High-Intensity Sweeteners: An Overview

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9/23/2014
What is a High-Intensity Sweetener?

- Used as sugar substitute
- Many times sweeter than table sugar (sucrose)
- Contribute few to no calories to food
- Smaller amounts are needed to create high levels of sweetness
Regulatory Authority and Status

• Federal Food, Drug, and Cosmetic Act
  (FD&C Act or The Act)
  – FD&C Act Section 409 (Food additive authority)
  – FD&C Act Section 201(s) (Food additive definition and exemptions)

• High-intensity sweeteners are regulated as:
  – Food additives
  – GRAS substances
  – Substance prohibited for used in human food
Regulatory Status – Food Additive

• Food Additive Safety Evaluation
  • The petitioner must submit data in a food additive petition demonstrating the food additive will be safe under the intended conditions of use (21 CFR Part 171).
  • FDA evaluates the data in the petition, public comments to the petition, and other relevant data in FDA's files.
  • Standard of Review: Fair evaluation of the data
  • Safety standard: Reasonable certainty of no harm (21 CFR 170.3(i))
Review Team

Toxicologist  Chemist  Environmental  Consumer Safety Officer
Typical Safety Data Package

- Genetic toxicity tests
- Subchronic toxicity tests with mice and rats
- One year toxicity test with dogs
- Chronic toxicity tests/carcinogenicity tests with mice and rats
- Reproductive and developmental toxicity studies in rats and/or rabbits
- Neurotoxicity studies in rodents
- Metabolism and pharmacokinetic studies
- Human studies – glucose homeostasis in diabetics and non-diabetics
Poll: What is the safety standard for a food additive petition?

- A. Absolute proof
- B. Reasonable certainty of no harm
- C. Public consensus
- D. Beyond a reasonable doubt
Regulatory Status - GRAS

- Listed in 21 CFR
  - Substances Generally Recognized As Safe (21 CFR Part 182)
  - Substances Affirmed as GRAS (21 CFR Part 184)
- Self-affirmed GRAS
- FDA’s Voluntary GRAS Notification Program (GRAS Notice Inventory on FDA website)
  - Scientific procedures – Requires same quantity and quality of scientific evidence to obtain approval of a food additive regulation for the substance
  - Experience based on common use in food before 1958
Regulatory Status – Prohibited from use in human food

• Prohibited from use in human food (21 CFR Part 189)
  – Determination that prohibited substances present a potential risk to the public health
  – Have not been shown by adequate scientific data to be safe for use in human food
  – Partial list of prohibited substances (not all-inclusive)
  – New scientific data could support FDA’s decision to make changes to this regulation
Poll

FDA is responsible for the safety decision of high-intensity sweeteners that are approved as food additives. Does FDA also have to approve GRAS substances?

• A. Yes
• B. No
High-Intensity Sweeteners

Saccharin
Aspartame
Sucralose
Acesulfame potassium (ACK)
Neotame
Advantame
Steviol glycosides (Reb. A and stevioside)
Luo Han Guo fruit extracts (monk fruit)

Non-nutritive sweeteners have less than 2 percent of the calories in an equal amount of sugar
Nutritive sweeteners have 2 percent or greater the calories in an equal amount of sugar
High-Intensity Sweeteners Regulated as Food Additives

Saccharin - §180.37
Aspartame - §172.804
Acesulfame potassium - §172.800
Sucralose - §172.831
Neotame - §172.829
Advantame - §172.803

Typically paired with other substances to add bulk, viscosity, mouthfeel (e.g., polydextrose, starches, gums)
Saccharin (History)

- Discovered in 1878
- Saccharin and its salts on original GRAS list
- Delisted from GRAS regulation and interim listed as a food additive in 1972
- More than 30 human studies demonstrated that saccharin is safe for human consumption.

