maltitol, maltitol syrup, maltitol solution, isomalt, lactitol, and mixtures of sugar alcohol substances, i.e., hydrogenated glucose syrup (HGS) and hydrogenated starch hydrolysate (HSH) products.

Xylitol is a monosaccharide polyhydric alcohol with a 5-carbon backbone. It occurs naturally in fruits (e.g., plums, strawberries, and raspberries) and vegetables (e.g., cauliflower and endive) (Refs. 82 and 83). Xylitol is made commercially by the hydrogenation of D-xylose.

Sorbitol is a monosaccharide polyhydric alcohol with a 6-carbon backbone. It is found naturally in many types of berries and fruits and in seaweeds and algae (Ref. 82). Sorbitol is made by hydrogenation of glucose.

Mannitol is also a 6-carbon, monosaccharide polyhydric alcohol. It occurs widely in nature in plants (e.g., pumpkins, mushrooms, onions, beets, celery, and olives), algae, and fungi. Like sorbitol, mannitol is made commercially by the hydrogenation of glucose.

Maltitol is a disaccharide alcohol (4–D-glucopyranosyl-D-sorbitol) with a 12-carbon backbone. It is produced commercially by hydrogenation of maltose.

Lactitol is also a disaccharide alcohol (β-D-galactopyranosyl D-sorbitol) with a 12-carbon backbone. It is produced by hydrogenation of lactose (Ref. 84).

HSH and HGS are mixtures of sugar alcohols manufactured by hydrogenation of corn starch or glucose syrups. The composition of the sugar alcohols in the final product will depend on the manufacturing process. Therefore, HSH and HGS products from different manufacturers may contain different proportions of the same sugar alcohols. One HSH product, under the trade name ''Lycasin,'' was first produced in Sweden by hydrogenation of potato starch. The Swedish product contained a mixture of sorbitol, maltitol, maltotrititol, and hydrogenated dextrines of various molecular weights. When the manufacturing process was moved to France in the 1970's, the production process was also changed (Ref. 85). The French product, ''Lycasin 80/55,'' was made from the hydrogenation of corn starch and contained 6 to 8 percent sorbitol, 50 to 55 percent hydrogenated disaccharides, 20 to 25 percent trisaccharides, and 10 to 20 percent hydrogenated polysaccharides (Ref. 75). Lycasin 80/55, or HSH 80/55, is less fermentable and produces less acid than the Swedish product (Ref. 85).

Isomalt, also known by the commercial name ''Palatinit,'' is an equimolar mixture of the disaccharide alcohols of ∝-D-glucopyranosyl-D-sorbitol and ∝-D-glucopyranosyl-D-mannitol. It is produced by treating sucrose with enzymes, followed by hydrogenation of the resulting mixture.

2. The Substances are Associated With a Disease for Which the U.S. Population is at Risk

Dental caries is recognized in *The Surgeon General's Report on Nutrition and Health* (Surgeon General's report) as a disease or health-related condition for which the United States population is at risk (Ref. 7). The overall prevalence of dental caries imposes a substantial burden on Americans. Of the 13 leading health problems in the United States, dental diseases rank second in direct costs (Ref. 7).

Based on this fact, FDA tentatively concludes that sugar alcohols meet the requirement in § 101.14(b)(1).

3. The Substances Are Food

Sugar alcohols are used as replacements for simple and complex sugars as sweeteners and bulking agents in foods (Ref. 1). Thus sugar alcohols are consumed for their taste and for their effect as a stabilizer and thickener (21 CFR 170.3(o)(28)). Therefore, FDA tentatively concludes that these substances satisfy the preliminary requirements of § 101.14(b)(3)(i).

4. The Substances Are Safe and Lawful

Several of the sugar alcohols that are the subject of this proceeding are currently listed in FDA's food additive and generally recognized as safe (GRAS) regulations, i.e., xylitol (21 CFR 172.395), mannitol (§ 180.25 (21 CFR 180.25)), and sorbitol (§ 184.1835 (21 CFR 184.1835)). Moreover, GRAS affirmation petitions have been submitted for each of the remaining substances, i.e., maltitol (GRASP 6G0319), maltitol syrups (HGS syrups) (GRASP 3G0286), isomalt (GRASP 6G0321), lactitol (GRASP 2G0391), HSH (GRASP 5G0304) and HSH syrups (GRASP 1G0375).

The agency notes that these GRAS affirmation petitions are under consideration and that any positive action resulting from this proposed rule should not be interpreted as an indication that the agency has affirmed those uses of the sugar alcohols as GRAS. Such determinations can only be made after the agency has completed its review of the GRAS petitions. A preliminary review of the GRAS affirmation petitions reveals that they contain significant evidence supporting the safety of these substances.

The agency also points out, however, that some concerns about the safety of sugar alcohols do exist. For example, in a filing notice for the affirmation of the GRAS status of lactitol (58 FR 47746, September 10, 1993), FDA stated that ''the agency's notice of filing of GRASP 2G0391 should not be interpreted either as a determination, preliminary or otherwise, that the issue of Leydig cell tumors has been resolved or that lactitol qualifies for GRAS affirmation.'' Also, by notice in the **Federal Register** of December 13, 1994 (59 FR 64207), the agency announced the filing of a food additive petition (FAP 4A4412) to amend the interim food additive status of mannitol to permit an alternate method of manufacture. In this notice, the agency pointed out concerns about data from studies on mannitol that demonstrate a significant incidence of benign thymomas, and an abnormal growth of thymus gland tissue, in female rats fed mannitol. In addition, the safety of sugar alcohols has been examined by the Federation of American Societies for Experimental Biology (FASEB) (Ref. 90), as well as internationally by the Joint Expert Committee on Food Additives (Ref. 91). The agency also notes that two of the sugar alcohols that are listed in FDA's food additive and GRAS regulations, i.e., mannitol (§ 180.25) and sorbitol (§ 184.1835), require a warning label regarding laxation if daily consumption of these sugar alcohols is expected to exceed 20 grams (g) per day for mannitol and 50 g per day for sorbitol. Nothing in this proposal alters these requirements.

Based on the totality of the evidence, the agency is not challenging, at this time, the petitioner's position that the use of sugar alcohols is safe and lawful. Although FDA tentatively concludes that the petitioner has satisfied the requirements of § 101.14(b)(3)(ii), the agency requests comments on its tentative conclusion.

III. Review of Scientific Evidence

A. Introduction

The development of dental caries is the result of an interaction between sugars (and other fermentable carbohydrates, such as refined flour) and oral bacteria in a suitable environment (Ref. 71). Microorganisms, and *Streptococcus mutans* (*S. mutans*) in particular, in dental plaque metabolize available dietary sugars, producing acid and sticky polysaccharides that adhere to the tooth as plaque. Acid produced from rapid and complete fermentation of sugars creates an acid environment within the