# Short-Chain Fructooligosaccharides

## Handling/Processing

### Identification of Petitioned Substance

**Chemical Name:**
Short-chain fructooligosaccharides

**CAS Number:**
308066-66-2

**Other Names:**
FOS
scFOS

**Other Codes:**
none

**Trade Names:**
Actilight®
FortiFeed®
scFOS®
Meioligo®
Neosugar
Nutraflora™
Nutraflora® P-95

### Characterization of Petitioned Substance

**Composition of the Substance:**

Fructooligosaccharides is a carbohydrate consisting of glucose and fructose units. More specifically, fructooligosaccharides is generally thought of as a mixture of 1-ketose (1-kestotriose; GF2), nystose (1,1-kestotetraose; GF3), and 1F-β-fructofuranosyl-nystose (1,1,1-kestopentaose; GF4) (Hussein et al., 1998). The petitioner is seeking approval for use of short-chain fructooligosaccharides. Short-chain fructooligosaccharides (sFOS) has a chain length from 2 to 10 monomers. Monomers are small molecules that may become chemically bonded to other small molecules. According to the U.S. Food and Drug Administration (FDA), no literature references were identified that specifically define or distinguish fructooligosaccharides as short-chain, medium-chain, or long-chain (FDA 2000).

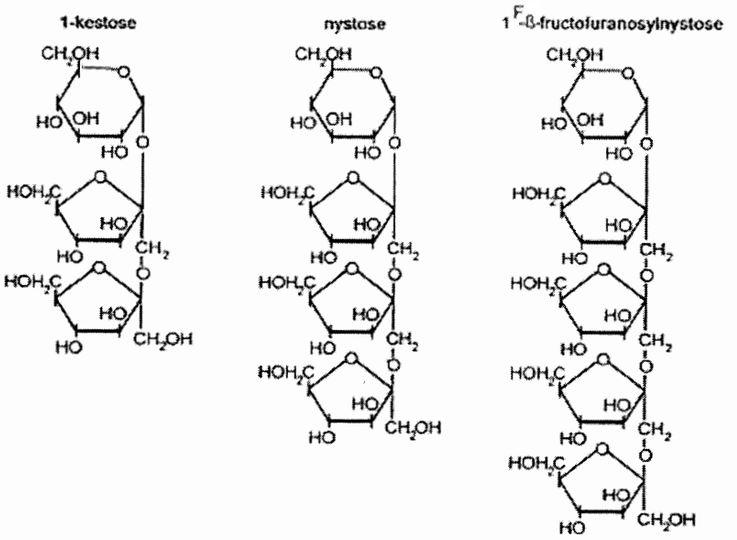


**Figure 1. Chemical Structure and Main Components of Fructooligosaccharides (Hussein et al. 1998)**

**Properties of the Substance:**
In liquid form, short-chain fructooligosaccharides is a clear, colorless, or yellow syrup-like liquid with a fruity smell and sweet taste (JCBEC 2006). In powder form, short-chain fructooligosaccharides is white to light yellow with a fruity smell and sweet taste. Short-chain fructooligosaccharides is soluble in water.

**Specific Uses of the Substance:**
Short-chain fructooligosaccharides is being petitioned for use as an ingredient in food and feed products to provide a selective energy source in the digestive tract of humans and animals.

The carbohydrate mixture already has been added to many food products, including infant foods, yogurt, and medical foods[1] (Garleb et al. 2002, Hussein 2003). Fructooligosaccharides can be taken as a dietary supplement in either capsule or powder form. Ingestion of fructooligosaccharides may help with gastrointestinal problems such as constipation, irritable bowel syndrome, inflammatory bowel disease, and lactose intolerance (Pharmasave 2006). It also has been thought to prevent yeast infections when taken as a supplement (Wikipedia 2006a).

Fructooligosaccharides also is used in pet foods and animal feed. Recently, the Association of American Feed Control Officials (AAFCO) adopted an official definition for fructooligosaccharides (Watt Feed E-News 2006).

The use of fructooligosaccharides is very popular in Japan where it is used as a sweetening agent, flavor enhancer, bulking agent, and humectant[2] (Scdiet.org 2001). It is added to food products like cookies, cakes, breads, candies, dairy products, and some beverages as a low-calorie sucrose-replacement. It is also is added to some Japanese health foods to promote the growth of beneficial bacteria in the gastrointestinal tract.