**Nonnutritive Sweeteners**

- Calcium cyclohexyl sulfamate
- Calcium saccharin
- Saccharin
- Sodium cyclohexyl sulfamate
- Sodium saccharin
Saccharin

- Remains interim listed as a food additive (21 CFR 180.37)
- 200 to 700 times sweeter than table sugar
- Used as a tabletop sweetener and in a variety of foods (e.g., beverages, baked goods, jams, chewing gum, canned fruit, candy, dessert toppings and salad dressings).
- Brand names Sweet and Low®, Sweet Twin®, Sweet'N Low® and Necta Sweet®
Aspartame

- 200 times sweeter than table sugar
- 1981 - Approved for uses in tabletop sweeteners, chewing gum, cold breakfast cereals, gelatins, and puddings
- 1983 - Approved for use in carbonated beverages
- 1996 – Approved as a general purpose sweetener
- There is a reasonable certainty of no harm to the general population from the use of aspartame as a sweetener in food
  - Exception: People with phenylketonuria (PKU) should not consume.
- It is one of the most exhaustively studied substances in the human food supply.
- Brand names include NutraSweet®, Equal®, and Sugar Twin®
Acesulfame Potassium

- 1988 - Approved as a non-nutritive sweetener for uses including table-top sweetener, in chewing gum, confectionaries, hard and soft candy, puddings and beverage categories
- 2002 - Approved as a general purpose sweetener (except in meat and poultry)
- Also known as acesulfame K (Ace-K)
- Ace-K is ~200 times sweeter than sugar and is often combined with other sweeteners
- More than 90 studies verify safety
- Used in over 4,000 foods including baked goods, frozen desserts, candies and beverages
- Brand name Sunett®
Sucralose is modified sucrose.
Sucralose is ~600 times sweeter than sucrose.
1998 – Approved as a non-nutritive sweetener for use in 15 food categories including baked goods, confections, gelatins, puddings, and beverages
1999 – Approved for use as a general purpose sweetener in foods
Extensively studied with more than 110 studies supporting its safety
It is currently used in over 4,500 products, including baked goods, ice creams, candy bars, jams, and carbonated beverages
Brand name Splenda®
Neotame

• 2002 - Approved as a non-nutritive sweetener for use as general purpose sweetener (except in meat and poultry)
• Chemically related to aspartame but does not contain phenylalanine
• Neotame is ~ 7,000 to 13,000 times sweeter than table sugar
• Heat-stable and can be used in cooking and baking
• Data from more than 113 animal and human studies designed to identify possible toxic effects, such as cancer-causing, reproductive, and neurological effects
• Sold under the brand name Newtame®
Advantame

• 2014 - Approved as a non-nutritive sweetener for use as general purpose sweetener and flavor enhancer (except in meat and poultry)
• Chemically related to aspartame but does not contain phenylalanine
• Advantame is ~ 20,000 times sweeter than table sugar
• Heat-stable and can be used in cooking and baking
• Data from more than 37 animal and human studies designed to identify possible toxic effects, including effects on the immune system, reproductive and developmental systems, and nervous system. FDA also reviewed pharmacokinetic and carcinogenicity studies, as well as several exploratory and screening studies
• Currently no brand names
High-Intensity Sweeteners Regulated as GRAS Substances

- High purity Steviol glycosides
- Purified Luo Han Guo fruit (Monk fruit) extracts
Steviol glycosides

- Steviol glycosides purified from the leaves of *Stevia rebaudiana* (Bertoni) Bertoni plant
  - ≥95% glycosides
- Sweetener in foods generally, except meat and poultry
- ~200-300x sweeter than sugar
- Non caloric
- Brand names include Truvia®, PureVia® and Enliten®
- Stevia leaf and crude stevia extracts are not considered GRAS
- Rebaudioside A and steviosides: subject of several GRNs – FDA had no questions about the notifiers determination that the use is GRAS
Luo Han Guo fruit extracts

