

April 3, 2006

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Dockets Management Branch  
U.S. Food and Drug Administration  
5630 Fishers Lane  
Room 1061  
Rockville, MD 20852

Dear Sir or Madam,

Citizens for Health (CFH) submits this petition pursuant to 21CFR10.30.

**A. Action requested**

Citizens for Health requests the Commissioner of Food and Drugs to amend its regulations as follows:

1. Revoke its amendment of food additive regulations that provided for the inclusion and addition of sucralose as a nonnutritive sweetener in food (21CFR172, Docket No. 87F-0086, April 3, 1998 [1]).
2. Regardless of whether the Agency revokes (or pending the revocation of) its 1998 approval of sucralose in a timely manner or at all, the Agency must either officially add sucralose (and Splenda®) to the existing FDA Safety Information and Adverse Events Reporting Program (establishing a separate reporting sub-category of Special Nutritional Products called "non-nutritive sweeteners" or "artificial sweeteners" and adjusting its Form FDA 3500 [2] and all other linked reporting/gathering forms, instructions and informational paperwork for health professionals and consumers) or (3) establish a separate and fully dedicated reporting system for sucralose and Splenda.
3. The Agency should ask the Inspector General of the Department of Health and Human Services to investigate consumer health concerns and publicly posted adverse event reports related to the widespread use of sucralose (Splenda) as a result of the Agency's approval of sucralose in 1998 despite serious safety concerns that the Agency originally acknowledged but ultimately set aside (precedent for FDA request for IG investigation: in March 2003, the Agency asked the HHS Inspector General to investigate the FDA's own conduct of the "Bone 97" clinical trial) (3).
4. The Agency should initiate a full-scale public-health investigation (involving U.S. Public Health Service environmental health officers) in and around McIntosh, Alabama, into local residents' reports of environmental exposure effects related to the transport and use of chlorine and the release of cyclohexane, a known toxin, from the Splenda plant in McIntosh, Alabama, looking into health problems than can be caused by exposure to cyclohexane, including but not limited to: coma; encephalopathy; liver abnormalities; chronic "painter's syndrome; psycho-organic solvent syndrome; organic solvent dementia; difficulty concentrating; dementia; memory loss; mood disturbance; arrhythmia; confusion; dermatitis; dizziness; fatigue; headache; in-coordination; inebriation; irritability; lethargy; impaired speech and stupor and ecological effects such as fish die-off, and into other health concerns related to the transport, use and/or

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- release of chlorine, dimethylamine, N,N-dimethylformamide; nitrate compounds and phosgene gas (4-14).
5. Based on all of the above-cited (and below-detailed) release of toxins (including cyclohexane) in the toxic, chlorine-based factory manufacturing of sucralose (Splenda), it is inappropriate and misleading (15) to consumers for Splenda to include "Made from Sugar So It Tastes Like Sugar" or any variation of this on its packaging and marketing materials and, therefore, the Agency must disallow or prohibit this slogan and its variants.
  6. Based on the fact that there has never been a human clinical trial on the finished product (Splenda) (which also includes dextrose and maltodextrin) the Agency should instruct the manufacturer to immediately remove the following slogan (and any variation) from its product packaging and marketing materials: "Suitable for people with diabetes" as this is false and misleading. Splenda has never been established as safe for people with diabetes contrary to its marketing.
  7. Based on the fact that galactosemia is an inherited metabolic disorder similar to phenylketonuria (PKU)—relating to which there is a warning required for aspartame—the fact that sucralose contains a galactose monosaccharide should be made public knowledge so that people with galactosemia, or pregnant women who carry genetic trait for this disorder and are at risk for having a baby with galactosemia, can avoid sucralose- and Splenda-containing products entirely. We are further urging you to order that all sucralose and Splenda products now bear a galactosemia warning because it contains a "galactose monosaccharide," and call on the Agency to inform all U.S. physicians, public health officials and galactosemia support groups about this health danger.
  8. If the Agency does not revoke its approval and (a) does not officially add sucralose (Splenda) to the existing FDA Safety Information and Adverse Events Reporting Program (establishing a separate sub-category of Special Nutritional Products called "non-nutritive sweeteners" or "artificial sweeteners" and adjusting its Form FDA 3500 (2) and all other linked reporting/gathering forms, instructions and informational paperwork for health professionals and consumers) or establish a separate and fully dedicated reporting system for sucralose (Splenda) and/or (b) ask for an investigation by the HHS Inspector General, and/or (c) initiate an independent full-scale public health investigation, and/or (d) instruct the manufacturer to immediately remove the above-cited inappropriate and misleading statements/slogans from product packaging and marketing materials, and (d) order that all sucralose- and Splenda-containing products bear a galactosemia warning, then CFH, in any and all of these cases, calls on the Agency to schedule a Public Hearing at its very earliest opportunity so that consumer and other stakeholder concerns can be fully heard and considered.