**Approved Legal Uses of the Substance:**
The petitioner submitted a "Generally Recognized as Safe" (GRAS) notice (GRN 000044) to FDA in 2000 stating that it had self-affirmed fructooligosaccharides as GRAS for use as a bulking agent (FDA 2000). A manufacturer may self-affirm that a compound is GRAS by performing all necessary research, including review by qualified experts (FDA 2004). Note, the manufacturer does not need to obtain approval from FDA or notify FDA of the results of its investigation, as long as qualified experts agrees that the substance is safe (Ziker 2002). However, the manufacturer may choose to notify FDA of the results of its investigation under the voluntary GRAS notification program.[3] In the case of fructooligosaccharides, FDA reviewed the information provided in GRN 000044 and indicated that it has no questions regarding GTC Nutrition's conclusion that fructooligosaccharides is GRAS under the intended conditions of use (FDA 2000). FDA stated, however, that it has not made its own determination regarding the GRAS status of the subject use of fructooligosaccharides.

In addition, according to the petitioner, fructooligosaccharides was self-affirmed as GRAS for use in yogurt in 1994 and for medical foods and poultry in 1990. According to the petitioner, fructooligosaccharides also was approved as a dietary supplement in 1994. However, the petition does not state who approved the compound as a dietary supplement. No references or supporting information were provided in the petition to support these statements, and none could be located in the published literature or on the Internet.

[1] A medical food is a food that is formulated to be consumed or administered under the supervision of a physician and that is intended for the specific dietary management of a disease or condition for which distinctive nutritional requirements have been established by medical evaluation.
[2] A humectant is a substance added to food to maintain moisture.
[3] The GRAS notification program is a voluntary procedure operating under a proposed rule published by FDA on April 17, 1997 (62 FR 18936).

**Action of the Substance:**
Short-chain fructooligosaccharides is a non-digestible carbohydrate and is used for its prebiotic effects (i.e., food substances which promote the growth of certain generally beneficial bacteria in the human digestive tract) (Wikipedia 2006a). Because it is not digested in the upper intestine, short-chain fructooligosaccharides serves as a nutritional source for beneficial bacteria that naturally populate the colon and increases their ability to benefit overall gastrointestinal system health, especially proper digestion (Wikipedia 2006a). In addition, short-chain fructooligosaccharides is thought to increase the production of volatile fatty acids, increase bifidobacteria and other beneficial microorganisms in the intestine, decrease intestinal pH, decrease constipation, ameliorate antibiotic-associated diarrhea, and reduce serum triglycerides and cholesterol (Wellnessweb.com 2006). The inclusion of fructooligosaccharides in medical foods (i.e., liquid food fed to patients by tube) may benefit patients by normalizing bowel function, maintaining large intestine integrity, restoring colonization resistance, altering the route of nitrogen excretion, and improving calcium absorption (Garleb et al. 2002). Studies in mice indicate that fructooligosaccharides may provide some protection against colon cancer by stimulating certain immune functions (Bornet et al. 2002)

## Status

**International:**
As noted previously, the use of fructooligosaccharides is very popular in Japan (Scdiet.org 2001). In 1993, Japan created the "foods for specified health uses (FOSHU)" program, which includes a wide variety of foods (e.g., cookies, dairy products, some beverages) that have been recognized by health regulatory officials as having sufficient scientific evidence to support health claims (Farnworth 1997). Fructooligosaccharides is currently on this list.

The petitioner provided summary information documenting the regulatory status of fructooligosaccharides in 18 countries for use as a food ingredient, acceptance as a fiber (e.g., ANZFA 2001), and supporting claims of its bifidogenic properties (i.e., promoting growth of beneficial bacteria).

Fructooligosaccharides is not specifically listed for the petitioned use (i.e., an ingredient in food and feed products to provide a selective energy source in the guts of humans and animals) or other uses in the following international organic standards:

- Canadian General Standards Board
- CODEX Alimentarius Commission
- European Economic Community (EEC) Council Regulation 2092/91
- International Federation of Organic Agriculture Movements
- Japan Agricultural Standard for Organic Production

## Evaluation Questions for Substances to be used in Organic Handling

**Evaluation Question #1: Is the petitioned substance formulated or manufactured by a chemical process? (From 7 U.S.C. § 6502 (21).)**

Although fructooligosaccharides occurs in nature, commercial formulations of short-chain fructooligosaccharides are manufactured. In the manufacturing process, a mixture of sucrose is fermented under heated conditions using an enzyme derived from the fungus *Aspergillus japonicus*. The sucrose is changed by the enzyme to GF2, GF3, and GF4 (shown in Figure 1). Processing inputs listed in the petition are sucrose, water, enzyme, hydrochloric acid or sodium hydroxide (for pH control), and active carbon.

