do not justify a different compliance date. Action is appropriate now because the current uniform compliance date is less than 1 year away. The agency has selected January 1, 1991, to ensure adequate time for implementation of any changes in food labeling that may be required by FDA final regulations published after January 1, 1988, and before January 1, 1990.

The agency encourages industry, however, to comply with new labeling regulations earlier than the required date wherever this is feasible. Thus, when industry members voluntarily change their labels, FDA believes that it is appropriate that they incorporate any new requirements that have been published as final regulations up to that time.

The new uniform effective date will apply only to final FDA food labeling regulations published after January 1, 1988, and before January 1, 1990. Those regulations will specifically identify January 1, 1991, as their compliance date. If any food labeling regulation involves special circumstances that justify a compliance date other than January 1, 1991, the agency will determine for that regulation an appropriate compliance date that will be specified when the regulation is published.

This notice is not intended to change existing requirements. Therefore, all final FDA food labeling regulations previously published in the **Federal Register** that announced January 1, 1989, as their compliance date will still go into effect on that date. Final regulations published in the **Federal Register** with compliance dates earlier than January 1, 1989 (e.g., July 1, 1987), are also unaffected by this notice.

The current uniform effective date of January 1, 1989, for new final regulations affecting the labeling of food products was announced in the **Federal Register** of September 25, 1986 (51 FR 34085). Foods initially introduced or initially delivered for introduction into interstate commerce on or after January 1, 1989, are still required to comply with any final FDA regulations that identify January 1, 1989, as their compliance date.

Dated: November 1, 1988.

John M. Taylor,

Associate Commissioner for Regulatory Affairs.

[FR Doc. 88-25664 Filed 11-4-88; 8:45 am]

BILLING CODE 4160-01-M

21 CFR Parts 182 and 184

[Docket Nos. 79N-0141 and 79N-0142]

GRAS Status of Corn Sugar, Corn Syrup, Invert Sugar, and Sucrose

AGENCY: Food and Drug Administration.

ACTION: Final rule.

SUMMARY: The Food and Drug Administration (FDA) is affirming that corn sugar, corn syrup, invert sugar, and sucrose are generally recognized as safe (GRAS) as direct human food ingredients. The safety of these ingredients has been evaluated under a comprehensive safety review conducted by the agency. Elsewhere in this issue of the **Federal Register**, FDA is proposing to affirm the GRAS status of the use of high fructose corn syrup as a direct human food ingredient.

DATES: Effective December 7, 1988. The Director of the Federal Register approves the incorporation by reference of certain publications at 21 CFR 184.1857 effective on December 7, 1988.

ADDRESS: Background information and references are on display under the docket number found in brackets in the heading of this final rule in the Dockets Management Branch (HFA-305), Food and Drug Administration, Rm. 4-62, 5600 Fishers Lane, Rockville, MD 20857.

FOR FURTHER INFORMATION CONTACT: John W. Gordon, Center for Food Safety and Applied Nutrition (HFF-334), Food and Drug Administration, 200 C Street SW., Washington, DC 20204, 202-426-5487.

SUPPLEMENTARY INFORMATION:

I. Introduction

A. Definitions

This document discusses the agency's evaluation of the safety of sucrose, corn sugar, corn syrup, and invert sugar. To clarify the agency's discussions of the GRAS status of these ingredients, the agency is defining and explaining pivotal terms in this safety review.

FDA will use the term "sugar" to refer to any free mono- and disaccharide present in food such as glucose, fructose, sucrose, maltose, or lactose. It will use the term "sugars" to describe collectively all forms of sugar present in food.

FDA will use the term "sweetener" to refer to any one or more food ingredients containing sucrose, invert sugar, corn sugar, corn syrup and solids, high fructose corn syrup, honey, and other edible syrups. The term "sweetener," as used in the document is not intended to include any other nutritive or nonnutritive sweetener that is added to food.

In discussing intakes of sugars, the agency will use several additional terms. The agency will use the term "added sugars" to describe all sugars that are added to a food, i.e., all sugars from sweeteners added to foods. The term "naturally occurring sugars" is used to refer to all sugars present naturally in a food. The term "total sugars" is used to refer to the total amount of sugars present in a food, that is, the sum of the added and naturally occurring sugars.

The term "sugar" has traditionally been used by consumers and by the agency (see 21 CFR 145.3(f), 146.3(f), and 170.3(n)(41)) as a synonym for the sweetener sucrose. In this document, however, the sweetener sucrose is identified as "sucrose." Because sucrose also occurs naturally, the term "added" is inserted where it is necessary to make a distinction between added and naturally occurring sucrose. The term "complex carbohydrate" is used in this document to describe any carbohydrates other than those defined as sugars or as specific oligo- or polysaccharides.

B. Regulatory History

In the **Federal Register** of November 30, 1982 (47 FR 53917 and 53923), FDA published proposals to affirm that (1) corn sugar, corn syrup, and invert sugar and (2) sucrose are GRAS for use as direct human food ingredients. FDA published these proposals in accordance with its announced review of the safety of GRAS and prior-sanctioned food ingredients.

In accordance with § 170.35 (21 CFR 170.35), copies of the scientific literature reviews and the reports of the Select Committee on GRAS Substances (the Select Committee) on corn sugar, corn syrup, and invert sugar and on sucrose have been made available for public review in the Dockets Management Branch (HFA-305), Food and Drug Administration, Rm. 4-62, 5600 Fishers Lane, Rockville, MD 20857. Copies of these documents have also been made available for public purchase from the National Technical Information Service, as announced in the proposals.

The agency's proposals to affirm the GRAS status of corn sugar, corn syrup, invert sugar, and sucrose were based on the safety evaluations of these ingredients by the Select Committee. In its 1976 report entitled "Evaluation of the Health Aspects of Sucrose as a Food Ingredient" (SCOGS-69), the Select Committee concluded (Ref. 1):

Reasonable evidence exists that sucrose is a contributor to the formation of dental caries

when used at the levels that are now current and in the manner now practiced.

Other than the contribution made to dental caries, there is no clear evidence in the available information on sucrose that demonstrates a hazard to the public when used at the levels that are now current and in the manner now prescribed. However, it is not possible to determine, without additional data, whether an increase in sugar consumption—that would result if there were a significant increase in the total of sucrose, corn sugar, corn syrup, and invert sugar added to foods—would constitute a dietary hazard.

In another report entitled "Evaluation of the Health Aspects of Corn Sugar (Dextrose), Corn Syrup, and Invert Sugar as Food Ingredients" (SCOGS-50), also issued in 1976, the Select Committee concluded (Ref. 2):

Evidence exists that simple sugars, including glucose and fructose [and, therefore, corn sugar (dextrose), corn syrup, including high-fructose corn syrup, and invert sugars] are cariogenic. However, in the quantities that these simple sugars are now consumed in processed foods, their contribution to formation of dental caries should be relatively small. If increased usage should occur, as seems likely, the contribution of these sugars to the occurrence of dental caries might become more important.

Other than the contribution made to dental caries, there is no evidence in the available information on corn sugar (dextrose), corn syrup, and invert sugar that demonstrates a hazard to the public when they are used at levels that are now current and in the manner now practiced. However, it is not possible to determine, without additional data, whether an increase in consumption—that would result if there were a significant increase in the total of corn sugar, corn syrup, invert sugar, and sucrose added to foods—would constitute a dietary hazard.

In its proposals on sucrose and on corn sugar, corn syrup, and invert sugar, FDA concurred with the Select Committee's conclusions and proposed to affirm the GRAS status of these ingredients. Based on the Select Committee's conclusion that the safety of possible expanded consumption of these ingredients could not be ascertained, the agency ordinarily would have proposed to establish specific limitations on the use of these ingredients in food. The agency tentatively decided against establishing such limitations, however, because they would be impractical to enforce and would not effectively prevent an expansion in total dietary sugars consumption from the voluntary selection by consumers of high sugar content foods. The proposals noted that the agency has no authority to regulate an individual's choice among available food products. Nonetheless, the agency stated that it would monitor average dietary consumption of these ingredients, and that it would undertake a new evaluation of the safety of the use of sweeteners if total dietary consumption would increase significantly.

In its proposals, the agency also announced that it had received a letter from the Center for Science in the Public Interest (CSPI) dated July 2, 1981, as well as a letter from the Sugar Association, dated July 13, 1981. CSPI alleged that current sweetener consumption presented a risk to the public health and suggested that an association exists between sucrose consumption and many serious health problems, including heart disease, diabetes, hypertension, nutrient deficiencies, and behavior disorders. Based on these concerns and on new scientific literature on these issues, CSPI requested that the Department of Health and Human Services (HHS) convene a special expert committee to evaluate the impact of sweeteners on health. The letter from the Sugar Association responded to these allegations. In the proposals, the agency invited comments on the issues raised in these letters.

Finally, the proposals requested information on lead and cadmium levels in corn sugar, corn syrup, invert sugar, and sucrose and also the submission of any evidence of prior sanctions for use of these ingredients.

FDA gave public notice that it was unaware of any prior-sanctioned food uses for these ingredients other than for the proposed conditions of use. Persons asserting additional uses in accordance with approvals granted by the U.S. Department of Agriculture (USDA) or FDA before September 6, 1958, were given notice to submit proof of those sanctions so that the safety of any prior-sanctioned uses could be determined. That notice also provided an opportunity to have prior-sanctioned uses of these ingredients recognized by issuance of an appropriate regulation under Part 181—Prior-Sanctioned Food Ingredients (21 CFR Part 181) or under Part 184 or 186 (21 CFR Part 184 or 186), as appropriate. FDA also gave notice that failure to submit proof of an applicable prior sanction in response to the proposals would constitute a waiver of the right to assert that sanction at any future time.

Two comments asserting prior sanctions were received in response to the proposals. Both comments claimed prior sanctions for the use of corn sugar, corn syrup, invert sugar, and sucrose in chewing gum and soft drinks. Each comment submitted published documents to support its claim. One of the comments contained Trade Correspondence No. 63 and No. 65 published by FDA in 1939 and 1940, respectively. The other comment contained excerpts from agency advisory opinion letters written before 1958.

On the basis of documentation submitted in the comments, the agency acknowledges that prior sanctions exist for the use of corn sugar, corn syrup, invert sugar, and sucrose in chewing gum and soft drinks. However, the agency has determined that issuance of prior-sanction regulations in 21 CFR Part 181 is not necessary because the conditions of use for these ingredients set forth in the GRAS affirmation regulations in this final rule include the use of these sweeteners in chewing gum and soft drinks under the conditions identified by these comments. Therefore, the agency is not issuing a prior-sanction regulation based upon these comments. In accordance with the proposals for corn sugar, corn syrup, and invert sugar and for sucrose, prior sanctions for conditions of use other than in chewing gum and soft drinks have been waived.

II. Updated Safety Review of Sweeteners

A. Introduction

CSPI and several of the comments on the agency's GRAS affirmation proposals on corn sugar, corn syrup, and invert sugar and on sucrose, requested an updated safety review of sweeteners. Because of the nature of the health-related issues raised by the comments and the length of time since the issuance of the Select Committee's reports on these sweeteners, the agency decided that such a review was appropriate. FDA decided to conduct one complete review for all sweeteners, and not several separate reviews for different individual sweeteners, because the sweeteners are used interchangeably in food, and these sweeteners are closely related and can be expected to have comparable health effects.