## **B. Statement of grounds**

### *Actions 1-3.*

The Agency should revoke its approval of sucralose (1) since serious potential and demonstrated health concerns were glossed over and ruled out but should not have been (<http://www.cfsan.fda.gov/~lrd/t1980403.html>).

For example, FDA-reviewed tests for clastogenic activity in a mouse micronucleus test and a chromosomal aberration test in cultured human lymphocytes were inconclusive; in the mouse lymphoma assay, sucralose exhibited some mutagenicity (1, page 6). In addition, products of hydrolysis were either inconclusive or mutagenic in the Ames test (1). Other effects were seen in FDA-reviewed teratologic studies, including significantly decreased thymic weight (1, page 7). In

rabbits, treatment-related deaths were noted and reviewed by FDA, as were infertility and spontaneously aborted fetuses. Body weight gain was also significantly decreased (1, page 8).

In FDA-reviewed carcinogenicity tests, there was an increase (in male rats) of hepatocellular clear cell foci and incidence of renal pelvic mineralization and epithelial hyperplasia, but, again, these findings were discounted (1, pages 9-10). Repeat tests (reviewed by FDA) also showed an increase in hepatocellular clear cell foci, but, again, this was dismissed (1, page 11).

In chronic dosing tests reviewed by FDA, the kidney weight in the high-dose group was significantly increased and body weight gain was significantly decreased (1, page 16). In a 4-to-8-week range-finding study reviewed by FDA, decreased thymus and spleen weights were seen, lymphocytopenia (low white blood cell count) was observed and cortical hypoplasia of the spleen and thymus was observed, effects that were all attributed to palatability and cast aside by the petitioner--and by the FDA as well (1, page 16).

Follow-up studies to address the above findings were conducted in animals, however the animals in the follow-up tests received sucralose intravenously (I.V.) to avoid the palatability issue. These follow-up studies in which no adverse health effects were seen are not relevant to oral human consumption. Long-term follow-up studies using oral administration need to be conducted but, until then, all of the non-oral tests should be dismissed as not relevant for humans (to whom sucralose is marketed).

#### *Action 4.*

In addition to issues relating to pre-market testing, there is good documentation as to the carcinogenic toxins that are released in the production of sucralose (4-14). Residents of McIntosh, Alabama, where Splenda is produced, have told CFH about elevated rates of health effects, birth defects and cancer in and around the Tate & Lyle (formerly McNeil Nutritionals) sucralose plant. These claims need to be independently investigated fully as well, moreso than what has already been looked into by the U.S. EPA and the Alabama Department of Environmental Management (ADEM).

The sole sucralose (Splenda) facility (McNeil/Tate & Lyle plant) in McIntosh, Alabama, is in the process of doubling its production capacity by the end of this year (17) despite the fact that the hazardous waste discharge points from this plant are located approximately 1/3 mile from a local church and 1 mile in each direction from another church and a school (10-14). Although the sucralose factory has received a positive rating from the EPA and ADEM as being in compliance, the fact that release of cyclohexane at this plant has increased by six-fold between 2002 and 2003 (3,478 lbs. in 2002 vs. 23,922 lbs. in 2003; EPA) is of grave concern.

#### *Action 5.*

Based on the above-cited release of toxins (including cyclohexane) in the chlorine-based factory production of sucralose (Splenda) (4-14), it is highly inappropriate and misleading to consumers for Splenda to include "Made from Sugar So It Tastes Like Sugar" or any variation of this on its packaging and marketing materials and, therefore, that is why the Agency must disallow or prohibit this slogan and its variants. A report (15) from the Advertising Standards Complaints Board of New Zealand ruled, on June 20<sup>th</sup>, 2005, that the "made from sugar"-related statements on packaging and marketing materials for Splenda are misleading.