- Purified extract from *Siraitia grosvenorii* Swingle fruit (Luo Han Guo or Monk fruit)
  - 25%, 45%, or 55% Mogroside V
- Mogrosides are the primary sweetening components
- Sweetener and flavor enhancer in all food, except meat and poultry
- ~160-250x sweeter than table sugar – depends on mogroside level
- Luo Han Guo fruit extracts: subject of GRNs 301 and 359 – FDA had no questions about the notifiers’ determinations that the use is GRAS
- Brand names include Monk Fruit in the Raw® and Nectresse®
Sweetener prohibited from use in human food - Cyclamates

Prohibited from use in human food (21 CFR Part 189)

- Discovered in 1937
- Use originally considered GRAS
- GRAS status rescinded in 1969
- Regulation prohibiting its use issued on 9/23/1974 (39 FR 34172)
Poll: Which sweetener is not a high-intensity sweetener?

- A. Sucralose
- B. Advantame
- C. Honey
- D. Steviol glycosides
- E. Aspartame
# Sweetness Intensity Comparison

<table>
<thead>
<tr>
<th>Sweetener</th>
<th>Sweetness Intensity vs. Table Sugar</th>
</tr>
</thead>
<tbody>
<tr>
<td>Luo Han Guo fruit extracts</td>
<td>~160-250x</td>
</tr>
<tr>
<td>Aspartame</td>
<td>~200x</td>
</tr>
<tr>
<td>Acesulfame potassium</td>
<td>~200x</td>
</tr>
<tr>
<td>Steviol glycosides</td>
<td>~200-300x</td>
</tr>
<tr>
<td>Saccharin</td>
<td>~300x</td>
</tr>
<tr>
<td>Sucralose</td>
<td>~320-1000x</td>
</tr>
<tr>
<td>Neotame</td>
<td>~7000-13,000x</td>
</tr>
<tr>
<td>Advantame</td>
<td>~20,000x</td>
</tr>
</tbody>
</table>
High-Intensity Sweeteners: Pros and Cons

Pros:
• Small amounts are needed for sweetening purposes
• Can be applied to many different products and foods
• Contains no carbohydrates
• They do not contribute to tooth decay and cavities
• Generally don't raise blood sugar levels
• They contain no or low calories, or at least much fewer calories than table sugar

Cons:
• Persons with PKU should not consume aspartame
• Aspartame is not heat stable
• People continue to question the safety of these substances, despite evidence to the contrary
Poll: Why do some consumers choose to use high-intensity sweeteners?

- A. They contribute few to no calories when added to food
- B. They generally will not raise blood sugar levels
- C. They are many times sweeter than sugar
- D. All of the above
Conclusion

• FDA continues to monitor and review scientific literature on the safety of sweeteners in food.

• If new evidence suggests that a product already in use may be unsafe, FDA will take action.

• Adverse events believed to be caused by sweeteners may be reported to FDA’s CAERS (CFSAN Adverse Events Reporting System) or FDA District Office.
Resources

Ingredients, Packaging, and Labeling homepage
http://www.fda.gov/Food/IngredientsPackagingLabeling/default.htm

EAFUS (Everything Added to Food in the United States) database
http://www.fda.gov/Food/IngredientsPackagingLabeling/FoodAdditivesIngredients/ucm115326.htm

Food Additive Status List
http://www.fda.gov/Food/IngredientsPackagingLabeling/FoodAdditivesIngredients/ucm091048.htm

High-Intensity Sweeteners
http://www.fda.gov/Food/IngredientsPackagingLabeling/FoodAdditivesIngredients/ucm397716.htm

Title 21 of the Code of Federal Regulations
http://www.fda.gov/Food/GuidanceRegulation/GuidanceDocumentsRegulatoryInformation/IngredientsAdditivesGRASPackaging/ucm082463.htm

Generally Recognized as Safe (GRAS)
http://www.fda.gov/Food/IngredientsPackagingLabeling/GRAS/default.htm
Thank You

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