The Select Committee conducted separate safety reviews of corn sugar, corn syrup, and invert sugar and of sucrose. In its conclusions, however, the Select Committee also acknowledged that the safety of these individual sweeteners was related to total sweetener consumption. In addition, although the Select Committee did not specifically address the safety of high fructose corn syrup, it considered high fructose corn syrup consumption as an integral part of the overall safety assessment of sweeteners (Ref. 2).

The agency recognizes that a safety assessment of corn sugar, corn syrup, invert sugar, and sucrose cannot be separated from a safety assessment of high fructose corn syrup. Therefore, the agency's updated safety review of sweeteners has included high fructose corn syrup, even though the agency is instituting a separate proceeding on that substance.

In the **Federal Register** of February 8, 1983 (47 FR 5716), FDA issued a final rule on high fructose corn syrup that listed that substance as GRAS in 21 CFR Part 182. The agency stated that it would consider whether it could affirm the use of high fructose corn syrup as GRAS upon completion of its safety review of the GRAS status of the use of corn sugar, corn syrup, invert sugar, and sucrose. Elsewhere in this issue on the **Federal Register**, FDA is proposing to affirm that the use of high fructose corn syrup as a direct human food ingredient is GRAS.

B. Description of the Review

In November 1983, the agency established a Sugars Task Force (the Task Force), composed of scientists from FDA's Center for Food Safety and Applied Nutrition (CFSAN), to assess the safety of dietary sugars (excluding lactose) as currently consumed in the American diet. The Task Force initiated its review by undertaking a search of the published literature for safety studies on sucrose, corn sugar, corn syrup, and invert sugar or their component sugars. The Task Force compiled an initial literature update on health effects of sugars consumption from the computer data banks Medline, Toxline, Cancerline, and Biological Abstracts, as well as from other available sources. The Task Force contacted each person that submitted a comment on the proposal and requested that he/she submit a copy of the references supporting his/her comments for evaluation.

The agency also published notices in the **Federal Register** of June 6, 1984 (49 FR 23457), and December 5, 1984 (49 FR 47505), announcing an opportunity for public review and comment on the bibliographic compilation of scientific articles retrieved through its literature search. The notices also solicited copies of any relevant data, published or unpublished, not included in the agency's compilation. In addition, the notices explained that the final rules on the GRAS status of the use of corn sugar, corn syrup, invert sugar, and sucrose would be based on the data evaluated during the Selected Committee's 1976 reviews of the safety of these ingredients, the data submitted in the comments on the proposals published in the **Federal Register** of November 30, 1982 (47 FR 53917 and 53923), and the data and information generated in response to the notices announcing the sugars bibliography. These data, along with the Task Force's estimate of sweetener consumption by the U.S. population, formed the basis for the Task Force's updated safety evaluation of sugars. The Sugars Task Force report was published in the *Journal of Nutrition* (Ref. 3).

The agency has received more than 65 comments including a detailed letter from the Center for Science in the Public Interest (CSPI) and a citizen petition from Maura (Jinny) Zack concerning the Sugars Task Force report. The comments, CSPI's letter, and the citizen petition asked that the Sugars Task Force report be revoked, amended, or clarified to make it clear that sugars consumption may be a health hazard to certain specific segments of the population. The CSPI letter urged the agency to reissue the report with revised sugars intake estimates and to rewrite some of its conclusions regarding the role of sugars in certain disease states. The letter also asked that the revised report include advice for consumers who are interested in eating a nutritious diet that will minimize their risk of health problems.

The citizen petition requested that the Commissioner revoke the Sugars Task Force report and prohibit further advertisements concerning the safety of sugar. The petition also called for a retraction of the advertisements already done by the Sugar Association and urged the Commissioner to make public announcements that processed sugars may have adverse health effects on certain segments of the population. In addition, the petition requested that if, after further investigation by the agency, the alleged harmful effects of sugars are confirmed, labeling should be ordered for the food containing sugars stating: "This product contains processed (or refined) sugar which may be injurious to your health".

The agency has reviewed the comments, the letter from CSPI, and the citizen petition concerning the Sugars Task Force report. The agency finds that the vast majority of the comments restated the allegations made in the citizen petition but provided no data to support their claim.

The issues raised in the CSPI letter relative to the Sugars Task Force report have been addressed in a separate agency action. (See the letter of September 26, 1988, from the Acting Director of CFSAN to CSPI (Ref. 4).) In general, the agency found that CSPI did not provide any scientifically sound data to warrant the revision of the report or of any of the conclusions contained in the report. Similarly, the agency addressed the issues raised in the citizen petition in a separate action. (See the letter of March 4, 1988, from the Associate Commissioner for Regulatory Affairs to Maura (Jinny) Zack (Ref. 5).) The agency found that the petition failed to provide scientifically valid data to support the allegations made in the petition. Moreover, some of the actions requested by the petitioner were either inappropriate under agency regulations or not within the jurisdiction of FDA.

C. Exposure Estimates

As part of its review, the Task Force estimated current intakes of sugars in the United States.

In its reports on sucrose and on corn sugar, corn syrup, and invert sugar, the Select Committee used an estimate of sweetener consumption prepared from the 1970 National Academy of Sciences/National Research Council (NAS/NRC) comprehensive survey of industry on the use of GRAS food ingredients (Ref. 6). Because no recent update of this survey was available and there was a need for an estimate that more accurately reflected the true consumption, the Task Force developed a method to estimate sugars (and thus sweetener) consumption. Under this method, the Task Force integrated food consumption data from the U.S. Department of Agriculture (USDA) Nationwide Food Consumption Survey of 1977–1978 with information on sugars content of food (Ref. 3). The information on the sugars content was compiled in 1984 from reported analytical data, direct laboratory analysis of foods, information obtained from manufacturer or product labels, calculation using recipes developed by USDA for estimating nutrient content of survey foods, and commercial product formula information. From these data, the Task Force estimated current average and the 90th percentile daily intakes of total sugars, adjusted total sugars, and individual sugars (e.g. fructose and sucrose) for the total population and 14 sex/age subgroups of the U.S. population. Adjusted total sugars represent total sugars excluding lactose. Lactose was excluded because it is not a subject of this GRAS review. The Task Force also estimated the relative contributions of added sugars (sugars from sweeteners) and naturally occurring sugars to total sugars intake. The 14 sex/age subgroups used by the Task Force are those used by NAS in its

estimates of the U.S. Recommended Dietary Allowances (Ref. 8).

The Task Force's method for estimating sweetener consumption was different from the method used by the Select Committee. Consequently, the estimates of sweetener consumption by the Task Force and by the Select Committee could not be directly compared. To compare sweetener consumption in 1976 and in 1985, the Task Force relied on a third set of data. The Task Force compared trends in sweetener usage (including a projected usage) based on USDA data on sweetener disappearance (USDA disappearance data) (Ref. 7). Disappearance data for sweeteners represent estimates of domestic shipments (deliveries) by refiners and importers of sweeteners to primary buyers such as food industries, trades, wholesalers, and retailers (Ref. 3). The data represent approximate estimates of the total amount (dry weight) of sweeteners available for consumption by the U.S. population and not the amount of sweeteners actually consumed.

These data tend to exaggerate average consumption levels and thus do not provide realistic estimates of actual sweetener consumption. A more accurate estimate of sweetener consumption, based on these data, would require adjustments to correct for loss and waste that can occur (1) during shipment and handling of the product; (2) during storage at wholesale, retail, and household levels from spillage and damage by insects and pests; (3) during commercial processing and home preparation of food; (4) during consumption at the table (plate waste) or other types of waste in households and food service institutions; and (5) in other miscellaneous usages of sweeteners (Ref. 3).

Nevertheless, because these disappearance data are collected regularly in a consistent and orderly manner, these data provide an appropriate basis to assess trends in sweetener usage. The Task Force used the USDA's disappearance data to determine whether the Select Committee's conclusions on the safety of corn sugar, corn syrup, invert sugar, and sucrose, which were predicated on a stable level of total sweeteners consumption, were still valid for 1985 levels of sweetener consumption.

D. Task Force's Review of Health Effects

During the course of gathering information, the Task Force evaluated approximately 1,500 articles relating to possible effects of dietary sugars on dental caries, glucose tolerance, diabetes mellitus, blood lipids, cardiovascular disease, behavior, obesity, malabsorption syndromes, food allergies, nephrocalcinosis, gallstones, nutrient deficiencies, and carcinogenicity.

The Task Force summarized the critical studies on each of these matters. In reviewing individual studies, the Task Force considered both the experimental design of the study and the observed effects. The Task Force also considered the allegations by CSPI relative to sugars consumption and adverse health effects, and whether the updated data established that adverse health effects were associated with the consumption of sugars. It then evaluated the significance of any adverse effects for the U.S. population or population subgroups at current levels of sugars consumption.

Based on its review, the Task Force developed a report on the health effects of sugars consumption entitled "Evaluation of Health Aspects of Sugars Contained in Carbohydrate Sweeteners" (Ref. 3). The report sets forth, for each matter the Task Force considered, summaries of the relevant studies, a discussion of the significant findings from the studies, and conclusions regarding these findings. The report also includes a final conclusion on the safety of current sugars consumption. A copy of the Task Force report has been placed on file in the Dockets Management Branch (address above). It is also available as the November 1986 supplement to the *Journal of Nutrition* (Ref. 3).

The Task Force concluded from its review of sugars that:

(1) Evidence exists that sugars, as they are consumed in the average American diet, contribute to the development of dental caries.

(2) Other than the contribution to dental caries, there is no conclusive evidence in the available information on sugars that demonstrates a hazard to the general public when sugars are consumed at the levels that are now current and in the manner now practiced (Ref. 3).

E. The Select Committee's Conclusions Compared to the Task Force's Conclusions

In their safety reviews, both the Select Committee and the Task Force recognized the unique toxicological position of sugars and sweeteners as food components and ingredients. Both groups recognized that sugars and sweeteners have low acute toxicity and are macronutrients that have a long history of consumption as major sources of calories in the United States (Refs. 1, 2, and 3). Both groups also recognized that the monosaccharide glucose has a central role in human metabolism (Refs. 2 and 3).

The Select Committee's conclusions on the safety of corn sugar, corn syrup, invert sugar, and sucrose were based on the level of consumption of these ingredients in 1976. To determine the continuing validity of these conclusions, as discussed above, the Task Force assessed the trend in sweeteners availability since the Select Committee issued its reports. These data show that, over this period, total sweetener availability has remained relatively stale (Ref. 3). Accordingly, FDA concludes that the Select Committee's safety conclusions are applicable to the current consumption of these sweeteners, and that the Task Force's findings and conclusions regarding the safety of these ingredients supplement the Select Committee's conclusions.

On the issue of dental caries, both the Task Force report (Ref. 3) and the Select Committee reports (Refs. 1 and 2) concluded that the current level of consumption of sweeteners, and of the sugars they contain, contributes to the incidence of dental caries in the general population, but that this consumption is not the only factor contributing to the incidence of dental caries.

The Task Force also found that dental caries incidence in the United States has declined significantly since the Select Committee issued its report in spite of the fact that sugars consumption has remained unchanged over that period. The Task Force attributed this decline, in part, to preventative dental methods (Ref. 3).

Both the Select Committee and the Task Force have concluded that there is no conclusive evidence that sugars consumption at present levels poses a health hazard to the general public, other than a contribution to dental caries.

III. Comments on the Proposals

A. Introduction

In response to its proposals, the agency received 16 comments from organizations or individuals regarding the proposed GRAS affirmation of corn sugar, corn syrup, invert sugar, and sucrose. The agency received nine comments from food manufacturers and trade organizations, two comments from professional societies, and five comments from individuals. As noted above, the agency had also received, before the publication of the proposals, two letters addressing health effects of

sweetener consumption. One letter was from CSPI, and the other was from the Sugar Association. FDA combined the letter from the Sugar Association with subsequent letters from that association on the proposal and treated these letters as one comment. Multiple submissions from a single company on the proposal were also combined and considered as a single comment.