**Evaluation Question #2: Is the petitioned substance formulated or manufactured by a process that chemically changes the substance extracted from naturally occurring plant, animal, or mineral sources? (From 7 U.S.C. § 6502 (21).)**

Commercial formulations of short-chain fructooligosaccharides are not obtained from a naturally occurring source. The manufacturing process converts sucrose to short-chain fructooligosaccharides.

**Evaluation Question #3: Is the petitioned substance created by naturally occurring biological processes? (From 7 U.S.C. § 6502 (21).)**

Although short-chain fructooligosaccharides is produced with a fungal enzyme β-fructofuranosidase on inulin (IOM 2001), commercial quantities are produced by a controlled process and combination of ingredients (sucrose, water, enzyme, hydrochloric acid or sodium hydroxide) that does not occur in nature.

**Evaluation Question #4: Is there a natural source of the petitioned substance? (From 7 CFR § 205.600 (b) (1).)**

Fructooligosaccharides occurs naturally in fruits and vegetables. Examples of produce that contain fructooligosaccharides include bananas, onions, chicory root, garlic, asparagus, barley, wheat, and tomatoes (Wikipedia 2006a). The Jerusalem artichoke has one of the highest concentrations of fructooligosaccharides (Wikipedia 2006a). Although fructooligosaccharides is produced naturally, there is no evidence that natural sources produce fructooligosaccharides in quantities sufficient for commercial uses.

**Evaluation Question #5: Is there an organic agricultural product that could be substituted for the petitioned substance? (From 7 CFR § 205.600 (b) (1).)**

No other organic agricultural products were identified that could be substituted for the petitioned substance.

**Evaluation Question #6: Are there adverse effects on the environment from the petitioned substance's manufacture, use, or disposal? (From 7 CFR § 205.600 (b) (2).)**

There is no information available from EPA or FDA to suggest that environmental contamination results from the manufacture, use, misuse, or disposal of short-chain fructooligosaccharides. According to the petitioner, it does not persist in the environment because it is water soluble and consists of biodegradable glucose and fructose units.

**Evaluation Question #7: Does the petitioned substance have an adverse effect on human health as defined by applicable Federal regulations? (From 7 CFR § 205.600 (b) (3).)**

There are no known harmful effects on human health after exposure to short-chain fructooligosaccharides. According to Joint FAO/WHO Expert Committee on Food Additives (JECFA 2005), abdominal complaints were reported after a single dose of ≥20 g in adults, while diet supplementation with fructooligosaccharides was tolerated in school-age children at a single dose of 3–9 g. Other studies that examined similar effects when ingesting fructooligosaccharide include one in Japan, one in the United States, and one in France (ECSCF 1997).

The Japanese study examined 85 healthy volunteers. The maximum dose of fructooligosaccharides that did not cause diarrhea was 0.3 g/kg for men and 0.4 g/kg for women. The dose that caused diarrhea in 50 percent of the subjects was 0.78 g/kg for men and 0.84 g/kg for women (ECSCF 1997).

In the U.S. study, volunteers were fed a constant dose of fructooligosaccharides (5 g three times a day with meals) or a control diet of sucrose. Volunteers fed fructooligosaccharides had a significant increase in flatulence, bloating, and abdominal discomfort; however, at this daily dose, effects were considered mild

and no subjects experienced diarrhea (ECSCF 1997). According to another publication that summarized this same feeding study (FNB 2005), the following responses were observed: a gaseous response when consuming 5 or 15 g/d; increased flatulence when consuming > 30 g/d, increased bloating when consuming > 40 g/d, and cramps and diarrhea when consuming 50 g/d; and increased flatulence and bloating when consuming 10 g/d of fructooligosaccharides.

