNCIL, *Petitioners*,

v.

U.S. FOOD AND DRUG ADMINISTRATION and ROBERT M. CALIFF, COMMISSIONER OF THE U.S. FOOD AND DRUG ADMINISTRATION, *Respondents*.

DECLARATION OF RICHARD LUCZYSKI

I, RICHARD LUCZYSKI, do hereby affirm and state:

1. I am a member of the Natural Resources Defense Council (NRDC), and have been for over twenty years.

2. I currently live in Pasadena, California.

3. As I see it, there is no voice for the environment except for whoever decides to be one. Our representatives in government are shortchanging us; they are not protecting us from so many of the threats to our planet and our health. I have sought to do my part in protecting the environment: I have advocated for better air quality in Pasadena, and as a fly fisherman, I have fought to protect trout streams in the San Bernardino National Forest from destruction by the United States Forest

Service. But I recognize that no individual can do enough on their own. I support NRDC because it is an effective voice for the environment.

4. I was diagnosed with hypothyroidism about fifteen years ago. Since then, I have taken medication to treat my hypothyroidism, and will have to do so every day for the rest of my life.

5. Managing my hypothyroidism has been difficult. In fall of 2015, I developed a reaction to my medication, which caused me to feel ill every day for a ninety-day stretch. While I was suffering this reaction, I feared that I would develop acute health problems that could impair my breathing. My doctors prescribed me a lower dosage of the same prescription. Though I have not yet had another adverse reaction to my medication, I now often worry about its effectiveness, and about whether it might cause adverse side effects. My doctor is currently looking to raise my dosage once more, because it is not clear that the lower dose will be equally effective.

6. My adult daughter also has hypothyroidism. She was diagnosed within the last four years.

7. I am aware that perchlorate is a chemical known to interfere with the proper functioning of the thyroid in humans. I am keenly aware of the dangers of perchlorate because Pasadena has a history of perchlorate contamination of drinking water caused by the NASA Jet Propulsion Laboratory.

8. I have been living in California since 1964, and have been drinking the tap water here that whole time. I worry that I have been exposed to perchlorate through drinking water, and that this exposure has contributed to—or even caused—my hypothyroidism.

9. I understand that, in addition to contaminating drinking water, perchlorate is a constituent in plastic packaging for dry foods. I also understand that perchlorate can transfer from such packaging to the foods contained therein, and that if I were to eat foods held in packaging containing perchlorate, I might ingest perchlorate.

10. I regularly eat certain dry packaged foods, including rice and sugar. I am aware that such foods might be held in packaging containing perchlorate, and might therefore be contaminated with perchlorate.

11. I am concerned that I might be exacerbating my hypothyroidism by unknowingly eating foods contaminated with perchlorate. I understand that the thyroid is responsible for the health of many other bodily functions, and so I am especially reluctant to mess around with it. If my thyroid medication fails, then I fail, and I fear dietary exposure to perchlorate might cause my thyroid medication to fail, by counteracting the medication's beneficial effects. I am also concerned that dietary exposure to perchlorate might require me to take a higher dosage of my thyroid medication than would otherwise be necessary, and that I might have another adverse reaction as a result. I cannot simply keep adding medications if my

treatment is unsuccessful. I believe I am already exposed to many threats to many forms of pollution that threaten my health, including perchlorate in my drinking water. I do not want to further endanger my health.

12. I am also worried about my daughter's health. When she was growing up, until twenty years ago, we ate the same foods and drank the same water, which I fear might have been contaminated with perchlorate. I also understand that perchlorate can be passed to children through breast milk. My wife breastfed both our children, and I worry that my children might have been exposed to perchlorate through my wife's breast milk. Now, my daughter has hypothyroidism. I am concerned that her health, like mine, continues to be at risk from dietary exposure to perchlorate from packaging for dry foods.

13. I am worried, too, about my grandchildren. My daughter has two children: one one-and-a-half years old, the other three-and-a-half. My daughter breastfed both of her children. I fear they might have been exposed to perchlorate through my daughter's breast milk, or through eating dry packaged foods, and that their health might suffer as a result.

14. I am aware that NRDC petitioned the United States Food and Drug Administration (FDA) in 2014 to ban uses of perchlorate in food packaging. I am aware that FDA has not yet responded to NRDC's petition, and that NRDC is suing FDA to compel FDA to do so.

15. In my view, FDA should at least find out what harm perchlorate in food packaging is doing to the health of all citizens, and make sure that everyone is aware of the risk. If FDA is putting citizens' health at risk, then FDA should ban uses of perchlorate in food packaging.