Thirteen comments addressed health issues associated with sugars consumption. Six comments addressed the labeling of sugars content of food. Four comments urged a possible educational campaign on sugars and health. Two comments, as mentioned previously, addressed prior sanctions for corn sugar, corn syrup, invert sugar, and sucrose. Three comments discussed lead and cadmium levels in these ingredients. Two comments requested specific changes in the agency's proposed GRAS affirmation regulations for corn sugar, corn syrup, and invert sugar.

B. Comments Raising Health Related Issues

The comments that addressed health issues associated with sugars consumption focused on the allegations made by CSPI. Five comments, including that from CSPI, claimed that consumption of sugars causes one or more adverse health effects. Eight comments, including that from the Sugar Assocation, generally denied that there is an association between sugars consumption and adverse health effects. Underlying the agency's review of the comments is the view that, given the long history of safe use of sugars in food, and the fact that the statute recognizes that such a history provides a basis for GRAS status (21 U.S.C. 321(s)), the burden of establishing the existence of an adverse health effect of consuming sugars lies with the person asserting that this adverse effect exists. In the absence of such a showing, no change in the GRAS status of the use of the ingredient under review is warranted.

1. Dental Caries

a. Three comments asserted that sucrose consumption is cariogenic, i.e., associated with the incidence of dental caries. Another comment argued that all fermentable sugars are cariogenic, whether they are added to food or occur naturally.

The agency has reviewed these comments and agrees that sugars consumption is a contributing factor in the incidence of dental caries. The agency finds that current data show that sugars that are fermentable by cariogenic bacteria and that are present in normal diets do contribute to the formation of plaque and dental caries.

These findings are consistent with those of the Select Committee, which found that the consumption of sweeteners contributes to the formation of dental caries in the general population.

b. Six comments questioned the role of sugars consumption in the formation of dental caries. One comment cited data (Refs. 9, 10, and 11) showing that there is no correlation between consumption of highly sugared foods and dental caries incidence. Two other comments asserted that the rate of caries formation depends upon a number of variables other than consumption of sugars. Other comments cited epidemiological evidence (Refs. 12 and 13) that showed that there has been a downward trend in caries formation during the past decade, while sugar consumption has remained stale over the same period.

The agency reviewed these comments and agrees that caries formation depends on a number of variables, and that sugars consumption is not the sole causative factor in dental caries. However, the agency does not agree that sugars consumption is not related to dental caries formation.

The Task Force found that the scientific literature and clinical trials do not establish a clear quantitative relationship between sugars consumption and dental caries incidence. The cariogenicity of dietary carbohydrates depends on the duration of food contact with the teeth and on the presence or absence of other food substances that can modify the cariogenic potential of sugars. Thus, there is no apparent simple relationship between the sugars content of food and cariogenic potential (Ref. 3).

The Task Force report confirmed the Select Committee's finding that the etiology of dental caries is multifactorial, with dietary factors being only one of the three major groups of factors that are involved in the development of carious lesions (Refs. 1 and 2). These factors include oral microbial flora (e.g., cariogenic bacteria and dental plaque) and host factors (e.g., resistance to dental decay and hardness of tooth surface), as well as dietary factors such as the residence time of fermentable carbohydrate and plaque acidity (Ref. 3). However, the finding that the etiology of dental caries is multifactorial is not inconsistent with the finding that a relationship exists between sugars consumption and dental caries formation because sugars represent a major source of fermentable carbohydrates in the diet.

c. Having considered the comments and the Task Force report, the agency finds that there is no basis for any more concern about the association between sugars consumption and the incidence of dental caries than that expressed in the Select Committee report. This finding is based on two factors:

(1) The Task Force report shows that total exposure to sweetners has not changed since the Select Committee report.

(2) The Task Force report shows that caries incidence in the United States has declined in the past decade. The data reviewed in the Task Force report suggest that further developments in caries prevention should augment this decline in the future.

Therefore, despite evidence that consumption of sucrose, corn sugar, corn syrup, and invert sugar is associated with dental caries, the agency does not believe it appropriate to modify the GRAS status of these ingredients.

2. Obesity

Two comments claimed that overconsumption of sucrose causes obesity but provided no data to support the assertion. Six comments disagreed with the contention that obesity is related to sugars consumption. Several comments cited data (Refs. 14, 15, and 16) to refute an association between sugars consumption and obesity. Several other comments asserted that obesity can result from overconsumption of any caloric source, and that the most important factor in obesity is the balance between calorie intake and energy expenditure.

The agency has reviewed the comments and the studies cited in the comments.

In one study, Walker studied black and white teenagers in South Africa and determined that sugars consumption by teenagers in the upper percentile for body weight was comparable to sugars intake in the lower percentile (Ref. 16). The agency finds that such studies tend to argue against a specific role for sugars consumption in obesity.

During the course of its review, the Task Force found that dietary manipulations leading to increased caloric intake have a potential for causing increased body weight. The Task Force also found, however, that the available data support the view that sugars do not have a unique role in the etiology of obesity. This finding of the Task Force is in agreement with the finding of the Select Committee, which noted that excessive consumption of sucrose may contribute to obesity as a nonspecific source of calories.

Thus, the agency concludes that the available data indicate that excess sugars consumption may contribute to obesity as a nonspecific source of calories but not because of any special property of sugars.

3. Glucose Tolerance

The agency received several comments related to disease conditions that are characterized by abnormal responses to a glucose tolerance test.

This induction of a permanent disease state as a result of changes in glucose tolerance brought about by sugars consumption would be of concern because, if found, such changes would implicate dietary sugars intake in the etiology of diabetes or hypoglycemia. (Hypoglycemia is a spectrum of disorders resulting in a decline of blood sugar either after fasting or after the ingestion of a meal.) (Ref. 3).

The Select Committee was of the opinion that there was not sufficient evidence to demonstrate that the consumption of sucrose, corn sugar, corn syrup, or invert sugar caused a deterioration of glucose tolerance in humans (Refs. 1 and 2). The Task Force also found no persuasive scientific evidence that supports the contention that current use levels of sugars or sweeteners directly contribute to the development of abnormal glucose tolerance in the general U.S. population (Ref. 3).

4. Hypoglycemia

One comment asserted that there is an association between hypoglycemia and high sugars consumption, and three comments claimed that there is not. Neither group of comments cited any data to support its position.

One comment claims that the incidence of hypoglycemia is increasing but provided no data to support its assertion. Other comments claimed that hypoglycemia is a rare disorder, and that its incidence has been exaggerated. Several comments claimed that the incidence of hypoglycemia is unknown.

The agency has reviewed these comments as well as the reports of the Task Force and the Select Committee and agrees that there is no evidence that suggests that hypoglycemia is other than a rare disorder. The agency can also find no evidence that the incidence of hypoglycemia is increasing.

In its review, the Task Force found a number of reports on human behavior related to "reactive" or postprandial hypoglycemia (decreased blood glucose after eating) (Ref. 3). A review of these reports including one by Harper and Gans (Ref. 17), reveals that there is a lack of scientific experimentation and interpretable data upon which to draw any conclusions about the relationship between sugars consumption and hypoglycemia.

Based on the available safety information, the agency concludes that there is insufficient data to demonstrate an association between sugars consumption and hypoglycemia in the general population.

5. Diabetes

Five comments asserted that there is no relationship between sugars consumption and diabetes. These comments cited other factors in the etiology of diabetes such as genetics, immune factors, and obesity. Several comments cited obesity as a major determinant in the emergency of adult onset diabetes.

Several comments asserted that control of diabetes requires restriction of total calorie intake, and that little scientific basis exists for singling out sugars for restriction in the diet of diabetics (Ref. 18).

One comment suggested that consumption of fructose by adult onset diabetics should be carefully controlled. In support of this suggestion, the comment cited data showing an increase in plasma insulin levels in rats fed fructose (Ref. 19), as well as data showing a decrease in insulin sensitivity in rats fed fructose (Ref. 20). The comment also cited data showing a significant reduction in both insulin binding to isolated monocytes and insulin sensitivity in humans fed 1,000 kilocalories of fructose per day for 1 week (Ref. 21).

Based on the findings of the Task Force, the agency agrees that factors other than sugars consumption (such as genetics and obesity) are important in the etiology of diabetes. The Task Force report reinforced the Select Committee's finding that consumption of sugars is not a causative factor in diabetes and is related to the onset of the disease only as a nonspecific source of calories. Although consumption of a diet with a very high level of sugars may produce adverse effects on glucose tolerance and insulin metabolism, the current level of sugars consumption has not been shown to be an independent risk factor for the development of impaired glucose tolerance (Ref. 3). The agency also agrees that control of diabetes requires careful monitoring of the entire diet and not just the monitoring of the sugars content of the diet.

The Task Force evaluated the data cited by the comment relating to plasma insulin levels and insulin sensitivity after consumption of fructose but did not find that the data supported a limitation of fructose in the diet of diabetics. The Task Force considered the data showing an increase in plasma insulin levels in rats fed fructose (Ref. 19). It found that because of the high level of fructose fed (66 percent of calories), the data did not provide a basis on which to estimate threshold levels of fructose consumption for adverse effects on blood glucose, insulin secretion, and tissue insulin sensitivity. Moreover, the Task Force concluded that, because of the flaws in the design of this study and of the excessive amounts of fructose fed to the animals, the data could not be used to determine the effects of fructose consumption under normal conditions.

With regard to the second study (Ref. 20), the Task Force found that it could not determine the significance of the study's findings because the study only lasted 7 days, and the data did not provide a basis on which to determine whether the observed effects represented normal adaptive mechanisms that are reversible or were effects associated with irreversible pathologic processes.

The Task Force reviewed studies investigating the effects of sugars (including fructose) consumption on blood glucose and insulin level in human diabetics (Ref. 21). However, the Task Force found that these studies did not show a consistent effect from consumption of sugars (or from consumption of a particular sugar). The Task Force noted that these studies emphasize the importance of assessing the glycemic or insulinogenic effects of diets and meal plans as opposed to single dietary components.

The agency concludes that neither the comments nor the Task Force report demonstrated that sugars consumption is associated with the etiology of diabetes in any way other than as a source of calories that can contribute to obesity, which is associated with adult onset diabetes.

6. Hyperlipidemia

Two comments claimed, based on data that they cited (Refs. 22, 23, and 24), that high sucrose consumption produced elevated blood lipid levels (hyperlipidemia) in the general population. One comment also cited data to show that sucrose consumption had a greater effect in elevating blood lipid levels than did consumption of other simple or complex carbohydrates (Refs. 22, 23, and 24).

One comment questioned the significance of the data cited to link sucrose consumption with hyperlipidemia (Refs. 25 and 26).

One comment asserted that the normal consumption of sucrose had little or no effect on serum triglyceride levels, but the comment provided no data to support this assertion. Another comment questioned the uniqueness of sucrose of fructose in causing hyperlipidemia in humans. This comment discounted the rat model data showing effects of fructose consumption because rats metabolize fructose differently than humans.

The Task Force found that studies in animals demonstrated that the effect of high carbohydrate or high sugars diets (65 to 75 percent of caloric intake) on blood lipids depends on a number of factors, including species, sex, strain, duration of experiment, dietary levels of noncarbohydrate components, physical activity, and meal patterns (Ref. 3). These findings support the Select Committee's finding that the ability of sucrose or fructose to modify serum lipid patterns depends on the animal's strain, sex, age, and species and on the adaptation response of the animal to prolonged exposure to sugars (Ref. 1).