#### *Action 6.*

Dextrose and maltodextrin are added to sucralose to make Splenda. There has never been a human clinical trial on the finished product (Splenda) (which also includes dextrose and maltodextrin). Caloric sweeteners such as these are known to impact blood sugar, insulin and

HbA1c levels in diabetics. Until Splenda, not sucralose, has been proven to be safe for use in diabetics, Splenda and sucralose must no longer be allowed to be marketed with the slogan, "Suitable for people with diabetes," as this is false and misleading. Splenda has never been established as safe for people with diabetes, contrary to its marketing.

*Action 7.*

Based on the fact that galactosemia is an inherited metabolic disorder similar to phenylketonuria (PKU)—relating to which there is a warning required for aspartame—the fact that sucralose contains a galactose monosaccharide should be made public knowledge so that people with galactosemia, or pregnant women who carry genetic trait for this disorder and are at risk for having a baby with galactosemia, can avoid sucralose- and Splenda-containing products entirely. We are further urging this Agency to order that all sucralose and Splenda products now bear a galactosemia warning because these products contain a "galactose monosaccharide," and call on the Agency to inform all U.S. physicians, public health officials and galactosemia support groups about this health danger.

*Action 8.*

If the Agency does not immediately revoke its approval of sucralose, then CFH calls for the Agency to hold a Public Hearing at its earliest opportunity so that consumer and other stakeholder concerns can be fully heard and considered.

**C. Environmental Impact**

As provided in 21CFR15.30, neither an environmental assessment nor an environmental impact statement is required.

That being said, the Agency should independently investigate the reported environmental exposure-linked health effects and reported disease incidence that is believed by McIntosh, Alabama, residents and others to be related to the EPA-approved release of poisons in McIntosh, Alabama, in the production of sucralose (4-14).

As noted, residents of McIntosh, Alabama, where sucralose (Splenda) is produced, have told local media outlets and our organization about elevated rates of health effects, birth defects and cancer in the vicinity of the Tate & Lyle (McNeil Nutritionals) plant. As stated above in Section B, these claims must be independently investigated fully as well, moreso than what has already been looked into by the U.S. EPA and the Alabama Department of Environmental Management (ADEM).

As noted, the sole sucralose (Splenda) facility (McNeil/Tate & Lyle plant) in McIntosh, Alabama, is in the process of doubling its production capacity by the end of this year (17) despite the fact that the hazardous waste discharge points from this plant are located approximately 1/3 mile from a local church and 1 mile in each direction from another church and a school (10-14). As also noted, despite the fact that the sucralose plant has received a positive rating from the EPA and ADEM as being in compliance, the fact that release of cyclohexane at this plant has increased by six-fold between 2002 and 2003 (3,478 lbs. in 2002 vs. 23,922 lbs. in 2003; EPA) is of grave concern.

If the Agency does not immediately revoke its approval of sucralose, then CFH calls for the Agency to hold a Public Hearing at its earliest opportunity so that consumer and other stakeholder concerns can be fully heard and considered.

#### **D. Economic Impact**

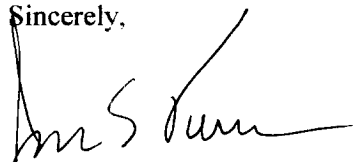
As provided in 21CFR15.30, economic impact information is to be submitted only when requested by the Commissioner following review of the petition.

That being said, the Agency should be aware of the degree of economic risk (and potential liability) in which the Agency would be placing the FDA and the U.S. government (from U.S. consumers) were the Agency not to follow all (or most) of the requested actions in this petition.

#### **E. Certification**

The undersigned certifies that, to the best knowledge and belief of the undersigned, this petition includes all available information and views on which the petition relies, and that it includes representative data and information known to the petition which are unfavorable to the petition.

Sincerely,



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#### **About Citizens for Health**

*Citizens for Health ([www.citizens.org](http://www.citizens.org)) is a national non-profit consumer advocacy group working to broaden healthcare options, create an integrative health system based on wellness, and advance the freedom to make health choices. The group promotes the fundamental policies needed to improve health choices and information in the U.S. and internationally. The group works with grassroots and education organizations and partners in the not-for-profit sector to ensure consumer access to dietary supplements, safe foods, a healthy environment and a wide range of healing therapies. Citizens for Health fosters active citizen leadership and organizes natural health consumers to create political and legislative solutions that support those rights.*

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