16. I would feel safer if FDA were to ban uses of perchlorate in food packaging. I would feel more confident eating dry packaged foods, such as flour and sugar, and would be relieved to know that my health, my daughter's health, and my grandchildren's health were exposed to one less threat. I would gain confidence that FDA could take appropriate steps to protect Americans from exposure to perchlorate and other toxic chemicals.

17. If FDA were to deny NRDC's petition, I would want NRDC to keep fighting to reduce people's exposure to perchlorate. I would want NRDC to examine FDA's reasons for denying the petition, and independently assess whether there are good reasons not to ban uses of perchlorate in food packaging.

18. I think it is important FDA respond to NRDC's petition, so that the public can know what analyses underlie FDA's policies regarding uses of perchlorate in food packaging. Right now, I am not sure if FDA is ignoring current science on the health effects of perchlorate due to inappropriate influence from manufacturers of food packaging or other industry groups. As a result, I do not feel I can fully trust FDA to protect public health.

19. For all the reasons stated above, I fully support NRDC in this matter.

I declare under penalty of perjury that the foregoing is true and correct.

Richard Luczyski — 3/15/2016

Richard Luczyski — Date

No. _____

UNITED STATES COURT OF APPEALS FOR THE NINTH CIRCUIT

IN RE BREAST CANCER FUND, CENTER FOR ENVIRONMENTAL HEALTH, CENTER FOR FOOD SAFETY, CENTER FOR SCIENCE IN THE PUBLIC INTEREST, ENVIRONMENTAL WORKING GROUP, and NATURAL RESOURCES DEFENSE COUNCIL, *Petitioners*,

v.

U.S. FOOD AND DRUG ADMINISTRATION and ROBERT M. CALIFF, COMMISSIONER OF THE U.S FOOD AND DRUG ADMINISTRATION, *Respondents*.

DECLARATION OF MATTHEW RAINBOW

I, MATTHEW RAINBOW, do hereby affirm and state:

1. I am a member of the Natural Resources Defense Council (NRDC), and have been for over twenty years.

2. I currently live in Lancaster, California.

3. I am Professor of General and Molecular Cell Biology at Antelope Valley College. As a molecular biologist, I have an acute sense of how fragile the ecosystems of the Earth are, and what serious trouble the planet is currently in. We live in a tiny, sealed ecosystem—the Earth—and that ecosystem is the only home that we have. We had better take care of it, if we want it to be habitable for future generations. I support NRDC because I feel it advocates for the world I want to

see, one in which my children and grandchildren can live in healthily when they are adults.

4. I have six children, of whom three are adults.

5. My children and I regularly consume dry foods sold in plastic packaging, particularly bread and rice, but also lentils, flour, and sugar. We also frequently consume foods that contain dry, previously packaged ingredients, such as breakfast cereals, bagels, and muffins.

6. I am aware that perchlorate is a chemical known to inhibit thyroid functioning in humans. I am also aware that the thyroid plays a crucial role in physical and cognitive development, and that exposure to perchlorate can therefore pose a significant health risk to children.

7. I understand that plastic packaging for dry foods may contain perchlorate, and that perchlorate can be transferred from such packaging to the food contained therein.

8. I am worried that my children and I are being exposed to perchlorate by eating dry packaged foods, and that such exposure could threaten our health. I am especially concerned about my children's wellbeing. I fear they might develop hypothyroidism, and that their development might be disrupted as a result. I am also worried that the carcinogenicity of perchlorate has not been sufficiently

studied. As a result, I cannot be certain that, later in life, my children will not develop thyroid cancer because they are being exposed to perchlorate now.

9. One of my children, my eight-year-old son, has high-functioning autism. I am particularly concerned about his health, and I worry that his condition might be adversely affected by exposure to perchlorate, given the role of the thyroid in cognitive development.

10. When I purchase food for myself and my children, I check to see if there are any labels indicating the presence of dangerous chemicals in the food or the packaging. I cannot recall seeing a label disclosing the presence of perchlorate in food packaging.

11. I understand that NRDC petitioned the United States Food and Drug Administration (FDA) in 2014 to ban uses of perchlorate in food packaging. I also understand that NRDC is now suing FDA to compel FDA to respond to that petition, because FDA has not yet done so.

12. I believe that if there is a clear association between exposure to perchlorate and developmental problems due to interference with thyroid function, then FDA should ban uses of perchlorate in food packaging. Since it seems to me such an association does exist, I believe FDA should ban uses of perchlorate in food packaging.