The agency acknowledges that, in some of the animal studies, sucrose and fructose appear to be associated with the elevation of blood lipids. However, the agency finds that it cannot make a definitive conclusion about the significance of this apparent association because of the number of variables that have an impact on the results. Moreover, because of differences in metabolism between experimental animals and humans, it is difficult to extrapolate from animal experiments to humans.

The Task Force evaluated the possible role of dietary carbohydrates in the regulation of blood lipids and lipoprotein levels in humans. It found that dietary manipulations can cause changes in blood lipid levels and in lipoprotein patterns. The Task Force found that both high fat and high carbohydrate diets have been reported to increase serum cholesterol or triglyceride levels. However, the Task Force also reports that these studies were inconsistent. In some studies, high sucrose or high fructose intake did not lead to any changes in serum cholesterol, triglyceride, or lipoprotein patterns, while, in others, all of these parameters were affected by sugars consumption. According to the Task Force, these discrepancies may be the results of differences in experimental protocols, including the composition of the noncarbohydrate components of the diet of the subjects and the duration of the study; in physical activity of the study subjects; in subjects' genetic variability; or in changes in the subjects' body weight during the course of the study. All of these factors have been shown to influence blood lipid levels (Ref. 3). Thus, because of the myriad of factors that influence blood lipid levels and because of inconsistency in the results from different experiments, the agency concludes that the available data are not adequate to demonstrate that a causal relationship exists between levels of sugars consumption and blood lipid levels in the normal population.

7. Carbohydrate Sensitivity

a. Two comments asserted that a subpopulation exists whose serum lipid levels and glucose tolerance parameters are more affected by sugars consumption than are those of the general population. The comments cited studies (Ref. 3) on the effects of diet on glucose tolerance and blood lipid levels in individuals classified as "carbohydrate sensitive."

One comment cited data to support the contention that this carbohydrate-sensitive subpopulation (as defined in the studies) may constitute 9 to 17 percent of the U.S. population (Refs. 27 and 28). Although no comments questioned the existence of this subpopulation, one comment claimed that the size of this population (as defined by the studies cited above) has been exaggerated.

One comment cited studies showing that a small segment of the population is carbohydrate-sensitive, a condition that is characterized by greater serum insulin and glucose response to sucrose load than that occurs in normal individuals (Ref. 29). Based on these studies, the comment suggested that sugars consumption might present an increased risk of diabetes for carbohydrate-sensitive individuals.

Several comments claimed that the consumption of high levels of fructose and sucrose (but not lower levels) caused abnormal serum lipid levels in carbohydrate-sensitive individuals. One comment cited data to support this claim (Refs. 30 and 31).

Two comments suggested a possible association between hyperlipidemia and normal sucrose consumption in carbohydrate-sensitive individuals. The comments claimed that data showing hyperlipidemia in carbohydrate-sensitive individuals after high sucrose consumption are evidence of this association (Ref. 30), and that these individuals are at greater risk than the general population at developing heart disease. However, several other comments claimed that carbohydrate sensitivity has not been shown to be a significant factor in the etiology of coronary heart disease.

The agency has reviewed these comments and the reports of the Task Force and the Select Committee. The agency finds that the significance of "carbohydrate sensitivity" is difficult to assess because various authors use different definitions of "carbohydrate sensitivity" and do not establish any relationship between the "carbohydrate sensitivity" observed in their study and a well-defined disease condition. For example, carbohydrate-sensitive individuals, as defined in the initial studies cited by the comments (Refs. 22 and 27), are individuals without overt disease who have the combination of elevated serum triglyceride levels (above 150–200 milligrams per deciliters) and an exaggerated insulin response (2.5 to 4 times normal) to oral sucrose loads. But the study provided no data to link these individuals with subsequent onset of diabetes.

One study (Ref. 22) cited by a comment associates "carbohydrate sensitivity" with type IV hyperlipoproteinemia. However, the study provides no data to substantiate the connection. This comment also cited data from this study (Ref. 22) to suggest that "carbohydrate sensitive" individuals are at increased risk in developing diabetes. However, the study provided no connection between "carbohydrate sensitivity" with the subsequent development of diabetes. Furthermore while prediabetics may exhibit hyperinsulinemic responses to carbohydrate meals, the subsequent development of diabetes in these individuals has not been linked to the ingestion of carbohydrate but rather to obesity and other factors (Ref. 3).

In its review, the Task Force was unable to confirm the frequency of occurrence of carbohydrate sensitivity in the U.S. population (alleged to be 9 to 17 percent) or the significance of the occurrence of carbohydrate sensitivity to the development of a disease condition. The frequency of occurrence figures (9 and 17 percent) cited by the comment were based on the results of two studies (Refs. 27 and 28, respectively) that investigated the blood lipid patterns of free-living populations without overt disease and identified subgroups within these populations that had blood lipid patterns that fell into one of five types of hyperlipoproteinemia (as defined by the authors of the studies). The populations studied were relatively small (1,118 and 1,301—Refs. 27 and 28, respectively), and the studies provided no data to demonstrate that these populations

were representative of the U.S. population as a whole. Furthermore, the blood lipid parameters used to define type IV hyperlipoproteinemia, which the comment identified as "carbohydrate sensitivity," differed between the two studies and also differed from the parameters used in Ref. 22, which was also cited by the comment. Finally, one of the studies (Ref. 27) acknowledged that the relationship between type IV hyperlipoproteinemia as defined in that study and premature coronary atherosclerosis is not well defined.

The Task Force found that carbohydrate sensitive individuals have a genetic predisposition to exaggerated insulin responses and elevated blood lipids with sucrose loading. However, the studies of high sucrose diets included several confounding variables, one of which was use of a gorging pattern of sucrose ingestion (Ref. 3). This pattern appeared to be necessary to elicit the response to sucrose. Furthermore, the Task Force found no evidence to show that prolonged high dietary sugars consumption will result in the development of diabetes mellitus in carbohydrate-sensitive individuals.

The Task Force questioned the relevance of data showing abnormal serum lipid levels in carbohydrate-sensitive individuals after consuming high levels of sucrose and fructose to the evaluation of health effects of normal sugars consumption in healthy individuals. The studies with sucrose had the same major problems as the studies on insulin response, including the gorging pattern of ingestion (Ref. 29).

In contrast, the study with fructose employed a conventional meal pattern. In this study (Ref. 31), plasma triglycerides increased significantly in carbohydrate-sensitive subjects but not in healthy controls after consumption of 7.5 and 15 percent dietary fructose. However, under these conditions, plasma cholesterol and LDL-cholesterol increased in both groups. The Task Force concluded that before the significance of this study could be fully evaluated relative to atherogenic risk, additional studies are needed to compare the observed effects of fructose with those occurring with other dietary sugars. The Task Force said that these studies should be carefully controlling for other dietary variables and for factors such as body mass index.

b. One comment questioned the applicability to humans of the animal model used in some studies to demonstrate carbohydrate sensitivity. The comment also questioned the relevance of data from the experimental animals fed high levels of sucrose to normal human consumption of sugars.

The agency agrees with this comment. Some of the animal data cited by the comment suggest the possibility that consumption of sugars at high dietary levels may result in an elevation of serum cholesterol and low-density lipoprotein and decreased insulin sensitivity. However, the Task Force found that clinical studies involving human subjects show no definitive relationship between sugars consumption and these effects (Ref. 3). Extrapolation of results from animal studies to humans is complicated by the differences that exist in sugar metabolism between some of the animals tested and humans, the lack of a dose-response relationship, and the presence of other factors that influence glycemic responses. Clinical studies that were conducted with normal humans and that were designed to evaluate the effect of current levels of sugars consumption on serum parameters (i.e., cholesterol, low-density lipoproteins, and insulin sensitivity) did not show any effect (Ref. 3).

c. The agency finds that, although there is evidence that a subset of the U.S. population experiences an elevation in serum lipids in response to a sucrose load, the data do not establish the size of this subset. Furthermore, based on the Task Force report, the agency finds that the available data do not demonstrate that sugars (including fructose), at current levels of consumption, had any different effects than other carbohydrates in inducing abnormal insulin and lipid levels in carbohydrate-sensitive individuals. Sugars have not been shown to present an increased risk of diabetes or coronary heart disease in this population.

8. Hypertension

Two comments asserted that high sucrose diets are linked to hypertension. One comment cited studies in humans, spider monkeys, and rats to support this assertion (Refs. 32, 33, and 34).

Four comments asserted that the link between sucrose consumption (either alone or in combination with salt) and hypertension is speculative. Several comments cited other data that showed no association between sucrose consumption and hypertension (Refs. 35 and 36).

The agency does not agree that sugars (including sucrose) consumption is linked to hypertension. In Sprague-Dawley rats, very high levels of sucrose in the diet can cause a slight rise in the systolic blood pressure. This rise in blood pressure is more pronounced when high levels of sodium chloride are also included in the diet. The interactive effects of other potentially important dietary factors, such as calcium, potassium, chloride, or fatty acids intake, have not been systematically examined.

Spontaneously hypertensive rats developed higher blood pressures with consumption of sucrose. The blood pressure increases from dietary sucrose and sodium in these rats were additive. However, in Wistar rats, blood pressure was not affected by ingestion of high levels of sucrose, although it was affected by ingestion of high levels of sodium chloride. These findings support the likelihood that the effect of sucrose on blood pressure is species and strain specific, and that in normal rats, the effect is dependent on high dietary levels of sodium chloride.

There is also some indication that at least some of the effects of sucrose on blood pressure are the result of increased body weight. Two studies in monkeys reported increased blood pressure as a result of consumption of diets with very high sucrose or high sucrose plus sodium chloride contents. In both studies, the body weights also increased during the experimental period, supporting the possibility that the observed effect on blood pressure was related to the body weight increase and not specifically to sucrose.

No data are available concerning the possible influence of long-term high sucrose consumption on blood pressure in humans. In normal human subjects, some sugars seem to have an acute, and possibly transient, effect on natriuresis (excretion of abnormal amounts of sodium in the urine). There is, however, no correlation between the potency of sugars as antinatriuretic agents and sugars' effect on blood pressure.

Based on its review of all the existing data, the Task Force found no convincing evidence to support the contention that current dietary intakes of sugars contribute to the development of hypertension (Ref. 3). The Select Committee, in its report on sucrose, reviewed preliminary data from a human study concerning the relationship between high sucrose diets and elevated blood pressure. The Select Committee found the data inadequate to draw any substantive conclusions (Ref. 1). Based on these findings, the agency concludes that current data are inadequate to establish a causal relationship between sugars consumption and hypertension.

9. Cardiovascular Disease

a. One comment hypothesized that diabetes and atherosclerotic disease are linked by hyperinsulinism. The comment suggested that sucrose consumption may

affect atherosclerotic disease by raising blood insulin levels and cited data showing effects of sucrose consumption on blood insulin levels (Ref. 37).

The agency does not agree with the comment. The Task Force noted that the major risk factors for cardiovascular disease identified by epidemiological studies include sex, positive family history of hypercholesterolemia, elevated low-density lipoprotein fraction of lipoproteins, hypertension, obesity, diabetes, cigarette smoking, and physical inactivity. Among these, hyperlipidemia, hypertension, obesity, and diabetes have a potential link with dietary practice, including the levels of dietary cholesterol and fat and the ratio of polyunsaturated to saturated fats.