In the French study, 6 females and 8 males were given candies containing either fructooligosaccharides or sucrose on a regular or occasional basis. Systemic responses and laxative thresholds were similar regardless of whether fructooligosaccharides was administered occasionally or regularly. When administered occasionally, 13 subjects experienced diarrhea, one with severe abdominal pain. When administered on a regular basis, nine subjects experienced diarrhea, one with flatulence and four not wanting to ingest any more candies. For flatulence, the dose where the symptom was significantly greater in those administered fructooligosaccharides was 30 g; for borborygmi (i.e., stomach growling), bloating, and abdominal cramping, the dose was 40 g. The mean threshold and laxative dose (i.e., where 50 percent of the subjects experienced diarrhea) was 50-60g (ECSCF 1997).

In an animal study by Clevenger et al. (1988), no adverse effects were observed in rats fed neosugar (trade name for sFOS) at dose levels up to 50,000 ppm for 104 weeks. Survival, growth, blood cells, blood chemistry, or organ weights were not affected by treatment. Although slight noncancerous changes in the lymph nodes and adrenal glands and also an increase in the occurrence of pituitary tumors were reported, they were not considered to be the result of treatment with neosugar. Clevenger and colleagues reached this conclusion because the severity of symptoms was not affected by the dose of neosugar and their level of occurrence was within the normal background range for the test animals.

**Evaluation Question #8: Is the nutritional quality of the food maintained when the petitioned substance is used? (From 7 CFR § 205.600 (b) (3).)**

An increase in carbohydrates occurs when short-chain fructooligosaccharides is added to food or animal feed. This increase is thought to provide beneficial health effects, including increases in the production of volatile fatty acids, increases in bifidobacteria and other beneficial microorganisms in the intestine, decreases in intestinal pH, decreased constipation, amelioration of antibiotic-associated diarrhea, and reduction of serum triglycerides and cholesterol (Wellnessweb.com 2006).

**Evaluation Question #9: Is the petitioned substance to be used primarily as a preservative? (From 7 CFR § 205.600 (b) (4).)**

Short-chain fructooligosaccharides is being petitioned for use as an ingredient in food and feed products to provide a selective energy source in the guts of humans and animals. It is not being petitioned for use as a preservative.

**Evaluation Question #10: Is the petitioned substance to be used primarily to recreate or improve flavors, colors, textures, or nutritive values lost in processing (except when required by law, e.g., vitamin D in milk)? (From 7 CFR § 205.600 (b) (4).)**

Short-chain fructooligosaccharides is being petitioned for use as an ingredient in food and feed products to provide a selective energy source in the guts of humans and animals. It is not being petitioned for use to recreate or improve flavors, colors, textures, or nutritive values lost in processing. According to the manufacturers of sFOS, the substance actually improves the taste and texture of foods when the product is added. Manufacturers of Actilight® (a trade name for sFOS) claim their product gives yogurt a fuller, smoother, and creamier feeling (Foodprocessing-technology.com 2005). Additionally, they claim Actilight® masks the aftertaste of intense sweeteners (Foodprocessing-technology.com 2005). Nutraflora® (another trade name for sFOS) also boasts that it improves the quality, taste, and texture of food, beverage, and supplement products (GTC Nutrition 2006).

**Evaluation Question #11: Is the petitioned substance generally recognized as safe (GRAS) when used according to FDA's good manufacturing practices? (From 7 CFR § 205.600 (b) (5).)**

As noted previously (see "Approved Legal Uses of the Substance"), the petitioner submitted a GRAS notice (GRN 000044) to FDA in 2000 stating that it had self-affirmed fructooligosaccharides as GRAS for use as a bulking agent (FDA 2000). In the case of fructooligosaccharides, FDA reviewed the information provided in the GRAS notice and indicated that the Administration has no questions regarding GTC Nutrition's conclusion that fructooligosaccharides is GRAS under the intended conditions of use (FDA 2000). FDA stated, however, that it has not made its own determination regarding the GRAS status of the subject use of fructooligosaccharides.

As also noted previously, according to the petitioner, fructooligosaccharides was self-affirmed as GRAS for use in yogurt in 1994 and for medical foods and poultry in 1990. However, no references or supporting information were provided in the petition to support this statement and none could be located in the published literature or on-line.

**Evaluation Question #12: Does the petitioned substance contain residues of heavy metals or other contaminants in excess of FDA tolerances? (From 7 CFR § 205.600 (b) (5).)**

Short-chain fructooligosaccharides does not contain residues of heavy metal or other contaminants in excess of FDA tolerances.

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