13. I am a strong advocate of the United States cutting down or eliminating use of plastics generally. I believe that plastics pollution of the oceans is environmentally horrific. That plastic food packaging might contain perchlorate, thereby making it dangerous to consumers, makes the use of plastics even worse.

14. If FDA were to grant NRDC's petition, and thereby ban uses of perchlorate in food packaging, I would feel more confident when my children or I eat dry packaged foods. I would rest easier knowing that no perchlorate was being transferred from the plastic packaging to our food and thereby threatening our health.

15. If FDA were to deny NRDC's petition, I would be frustrated that FDA was abetting the continued overuse of plastics. I would want FDA and advocacy organizations such as NRDC to closely examine the available science to determine how much perchlorate is being transferred from packaging to foods. I would want NRDC to carefully evaluate FDA's explanation of its decision, and, if warranted, use it as the basis for further future advocacy, including possible litigation.

16. I see NRDC's efforts to have FDA ban uses of perchlorate as part of a larger effort to rid our food system of the hundreds of chemicals that have not been adequately vetted, and that may be hazardous to human health. For NRDC to succeed in this litigation would, in my view, constitute an important step towards protecting the health of the public against such chemicals.

17. For all the reasons stated above, I fully support NRDC in this matter.

I declare under penalty of perjury that the foregoing is true and correct.

Matthew Rainbow

March 25, 2016

Matthew Rainbow

Date

No. _____

UNITED STATES COURT OF APPEALS FOR THE NINTH CIRCUIT

IN RE BREAST CANCER FUND, CENTER FOR ENVIRONMENTAL HEALTH, CENTER FOR FOOD SAFETY, CENTER FOR SCIENCE IN THE PUBLIC INTEREST, ENVIRONMENTAL WORKING GROUP, and NATURAL RESOURCES DEFENSE COUNCIL, *Petitioners*,

v.

U.S. FOOD AND DRUG ADMINISTRATION and ROBERT M. CALIFF, COMMISSIONER OF THE U.S. FOOD AND DRUG ADMINISTRATION, *Respondents*.

DECLARATION OF PAIGE TOMASELLI

I, PAIGE TOMASELLI, do hereby affirm and state:

1. I am a member of Center for Food Safety, and have been since 2008.

2. I currently live in Oakland, California.

3. I am a Senior Attorney at Center for Food Safety (CFS), and have been a litigator here since 2008. Prior to joining CFS, I worked as an attorney at Sher Leff, representing public water supplies and public agencies in mass tort litigation involving groundwater contamination and toxic torts, and also as counsel for a real estate law firm.

4. On November 24, 2015, I gave birth to my first child. I am currently breastfeeding him. I also purchase and prepare food for myself and my husband.

5. I am aware that perchlorate is a constituent in plastic packaging for dry foods. I understand that perchlorate can transfer from packaging to the foods it contains, and that I could consume perchlorate if I were to eat foods held in packaging containing perchlorate. I also am aware that perchlorate is found in drinking water in California.

6. I am aware that perchlorate is a chemical known to interfere with the proper functioning of the thyroid in humans, which is essential for brain development in infants and fetuses.

7. I have lived in California for the past 33 years, aside from three years when I was attending law school out-of-state. In all the time I have lived here, I have consumed tap water on a regular basis, nearly exclusively over bottled water.

8. I regularly purchase and eat dry foods in plastic packaging, including rice, quinoa, bread, tortillas, steel cut oats, sugar, pasta, crackers, cookies, chips, and seaweed. I am aware that such foods might be held in packaging containing perchlorate, and might therefore be contaminated with perchlorate. However, avoiding such packaging is exceedingly difficult, and I struggle to avoid it entirely.

9. I also purchase and eat bulk dry foods, including raw nuts, roasted nuts, oats, flour, granola, dried fruits, beans, and lentils. I choose bulk foods to save money and also to avoid unnecessary plastic packaging for both my health and the environment. However, I am aware that foods I purchase in bulk and feed to my

family might have been stored in plastic packaging containing perchlorate at some point in their production and distribution. I have no way of knowing whether these bulk foods were contaminated with perchlorate from such packaging, and therefore cannot avoid it. If I had a means of avoiding perchlorate in food packaging entirely, I would do so.

10. I understand that perchlorate can be passed to children through breastmilk, and that infant formula can also contain perchlorate. I am aware that children between six months and six years old have the greatest average exposures to perchlorate, which can inhibit their neurological development. I choose to breastfeed my son because I know that breastmilk provides optimal nutrition for infants, as well as antibodies to protect his health. I fear that my newborn son may be exposed to perchlorate through my breastmilk, and that his health and development might suffer as a result.