Although some animal data support the contention that dietary manipulations involving sugars may potentiate risk factors for cardiovascular disease such as hypertension, hypercholesterolemia, and insulin resistance, the Task Force found that these relationships are less clear in studies in human populations (Ref. 3). Changes in serum lipids in response to sugars ingestion were reported in short-term animal and clinical experiments (Ref. 3). However, the Task Force considered these changes to be of limited significance because the observed changes were transient and disappeared with prolonged exposure to high sugar diets. The mechanism for this apparent adaptation to changes in dietary composition is poorly understood.

In a 1-year study of pigs (Ref. 38), there were no indications of cardiovascular pathological processes as a result of high sucrose consumption. This finding is important because the pig is generally considered to be an excellent model for dietary requirements and metabolic processes in the human. The dietary levels of sugars in the pig study were substantially higher than the current level of sugars consumption by the general population.

b. Four comments asserted that there is no convincing epidemiological or clinical evidence of a relationship between sucrose consumption and coronary heart disease. Several comments claimed that the known risk factors in the development of heart diseases were unrelated to sugars consumption.

The agency agrees with these comments. The Task Force found that no epidemiological or clinical survey evidence that would establish a link between sugars intake and cardiovascular disease had been reported since the Select Committee review of the safety of sucrose (Ref. 1). Accordingly, the Task Force concluded that there is no credible evidence that dietary sugars are an independent risk factor for coronary artery disease in the general population (Ref. 3).

The Select Committee report did not establish that sugars consumption is a primary dietary factor in the etiology of cardiovascular disease. The Select Committee emphasized that the primary dietary factors involved in the etiology of the disease are the nature and amount of fat in the diet.

c. Based on its review and evaluation of the comments and the reports of the Select Committee and the Task Force, the agency concludes that current data do not support the contention that sugars are a primary or an independent risk factor for cardiovascular disease such that the reduction in current levels of sugars intake in the general population would reduce the risk of this disease.

10. Nutritional Deficiencies

a. One comment asserted that current levels of sucrose consumption may cause nutritional deficiencies and suggested limiting consumption of sweeteners in any form in which they are not combined with significant proportions of other foods of high nutritive value. The comment cited two studies in support of its arguments (Refs. 39 and 40). One study showed thiamine deficiencies in certain populations when diets high in "empty calories" are consumed, and the other study showed riboflavin deficiency in an urban teenage population that relies heavily on snack food.

The agency has considered this comment along with the references cited and the reports of the Task Force and the Select Committee. In its report, the Task Force determined that any serious and sustained disturbance of the dietary balance has the potential to cause nutritional deficiencies, but that sucrose and other sweeteners do not have a unique ability to cause such a disturbance (Ref. 3). The Select Committee found that sucrose intake in excessive amounts could have an effect on intake of other nutrients and could result in a nutrient imbalance (Ref. 1). The agency, however, cannot prevent consumers from adopting poor diets.

The Task Force concluded that the studies cited by the comments to show that sugars consumption caused deficiencies in certain vitamins can also be interpreted as demonstrating the failure of the test population (teenagers) to consume foods that are rich in riboflavin and thiamine (Ref. 3). The vitamin deficiency can be seen not as a result of sucrose consumption per se but as a result of diet selection. Supporting this view is the fact that the Task Force found no firm evidence that sugars interfere with the bioavailability of vitamins, minerals, or trace nutrients (Ref. 3). Thus, under ordinary conditions of use, there is no evidence that sugars cause vitamin deficiencies.

b. Five comments asserted that sugar consumption does not cause nutritional deficiencies. Three comments questioned the validity of the results of the studies cited above because of design deficiencies in those studies. Other comments stated that it is the absence of nutrients in the diet that causes nutritional deficiencies. One comment cited an article that it claimed contained data that suggested that sucrose consumption could have a positive effect on nutrient availability because sucrose can be used as a vehicle for vitamin enrichment (Ref. 41).

The agency evaluated the article cited in the latter comment. This article generally addressed sucrose as a vehicle for fortification but did not provide convincing evidence that sucrose actually enhanced the uptake of these nutrients. Therefore, this article does not provide an adequate basis for concluding that sucrose has a positive effect on nutrient availability.

The Select Committee in its report on sucrose found that overconsumption of sucrose could possibly result in dietary imbalances (Ref. 1). The Select Committee also found that it is possible that some individuals who consume excessive amounts of sucrose may exclude adequate amounts of other foods that furnish required nutrients. However, these individuals do not represent the normal population.

c. The agency concludes that any sustained disruption of dietary balance has the potential to cause nutrient deficiencies, but that sweeteners do not have a unique ability to cause dietary imbalances. This conclusion is in agreement with findings reported in the Select Committee reports. The agency further concludes that neither the comments nor the Task Force report demonstrated that there is a unique relationship between sugars consumption and nutritional deficiencies.

11. Behavior

One comment suggested possible behavioral effects from sugars consumption and suggested that the effects of sugars consumption on hypoglycemia, which may affect behavior, be investigated. This comment, however, did not provide any data to support the suggestion. Five

comments claimed that the available data do not demonstrate an association between sucrose consumption and hyperactive behavior (i.e., attention-deficit disorder) in either hyperkinetic or normal children.

The agency has reviewed the comments relative to sugars consumption and behavior. The agency notes that several scientific conferences on diet and behavior (Refs. 46 and 47) have reviewed the effects of foods on behavior since the Select Committee's reviews in 1976. General scientific concerns have centered on: (1) The effects of sugars consumption on neurotransmitter concentrations in the central nervous system and on behavior in animals; (2) the effects of sugars on human behavior (principally hyperactivity, i.e., attention-deficit syndromes in children); and (3) the influence of sugars consumption on appetite, hunger, and food consumption. Sucrose has been a central focus, although limited data exist for the other sugars.

A number of the reports on human behavior relate to "reactive" of postprandial hypoglycemia, which is marked by decreased blood glucose after eating and is associated with a characteristic group of clinical symptoms (sweating, palpitation, piloerection, trembling, and other stress symptoms) coincident with the low level of plasma glucose and subsiding as glucose levels rise. Reactive hypoglycemia has been reported, particularly in the psychological literature and the lay press, to be correlated with a wide range of behavioral and mood changes in adults, including difficulty in thinking, depression, irritability, and neurological disturbances.

The Task Force reported that there is a paucity of well-controlled scientific studies on this subject (Ref. 3). With respect to the well-controlled studies that do exist, the Task Force concluded that there is no substantial evidence that the consumption of sugars is responsible for adverse behavioral changes in children or in adults (Ref. 3).

Based on the data available to the Task Force, the agency concludes that:

(1) There is no conclusive experimental evidence that sugars consumption causes significant changes in the behavior of children or adults. While some authors have reported a correlation between sugars consumption and behavioral changes such as hyperactivity, restlessness, and distractibility in children, these studies were in many cases poorly controlled. Other investigations, working under more controlled conditions, have failed to demonstrate increased activity or have demonstrated instead drowsiness and decreased activity.

(2) The suggestion that reactive hypoglycemia is correlated with behavioral or mood changes likewise cannot be substantiated by available experimental evidence. The possibility cannot be ruled out that a relatively small group of individuals may react idiosyncratically to sugars consumption. However, there is no scientifically validated evidence demonstrating that current levels of sugars consumption adversely affect behavior.

12. Sucrose and Caffeine

One comment suggested that caffeine and sucrose act synergistically on behavior. Three comments, however, asserted that there are no data that demonstrate that sucrose and caffeine have such an effect on behavior.

The agency has reviewed these comments and notes the absence of data on this subject. The agency finds that there is no scientific basis for suggesting that sugars and caffeine consumption would have synergistic effect on behavior.

13. Brain Neurochemistry

One comment suggested that sucrose may affect behavior by altering neurotransmitter levels in the brain and cited data showing a link between high carbohydrate meals and increased brain serotonin levels (Refs. 42 and 43). Another comment asserted that there are no data that establish a connection between behavior and brain serotonin levels, and that this alleged connection is merely conjectural.

The agency has reviewed these comments. The Task Force determined that some evidence exists from animal studies that high levels of intake of carbohydrates (including sugars) may modify the transport of amino acid precursors of neurotransmitters into the brain and may alter neurotransmitter levels in the brain (Ref. 3). The Task Force also found that the ability of the changes in neurotransmitter levels to modify behavior, although speculated upon, has not been shown by controlled clinical or preclinical experiments (Ref. 3).

The Task Force concluded that the ability of dietary sugars intake to modify behavior through effects on central nervous system neurotransmitter metabolism has not been demonstrated (Ref. 3).

The agency finds that, considered together, the comments and the Task Force report do not provide any basis for substantive health concerns about sugars consumption and behavior that would call into question the GRAS status of the use of corn sugar, corn syrup, invert sugar, and sucrose.

14. Consumption

a. One comment made several assertions regarding the current level of sweetener consumption. The comment stated that the average American consumes 2 pounds of refined sweeteners a week, and that refined sweeteners constitute one-fifth of the American diet. It stated that a study showed that some 10-year-olds consumed up to 48 percent of their total calories as refined sweeteners (Ref. 35).

The agency disagrees with the conclusions that the comment drew from the data on current levels of sweetener consumption by the American population. Specifically, the agency does not agree that the average American consumes 2 pounds of sweeteners per week. This figure appears to be based on USDA disappearance data. It is an overestimate of intake and would be a misuse of these data. The USDA per capita disappearance data represent approximate estimates of the total amount of sweeteners available for consumption by the U.S. population. These data do not account for the losses and wastes of sweeteners that occur between the time the sweeteners are shipped from manufacturers and the time they are actually consumed. However, these data are useful for estimating trends of sugars consumption over the years.

The agency estimates, based on USDA Nationwide Food Consumption Survey data, that the average American consumes less than 1 pound of added sugars per week (Ref. 3). In evaluating the comment's assertion that one-fifth (20 percent) of the American diet consists of sweeteners, the agency noted that this level of calorie intake from sugars added to the diet approximates the 90th percentile intakes in the United States. The Task Force estimated (Ref. 3) that average consumers obtain only 11 percent of total calorie intake from added sugars.

The agency has reviewed the reference (Ref. 35) cited by the comment to support its assertion that some 10-year-olds consume up to 48 percent of calories as refined sweeteners. FDA could not confirm this figure from the reference because the reference reported the amount of calories from total sugars (including both naturally occurring sugars and sugars added to foods) and not the amount from added sweeteners only, as claimed by the comment.

The agency concludes that the comment did not provide valid evidence to support its claim that the current level of sugars consumption is higher than that estimated by the Task Force. Therefore, the agency finds that there is no basis for modifying the Task Force's estimate of sugars consumption in response to this comment.

b. Three comments addressed changes in sweetener consumption over time. One comment stated that consumption of refined sweeteners has risen 50 percent (from a level of 12 percent to a level of 18 percent of calories) since 1910. However, another comment asserted that a comparison of today's refined sweetener consumption with that of 1910 is without significance because of changes in lifestyles. Two comments presented USDA disappearance data on sweetener availability. One comment asserted that sweetener consumption increased from 1900 to 1920 and remained relatively constant from 1920 to 1980. This comment also argued that recent data showed a downward trend in sucrose consumption and an increase in corn sweeteners consumption (Ref. 44). The other comment asserted that total sweetener intake has been constant from 1970 through 1985.

The agency agrees that per capita disappearance of sweeteners shows a trend toward increased consumption of sweeteners since 1910, the overall increase being about 50 percent. However, the agency finds that there was a relatively steep increase between 1910 and 1930, but that during the period from 1930 to 1970, the availability of sweeteners showed only a small overall increase with considerable yearly fluctuations (Ref. 3). Most importantly, the data show that the availability of sweeteners remained fairly constant from 1970 through 1985 (Ref. 3), suggesting that total sweetener consumption has remained relatively constant since the review by the Select Committee.

The agency concludes that the comments have not presented new data that show a significant increase in sweetener consumption that would call into question the safety of the current use of sweeteners. Therefore, the agency finds that these comments do not provide any reason to modify the Task Froce conclusions on the trends in sweetener usage.

c. One comment asserted that American consumption of sweeteners is excessive and is associated with various health problems. The comment made several allegations and cited the data discussed above on current levels of sweetener consumption and the 50 percent rise in sweetener consumption since 1910 to support its assertions concerning overconsumption of sweetener (Ref. 8). Two comments responded to the allegation of overconsumption of sweeteners by showing (through the trend data on sweetener availability discussed above) that total sweetener consumption has remained relatively constant.

The agency finds that none of the comments provided data that were relevant to proving or disproving the alleged overconsumption of sweeteners by the U.S. population. The two sets of data addressed either some absolute measure of current consumption or trends in consumption. Neither set of data establishes that the current level of sweetener consumption by the U.S. population is associated with a health risk.

d. Based on these assessments, the agency concludes that, with the exception of effects of sweetener consumption on dental caries formation, current levels of sweetener consumption do not constitute "overconsumptions."

Therefore, the agency finds that the comments did not provide a basis to call into question the Select Committee's conclusions on the safety of corn sugar, corn syrup, invert sugar, and sucrose. As a result, FDA finds that these comments do not provide a basis for modifying the GRAS status of the use of these ingredients.

15. Conclusions Regarding GRAS Status

The agency proposed to affirm the GRAS status of corn sugar, corn syrup, and invert sugar and of sucrose based on the safety evaluations and conclusions of the Select Committee. The agency has considered all the comments on these proposals, including those that asserted possible adverse health effects from sweetener consumption. In considering these comments, the agency has assessed whether the information in the comments together with information in the Task Force report provide evidence that raises significant doubts as to the safety of sugars.

The agency finds that, in most cases, the comments raised issues that had been addressed by the Select Committee in its reports on corn sugar, corn syrup, and invert sugar and on sucrose, and that the comments did not provide evidence that would warrant a change in the Select Committee's conclusions. In a few cases the comments provided new data and raised issues that had not been addressed by the Select Committee in its reports. In its review of the safety of sugars consumption, however, the Task Force evaluated these new data and issues, as well as other data on the issues that were available in the published literature. The Task Force found that these data did not provide sufficient evidence of any health concerns from sugars consumption to bring into doubt the Select Committee's conclusions regarding the safety of corn sugar, corn syrup, invert sugar, and sucrose. The agency has reviewed these comments, the Select Committee's report, and the report of the Task Force and agrees with the Task Force for the reasons previously set out. Therefore, the agency is not modifying the GRAS affirmation regulations that it proposed for these ingredients.

C. Comments Requesting Agency Action to Increase Consumer Information on Sugars

1. Sugars Labeling

Five comments supported some form of "sugar" labeling of food. The comments differed in what sugars they wanted labeled. One comment specifically requested that "added sugars" be labeled. Other comments requested declaration of "total sugars" because labeling only "added sugars" would not give a complete picture of the sugars content of the food.

The comments also varied in their concept of sugars labeling. One comment requested mandatory labeling of sugars in food without specifying what the label would say. Other comments wanted a modification of nutrition labeling either to include "sugar" or to separate the carbohydrate portion of nutrition labeling into "simple sugars" and "complex carbohydrates." One comment requested voluntary sugars labeling.

One comment that was opposed to sugars labeling asserted that no reason exists to single out sugars for mandatory declaration, and that more practical methods exist for disseminating information about the sugars content of foods. The comment requested that FDA consider sugars labeling only in the context of a reevaluation of nutrition labeling and the total food label.

The agency acknowledges that the Select Committee recommended that FDA require improved labeling of the sugars content of food. The agency further agrees that to provide useful information to consumers, any labeling system should include both added and naturally occurring sugars. However, because quantitative labeling of sweeteners involves issues beyond the scope of this safety review and is not necessary for the GRAS affirmation of corn sugar, corn syrup, invert sugar, and

sucrose, the agency is not taking any action in response to these comments. Individuals who wish to request agency consideration of a specific modification of the ingredient labeling or nutrition labeling regulations to provide for sugars labeling may submit a citzen petition under 21 CFR Part 10.

2. Educational Campaign

Four comments supported an educational program related to sugars and health. One comment specifically requested that HHS mount an educational compaign on health effects of sugars consumption. Two comments supported an educational campaign to disseminate scientific facts about sucrose's role in the diet and to refute popular mythology about sucrose. One comment supported an educational effort to help consumers practice better eating habits.

The agency has reviewed these comments and notes that these comments present differing views about the appropriate focus and content of an educational campaign. One comment wanted the campaign to promote the view that sugar consumption causes adverse health effects. Two comments appeared to want an educational campaign to counteract the view expressed in the first comment. The fourth wanted an educational campagn on total dietary management, with sugars discussed within this broader context.

The agency finds that the last approach is the most appropriate based on the findings both in the Select Committee's reports on corn sugar, corn syrup, and invert sugar and on sucrose and in the Task Force's review of sugars. USDA and HHS recently published "Dietary Guidelines for Americans" (Ref. 45), which contains seven dietary guidelines for staying healthy. One of these guidelines, "Avoid too much sugar," discourages overconsumption of sugars. The agency concludes that the current affects in promoting the dietary guidelines provide an adequate educational campaign on the health effects of sugars consumption.

D. Lead and Cadmium Content of Sweeteners

In the proposals on corn sugar, corn syrup, and invert sugar and on sucrose, FDA announced the results of a survey that the agency conducted in 1974 on heavy metals in food. The analytical results showed that 6 of 71 samples of refined sugar tested contained high levels of cadmium and lead. Because the agency was unable to confirm the results of this survey in a resurvey in 1980, FDA requested the submission of data on cadmium and lead levels in refined and unrefined cane and beet sugars, as well as in corn sugar, corn syrup, and invert sugar. The agency requested that the sugar industry report the levels of heavy metals found at each stage of the manufacturing process.

FDA received three comments in response to this request. One comment noted that a draft paper by the two FDA scientists attributed the occasional high cadmium and lead values in the 1974 survey of sucrose samples to difficulties in the method used to ash the samples. The comment stated that when the agency employed a new dry ashing procedure, the previous results could not be duplicated. Although the comment promised to submit more information on cadmium and lead analysis, the agency has never received this information.

One comment claimed that information on lead and cadmium levels in corn syrups and sucrose during processing is not generally available. As an alternative, the comment suggested that producers be allowed to furnish data on the finished product.

The final comment cited a report in the *Journal of Agriculture and Food Chemistry* (24(1), 1976) by the USDA's Southern Regional Research Center, which listed lead and cadmium levels in raw and refined sucrose at less than 0.1 part per million for lead and 0.01 part per million for cadmium. The comment claimed that its own recent analyses of the lead and cadmium content in refined and unrefined sweetners have confirmed these results.

The agency has reviewed these comments along with other information generated by the scientific literature update on sucrose and corn sugars. The agency has also reviewed results of FDA's 1980 resurvey which showed the estimated lead and cadmium intake levels from sucrose to be less than 0.01 and 0.008 microgram per day, respectively. These levels are much lower than those that were reported in the previous survey.

The agency, after analyzing all the available data, finds that the first survey may have been in error because of the ashing techniques used to prepare the samples. More recent data in which revised sample preparation techniques were used demonstrate that the contribution of lead and cadmium from sugar consumption to the total dietary load for these two contaminants is minimal and represents less than 1.5 percent of total dietary consumption of lead and cadmium. The agency, therefore, concludes that the levels of lead and cadmium in sucrose do not represent a hazard to the public health, and that it is not necessary to set limits for these contaminants in these regulations. Therefore, the agency has not modified the GRAS affirmation regulation for corn sugar, corn syrup, invert sugar, and sucrose to incorporate specifications for lead and cadmium.

E. Comments Regarding Proposed Identity and Specifications

1. Identity and Specifications for Corn Sugar and Corn Syrup

Two comments were received that asked that the proposed GRAS affirmation regulations for corn sugar (§ 184.1857) be made compatible with 21 CFR 168.110 (dextrose anhydrous) and 21 CFR 168.111 (dextrose monohydrate) by modifying the regulation to include the monohydrate form of the sugar. The comments also asked that the proposed regulation for corn syrup (§ 184.1865) be modified to make it consistent with 21 CFR 168.120 (glucose sirup) and 21 CFR 168.121 (dried glucose sirup). One of the comments asked that the title of the corn sugar regulation be changed to "Dextrose." One comment requested that the liquid form of corn sugar be included in the corn sugar regulation.

The agency has reviewed these comments and finds that its safety review covered both the monohydrate and the anhydrous forms of corn sugar, and that it is appropriate for the GRAS affirmation regulation for corn sugar to be modified to include both of these forms of corn sugar. The agency has also reviewed the request that the GAS affirmation regulation for corn syrup (glucose sirup) be made compatible with the descriptions in §§ 168.120 and 168.121. The agency concurs that it is appropriate for the GRAS affirmation regulation for corn syrup to be compatible with the descriptions in §§ 168.20 and 168.21, including use of the synonym "glucose sirup." The agency has modified the final rule to incorporate these changes.

The agency has concluded that no change in the title of the regulation for corn sugar is warranted because corn sugar is the name of the ingredient whose safety was reviewed by the Select Committee and evaluated during the GRAS review. The name adequately describes the material covered by the regulation and does not lead to deception of consumers. The agency will, however, include "dextrose" in the regulation as a commonly used synonym for corn sugar. FDA has modified the final rule to incorporate this change.

The agency has also reviewed the comment requesting that the liquid form of corn sugar be included in the corn sugar regulation. The agency finds that

although liquid corn sugar does not meet the specifications for corn sugar, it does meet the identity and specifications of corn syrup and is covered under that regulation. Accordingly, the agency is not modifying its final rule to incorporate the requested change.

The agency also notes that although the specifications for corn sugar describe a crystalline material, the description of corn sugar in proposed § 184.1857(a) did not describe the material as crystalline. Therefore, to resolve this confusion and to provide consistency between the description of corn sugar in § 184.1857(a) and the specifications for corn sugar in § 184.1857(b), the agency has added a sentence to paragraph (a) specifying that the hydrolyzed corn starch is refined and crystallized.

In addition, the agency notes that the description of sucrose in proposed § 184.1854(a) does not explicitly cover the extraction, by pressing, of sugar cane juice from sugar cane or beet juice from sugar beets and also does not mention the evaporation of the extracted sugar cane juice or beet juice. Therefore, the agency has modified § 184.1854(a) to include "pressing" as a possible extraction procedure and "evaporated" as a step in the refinement of sucrose.

The agency is also aware that glucose syrup and dextrose may be prepared from starch sources other than corn starch. The agency has not included these sources in this regulation because this safety review covered only the product derived from corn. The agency will consider modifying the regulations for corn syrup and corn sugar if adequate information on the possible impurities and the method of manufacture of these food ingredients from starch sources other than corn starch is submitted to the agency for consideration. Interested persons may petition the agency to amend the GRAS regulations for corn syrup and corn sugar by submitting a GRAS affirmation petition in accordance with 21 CFR 170.35.