11. My newborn's health is the most important thing to me, and I am meticulous about avoiding exposing him to unnecessary chemicals and additives either through his environment or breastmilk. I spend time and energy to avoid purchasing foods sold in packaging that contains harmful chemicals, and I also spend time, energy, and money to seek out chemical-free food storage containers to use in my home.

12. I am concerned about cumulative exposure to perchlorate from drinking water, food packaging, and other sources that together may result in harmful levels of perchlorate in myself and, by extension, my nursing infant.

13. I am aware that CFS and others petitioned the United States Food and Drug Administration (FDA) in 2014 to ban uses of perchlorate in food packaging. I am aware that FDA has not yet responded to the petition, and that CFS is now suing FDA to compel FDA to do so.

14. FDA's continued failure to respond to the petition harms me and my infant son by allowing our exposure to perchlorate to continue at unsafe levels. FDA's failure also curtails my ability to purchase dry foods with any confidence.

15. This harm would be significantly lessened if FDA were to grant CFS's petition and therefore ban uses of perchlorate in food packaging. I would be free from exposure to perchlorate from dry foods packaging and my cumulative exposure would be lessened, which in turn would protect my son from exposure through breastmilk. I would feel confident purchasing and eating dry packaged foods without fear of perchlorate exposure. I would also gain trust in FDA as the agency charged with keeping our food supply safe from harmful food additives.

16. If FDA were to deny the petition, my injuries would still be reduced because it would enable CFS to independently assess whether FDA's decision not to ban uses of perchlorate in food packaging was justified. I trust CFS to conduct this

assessment and to hold FDA accountable for protecting my health. If CFS were to conclude that FDA did not act appropriately to protect the public health, then it could take further action to challenge FDA's decision, which would protect my health.

I declare under penalty of perjury that the foregoing is true and correct.

Paige Tomaselli

3/18/ 16
Date

No. _____

UNITED STATES COURT OF APPEALS FOR THE NINTH CIRCUIT

IN RE BREAST CANCER FUND, CENTER FOR ENVIRONMENTAL HEALTH, CENTER FOR FOOD SAFETY, CENTER FOR SCIENCE IN THE PUBLIC INTEREST, ENVIRONMENTAL WORKING GROUP, and NATURAL RESOURCES DEFENSE COUNCIL, *Petitioners*,

v.

U.S. FOOD AND DRUG ADMINISTRATION and ROBERT M. CALIFF, COMMISSIONER OF THE U.S. FOOD AND DRUG ADMINISTRATION, *Respondents*.

DECLARATION OF GINA TRUJILLO

I, GINA TRUJILLO, do hereby affirm and state:

1. I am the Director of Membership for the Natural Resources Defense Council (NRDC). I have served in this position since January 2015.

2. My duties include supervising the preparation of materials that NRDC distributes to members and prospective members. Those materials describe NRDC and identify its mission.

3. NRDC is a membership organization incorporated under the laws of the State of New York. It is recognized as a not-for-profit corporation under section 501(c)(3) of the United States Internal Revenue Code.

4. NRDC's U.S. offices are located in New York, New York; Washington, D.C.;

Chicago, Illinois; Bozeman, Montana; San Francisco, California; and Santa Monica, California.

5. NRDC currently has approximately 294,800 members in the United States. There are NRDC members residing in each of the fifty United States and in the District of Columbia.

6. NRDC's mission statement declares that the organization's purpose is "to safeguard the Earth: its people, its plants and animals, and the natural systems on which all life depends." The mission statement goes on to declare that NRDC strives to "advance the long-term welfare of present and future generations," and that NRDC "affirms the integral place of human beings in the environment." Accordingly, protecting human health by preventing pollution ranks among NRDC's top institutional priorities. As set forth in NRDC's statement of priorities: "Toxic chemicals in our environment . . . have been linked to cancer, birth defects and brain impairments. Reducing or eliminating the load of these dangerous chemicals in . . . the air we breathe, the food we eat and the water we drink can help reduce the toll of human disease and suffering."

7. Protecting human health from the adverse effects of perchlorate in food packaging exemplifies NRDC's work. NRDC has sought for years to limit human exposure to toxics, and has undertaken both public advocacy and litigation aimed at limiting human exposure to perchlorate, in particular.

I declare under penalty of perjury that the foregoing is true and correct.

Gina Trujillo

Gina Trujillo

3/14/16

Date