2. Identity and Manufacture of Invert Sugar

FDA received two comments that requested that hydrolysis with safe and suitable acids be included in the methods of preparing invert sugar, and that the description for invert sugar be modified to include sucrose as a constituent of this substance.

One of the comments also requested that the method of manufacture described in the regulation include the use of ion exchange resins.

The agency has reviewed the comments as well as data in its files on the manufacture of corn sweeteners. The agency notes that safe and suitable acids have been used traditionally to hydrolyze polysaccharides and to manufacture corn sugar and corn syrup. Therefore, the agency is of the opinion that there are no safety reasons why safe and suitable acids should not be used in the manufacture of invert sugar from sucrose. Accordingly, the agency has modified the regulation for invert sugar to include hydrolysis of sucrose with safe and suitable acids in the description of how this substance is manufactured.

However, in the case of ion exchange resins, the agency has no basis to evaluate the safety or suitability of their use in the manufacture of invert sugar. In the past, the agency has listed ion exchange resins as food additives in 21 CFR 173.25 and has required specific food additive approval for their use. Section 173.25 has no listing for use of an ion exchange resin in the manufacture of invert sugar. In addition, the comment provided no information on the identity of the ion exchange resins or on the safety or the suitability of such use. Therefore, the agency has not modified the regulation for invert sugar to inlcude the use of ion exchange resins.

The agency has also reviewed the requests that the description of invert sugar include the presence of sucrose. The agency has confirmed that its definition of invert sugar in 21 CFR 145.3(e) and 146.3(e) provides for the presence of unhydrolyzed sucrose in invert sugar.

FDA is of the opinion that the GRAS regulation for invert sugar should be compatible with the standard of identity for invert sugar in §§ 145.3(e) and 146.3(e). Therefore, the agency has modified § 184.1859(a) to provide for the presence of unhydrolyzed sucrose in the description of invert sugar.

IV. Procedural Issues

In the proposals, FDA stated that it would work with the Committee on Codex Specifications (now known as the Committee on Food Chemicals Codex) of the National Academy of Sciences to develop acceptable specifications for sucrose and invert sugar used as direct human food ingredients. The agency also stated that it would incorporate these specifications into the regulations when they are developed. The date, however, work on the specifications is still incomplete. Until the specifications are developed, sucrose and invert sugar for direct food use must comply with the description in §§ 184.1854 and 184.1859, respectively, and be of food-grade purity in accordance with 21 CFR 182.1(b)(3) and 170.30(h)(1).

The agency has carefully considered the potential environmental effects of this action and has concluded that the action will not have a significant impact on the human environment and that an environmental impact statement is not required. The agency's finding of no significant impact and the evidence supporting that finding, contained in an environmental assessment, may be seen in the Dockets Management Branch (address above) between 9 a.m. and 4 p.m., Monday through Friday. This action ws considered under FDA's final rule implementing the National Environmental PolicyAct (21 CFR Part 25).

In accordance with the Regulatory Flexibility Act, the agency previously considered the potential effects that this rule would have on small entities, including small businesses. In accordance with section 605(b) of the Regulatory Flexibility Act, the agency has determined that no significant impact on a substantial number of small entities would derive from this action. FDA has not received any new information or comments that would alter its previous determination.

In accordance with Executive Order 12291, FDA has previously analyzed the potential economic effects of this final rule. As announced in the proposal, the agency has determined that the rule is not a major rule as determined by the Order. The agency has not received any new information or comments that would alter its previous determination.

The agency's findings of no major economic impact and no significant impact on a substantial number of small entities, and the evidence supporting these findings, are contained in a threshold assessment which may be seen in the Docket Management Branch (address above).

V. References

The following references have been placed on display in the Dockets Management Branch, and may be seen by interested persons between 9 a.m. and 4 p.m., Monday through Friday.

1. "Evaluation of the Health Aspects of Sucrose as a Food Ingredient" (SCOGS–69), Select Committee on GRAS Substances, Life Sciences Research Office, Federation of American Societies for Experimental Biology, 1976.

2. "Evaluation of the Health Aspects of Corn Sugar (Dextrose), Corn Syrup, and Invert Sugar and Food Ingredients" (SCOGS–50), Select Committee on GRAS Substances, Life Sciences Research Office, Federation of

American Societies for Experimental Biology, 1976.

3. Glinsmann, W.H., H. Irausquin, and Y.K. Park, "Evaluation of Health Aspects of Sugars Contained in Carbohydrate Sweeteners," Report of Sugars Task Force, 1986, *Journal of Nutrition*, 116(115):51, 1986.

4. Letter from Acting Director of the Center for food Safety and Nutrition to the Center for Science in the Public Interest, September 26, 1988.

5. Letter from Associate Commissioner for Regulatory Affairs to Maura (Jinny) Zack, March 4, 1988.

6. "Subcommittee on Review of the GRAS List (Phase II). A Comprehensive Survey of Industry on the Use of Food Chemicals Generally Recognized as Safe (GRAS)," Committee on Food Protection, Division of Biology and Agriculture, National Research Council, 1972.

7. Barry R.D., "High fructose corn sirup and pure fructose: potential consumption and substitution for sugar by 1990." Presented to the American Medical Association Resource Conference on HFCS and Fructose, Chicago, IL, October 2, 1984.

8. "Recommended Dietary Allowances," 9th Ed., National Research Council, 1980.

9. Burt, B., and S. Eklund, "Sugar Consumption and Dental Caries: Some Epidemiological Patterns in the United States," *in* "American Dental Association Health Foundation, Foods, Nutrition and Dental Health," Chicago, Pathotox, p. 171, 1981.

10. Johnsen, D., "Social Factors and Diet Diaries of Caries-Free and High Caries 2 to 7 Year-Olds Presenting for Dental Care in West Virginia," 2, No. 4, 1980.

11. Walker, A.R.P., et al., "Dental Caries in South African Black and White High School Pupils in Relation to Sugar Intake and Snack Habits," *Community Dentistry and Oral Epidemiology*, 9:37–43, 1981.

12. Changes in "The Prevalence of Dental Caries in United States Children, 1961–1980," *Journal of Dental Research*, 61:1346, 1982.

13. "The First International Conference on the Declining Prevalence of Dental Caries," *Journal of Dental Research*, 61:1301, 1982.

14. van Itallie, T.B., and J. Hirsches, "Calories: Appraisal of Excess Calories as a Factor in the Causation of Disease," *American Journal of Clinical Nutrition*, 32:2648, 1979.

15. Richardson, J.F., "The Sugar Intake of Businessmen and Its Inverse Relationship with Relative Weight," *British Journal of Nutrition*, 27:449, 1972.

16. Walker, A.R.P., "Studies on Sugar Intake and Overweight in South African Black and White School Children," *South African Medical Journal*, 48:1650, 1974.

17. Harper, A.E., and D.A. Gans, "Claims of Antisocial Behavior from Consumption of Sugar: An Assessment," *Food Technology*, 40:142, 1986.

18. Nuttall, F.Q., and M.C. Gannon, "Sucrose and Disease," *Diabetes Care*, 4:305, 1981.

19. Sleder, J., et al., "Hyperinsulinemia in Fructose-Induced Hypertriglyceridemia in the Rat," *Metabolism*, 29:303, 1980.

20. Zavoroni, I., et al., "Effect of Fructose Feeding on Insulin Secretion and Insulin Action in the Rat," *Metabolism*, 29:970, 1980.

21. Beck-Nielsen, H., O. Pedersen, and H.O. Lindskov, "Impaired Cellular Insulin Binding and Insulin Sensitivity Induced by High-Fructose Feeding in Normal Subjects," *American Journal of Clinical Nutrition*, 33:273, 1980.

22. Reiser, S., et al., "Isocaloric Exchange of Dietary Starch and Sucrose in Humans. I. Effects on Levels of Fasting Blood Lipids," *American Journal of Clinical Nutrition*, 32:1659, 1979.

23. Macdonald, I., "The Effects of Dietary Carbohydrate on High Density Lipoprotein Levels in Serum," *Nutrition Reports International*, 17:663, 1978.

24. Hayford, J.T., et al., "Triglyceride Integrated Concentrations: Effects of Variation of Source and Amount of Dietary Carbohydrate," *American Journal of Clinical Nutrition*, 32:1670, 1979.

25. Grande, F., "Sugars in Cardiovascular Disease," *in* "Sugars in Nutrition," New York, Academy Press, pp. 401–437, 1974.

26. Walker, A.R.P., "Sugar Intake and Coronary Heart Disease," *Atherosclerosis*, 14:137, 1974.

27. Woods, P.D.S., et al., "Prevalence of Plasma Lipoprotein Abnormalities in a Free-Living Population of the Central Valley, California," *Circulation*, 45:114, 1972.

28. Brown, D.F., and K. Daudiss, "Hyperlipoproteinemia Prevalence in a Free-Living Population in Albany, New York," *Circulation*, 47:558, 1973.

29. Reiser, S., et al., "Serum Insulin and Glucose in Hyperinsulinemic Subjects Fed Three Different Levels of Sucrose," *American Journal of Clinical Nutrition*, 34:2348, 1981.

30. Reiser, S., et al., "Blood Lipids and Their Distribution in Lipoproteins in Hyperinsulinemic Subjects Fed Three Different Levels of Sucrose," *Journal of Nutrition*, 111:1045, 1981.

31. Hallfrisch, J., et al., "Blood Lipid Distribution of Hyperinsulinemic Men Consuming Three Levels of Fructose," *American Journal of Clinical Nutrition*, 37:740, 1983.

32. McIntyre, M.L., et al., "Blood Pressure Changes Caused by Supplementing the Diets of Young, Adult Volunteers with Different Amounts of Sucrose," *Federation Proceedings*, 34:911, 1975.

33. Hall, C.E., and O. Hall, "Comparative Effectiveness of Glucose and Sucrose in Enhancement of Hypersalimentation and Salt Hypertension," *Proceedings of the Society for Experimental Biology and Medicine*, 123:370–374, 1966.

34. Beebe, C.G., et al., "Blood Pressure of Rats as Affected by Diet and Concentration of NaCl in Drinking Water," *Proceedings of the Society for Experimental Biology and Medicine*, 151:395–399, 1976.

35. Frank G.C. G.S. Berenson, and L.S. Weber, "Dietary Studies and the Relationship of Diet to Cardiovascular Disease Risk Factor Variables in 10–Year Old Children—The Bogalusa Heart Study 1978," 31:328–340.

36. Palumbo, P.J., "Sucrose Sensitivity in Patients With Coronary Artery Disease," *American Journal of Clinical Nutrition*, 30:394–401, 1977.

37. Crapo, P.A., G. Reaven, and J. Olefsky, "Plasma Glucose and Insulin Responses to Orally Administered Simple and Complex Carbohydrates," *Diabetes*, 25:741, 1976.

38. Bruckdorfer, K.R., and J. Yudkin, "A Comparison of Dietary Starch and Dietary Sucrose in the Pig, "*Nutrition and Metabolism*, 19:225–232, 1975.

39. Lonsdale, D., and R.J. Shamberger, "Red Cell Transkeltolase as an Indicator of Nutritional Deficiency," *American Journal of Clinical Nutrition*, 33:205–211, 1980.

40. Lopez, R., J.V. Schwartz, and J.M. Cooperman, "Riboflavin Deficiency in an Adolescent Population in New York City," *American Journal of Clinical Nutrition*, 33:1283–1286, 1980.

41. "Fortification of Sugar with Vitamin A in Central American and Panama," Institute of Nutrition for Central Americas and Panama, Guatemala, 1974.

42. Wurtman, R.J., "Precursor Control of Transmitter Synthesis," in "Nutrition and the Brain," Vol. 5, New York, Raven Press, 1979.

43. Fernstrom, J.D., and R.J. Wurtman, "Nutrition and the Brain," *Scientific American*, 230:84, 1974.

44. "Sugar and Sweetener: Outlook & Situation," U.S. Department of Agriculture, December 1982.

45. "Nutrition and Your Health: Dietary Guidelines for Americans," 2d Ed., U.S. Department of Agriculture, U.S. Department of Health and Human Services, 1985.

46. Lieberman, H.R., and R.J. Wurtman, editors, "Research Strategies for Assessing the Behavioral Effects of Foods and Nutrients," Proceedings of a conference at Massachusetts Institute of Technology, Pergamon Press, Elmsford, 1982.

47. "Diet and Behavior: A Multidisciplinary Evaluation," sponsored by American Medical Association, International Life Sciences Institute and the Nutrition Foundation, Arlington, VA 1984, *Nutrition Reviews*, 44 Supplement: 1–254, 1986.

List of Subjects

21 CFR Part 182

Food ingredients, Food packaging, Spices flavorings.

21 CFR Part 184

Food ingredients, Incorporation by reference.

Therefore, under the Federal Food, Drug, and Cosmetic Act and under the authority delegated to the Commissioner of Food and Drugs, Parts 182 and 184 are amended as follows:

PART 182—SUBSTANCES GENERALLY RECOGNIZED AS SAFE

1. The authority citation for 21 CFR Part 182 continues to read as follows:

Authority: Secs. 201(s), 402, 409, 701, 52 Stat. 1046–1047 as amended, 1055–1056 as amended, 72 Stat. 1784–1788 as amended (21 U.S.C. 321(s), 342, 438, 371); 21 CFR 5.10, 5.61.

§ 182.1 [Amended]

2. Section 182.1 *Substances that are generally recognized as safe* is amended in paragraph (a) by removing the word "sugar," from the second sentence.

§ 182.90 [Amended]

3. Section 182.90 *Substances migrating to food from paper and paperboard products* is amended by removing "Corn sugar (sirup)," "Invert sugar," and "Sucrose" from the list of substances.

PART 184—DIRECT FOOD SUBSTANCES AFFIRMED AS GENERALLY RECOGNIZED AS SAFE

4. The authority citation for 21 CFR Part 184 continues to read as follows:

Authority: Secs. 201(s), 402, 409, 701, 52 Stat. 1046–1047 as amended, 1055–1056 as amended, 72 Stat. 1784–1788 as amended (21 U.S.C. 321(s), 342, 348, 371); 21 CFR 5.10, 5.61.

5. Section 184.1854 is added to Subpart B to read as follows:

§ 184.1854 Sucrose.

(a) Sucrose ($C_{12}H_{22}O_{11}$, CAS Reg. No. 57–50–11–1) sugar, cane sugar, or beet sugar is the chemical β-D-fructofuranosyl-α-D-glucopyranoside. Sucrose is obtained by crystallization from sugar cane or sugar beet juice that has been extracted by pressing or diffusion, then clarified and evaporated.

(b) FDA is developing food-grade specifications for sucrose in cooperation with the National Academy of Sciences. In the interim, this ingredient must be of a parity suitable for its intended use.

(c) In accordance with § 184.1(b)(1), the ingredient is used in food with no limitation other than current good manufacturing practice.

(d) Prior sanctions for this ingredient different from the uses established in this section do not exist or have been waived.

6. Section 184.1857 is added to Subpart B to read as follows:

§ 184.1857 Corn Sugar.

(a) Corn sugar ($C_6H_{12}O_6$, CAS Reg. No. 50–99–7), commonly called D-glucose or dextrose, is the chemical α-D-glucopyranose. It occurs as the anhydrous or the monohydrate form and is produced by the complete hydrolysis of corn starch with safe and suitable acids or enzymes, followed by refinement and crystallization from the resulting hydrolysate.

(b) The ingredient meets the specifications of the Food Chemicals Codex, 3d Ed. (1981), pp. 97–98 under the heading "Dextrose," which is incorporated by reference in accordance with 5 U.S.C. 552(a) and 1 CFR Part 1. Copies are available from the National Academy Press, 2101 Constitution Ave., NW., Washington, DC 20418, or available for inspection at the Office of the Federal Register, 1100 L St. NW., Washington, DC 20408.

(c) In accordance with § 184.1(b)(1), the ingredient is used in food with no limitation other than current good manufacturing practice.

(d) Prior sanctions for this ingredient different from the uses established in this section do not exist or have been waived.

7. Section 184.1859 is added to Subpart B to read as follows:

§ 184.1859 Invert sugar.

(a) Invert sugar (CAS Reg. No. 8013–17–0) is an aqueous solution of inverted or partly inverted, refined or partly refined sucrose, the solids of which contain not more 0.3 percent by weight of ash. The solution is colorless, odorless, and flavorless, except for sweetness. It is produced by the hydrolysis or partial hydrolysis of sucrose with safe and suitable acids or enzymes.

(b) FDA is developing food-grade specifications for invert sugar in cooperation with the National Academy of Sciences. In the interim, this ingredient must be of a purity suitable for its intended use.

(c) In accordance with § 184.1(b)(1), the ingredient is used in food with no limitation other than current good manufacturing practice.

(d) Prior sanctions for this ingredient different from the uses established in this section do not exist or have been waived.

8. Section 184.1865 is added to Subpart B to read as follows:

§ 184.1865 Corn Syrup.

(a) Corn syrup, commonly called "glucose sirup" or "glucose syrup," is obtained by partial hydrolysis of corn starch with safe and suitable acids or enzymes. It may also occur in the dehydrated form (dried glucose sirup). Depending on the degree of hydrolysis, corn syrup may contain, in addition to glucose, maltose and higher saccharides.

(b) The ingredient meets the specifications as defined and determined in § 168.120(b) or § 168.121(a) of this chapter, as appropriate. FDA, in cooperation with the National Academy of Sciences, is undertaking a study to determine if additional food-grade specifications for corn syrup are necessary.

(c) In accordance with § 184.1(b)(1), the ingredient is used in food with no limitation other than current good manufacturing practice.

(d) Prior sanctions for this ingredient different from the uses established in this section do not exist or have been waived.

Dated: October 31, 1988.

John M. Taylor,

Associate Commissioner for Regulatory Affairs.

[FR Doc. 88–25583 Filed 11–4–88; 8:45 am]

BILLING CODE 4160–01–M

DEPARTMENT OF HOUSING AND URBAN DEVELOPMENT

Office of the Assistant Secretary for Public and Indian Housing

24 CFR Parts 904, 905, 913, 960, and 966

[Docket No. R–88–1020; FR–1164]

Tenancy and Administrative Grievance Procedure for Public Housing; Notice Suspending Effective Date

AGENCY: Office of the Assistant Secretary for Public and Indian Housing, HUD.

ACTION: Notice suspending effective date for the Tenancy and Administrative Grievance Procedure for Public Housing.

SUMMARY: A final rule to amend lease and grievance procedures for the public housing program was published on August 30, 1988 (53 FR 33216), Docket No. R–88–1020; FR 1164. On October 14, 1988, HUD published a notice announcing that the final rule would become effective on November 7, 1988 (52 FR 40220, 40221).

Pursuant to a Temporary Restraining Order in National Tenants Organization, *et al.* v. Samuel R. Pierce (United States District Court for the District of Columbia, Civil Action No. 88–3134), HUD hereby withdraws the notice of effective date previously published, to maintain the status quo pending hearing on a motion for preliminary injunction by plaintiffs in this action.

The prior lease and grievance regulations (24 CFR Part 966) remain in effect until publication of further notice by HUD. Accordingly, the effective date as published on October 14, 1988, as it applies to the Tenancy and Administrative Grievance Procedure for Public Housing published August 30, 1988, is suspended.

DATE: Effective date of this Notice: November 2, 1988.

FOR FURTHER INFORMATION CONTACT: Grady J. Norris, Assistant General Counsel for Regulations, Department of Housing and Urban Development, Room 10276, 451 Seventh Street SW., Washington, DC 20410, telephone (202) 755–7055. (This is not a toll-free number.)

Date: November 3, 1988.

Grady J. Norris,

Assistant General Counsel for Regulations.

[FR Doc. 88-25767 Filed 11-4-88; 8:45 am]

BILLING CODE 4210-33-M

DEPARTMENT OF DEFENSE

Office of the Secretary

32 CFR Part 159

[DoD Directive 5200.1]

DoD Information Security Program

AGENCY: Department of Defense.

ACTION: Final rule.

SUMMARY: This Part updates established policies and procedures of the DoD Information Security Program and implements Executive Order 12356, "National Security Program" and Information Security Oversight Office Directive No. 1, "National Security Information." This Part also delegates authority, assigns responsibilities, and authorizes the development, publication, and maintenance of DoD 5200.1-R, "Information Security Program Regulation" and other issuances that pertain to the DoD Information Security Program. At the present time, 32 CFR Part 159 is a combination of DoD Directive 5200.1, June 7, 1982, and DoD 5200.1-R. This revision separates the two documents. DoD 5200.1-R will be submitted as a separate part (32 CFR Part 159a) at a later date.

EFFECTIVE DATE: June 7, 1982.

FOR FURTHER INFORMATION CONTACT: Mr. F. Cook, Office of the Deputy Under Secretary of Defense for Policy, Directorate for Security Plans and Programs, The Pentagon, Washington, DC 20301-2200.

SUPPLEMENTARY INFORMATION:

List of Subjects in 32 CFR Part 159

Classified information, Foreign relations.

Accordingly, 32 CFR Part 159 is revised as follows:

PART 159—DOD INFORMATION SECURITY PROGRAM

Sec.

Authority: E.O. 12356 and 5 U.S.C. 301.

§ 159.1 Purpose.

(a) This part updates policies and procedures of the DoD information Security Program, implements Executive Order 12356 and 32 CFR Part 2001, delegates authority, and assigns responsibilities.

(b) This part authorizes the development, publication, and maintenance of the following documents, consistent with DoD 5025.1-M.

(1) DoD 5200.1-R, "Information Security Program Regulation";

(2) DoD 5200.1-H, "Department of Defense Handbook for Writing Security Classification Guidance";

(3) DoD 5200.1-I, "Index of Security Classification Guides";

(4) DoD 5200.1-PH, "A Guide to Marking Classified Documents"; and

(5) Other DoD 5200.1-PH series issuances necessary to ensure or facilitate compliance with and implementation of DoD 5200.1-R and E.O. 12356 and 32 CFR Part 2001.

§ 159.2 Applicability and scope.

(a) This part applies to the Office of the Secretary of Defense, the Military Departments, the Organization of the Joint Chiefs of Staff, the Unified and Specified Commands, and the Defense Agencies (hereafter referred to as "DoD Components").

(b) This part covers all information that is owned, produced by or for, or is under the control of the Department of Defense that shall be protected from unauthorized disclosure in the interest of national security under Executive Order 12356 and ISOO Directive No. 1 and all such information received by the Department of Defense from other sources, including that received from or produced pursuant to or as a result of a joint arrangement with a foreign government or international organization.

§ 159.3 Policy.

It is the policy of the Department of Defense to assure that information that warrants protection against unauthorized disclosure is properly classified and safeguarded as well as to facilitate the flow of unclassified information about DoD operations to the public.

§ 159.4 Procedures.

To carry out this policy, there is established a DoD Information Security Program that shall be administered to ensure that:

(a) Information requiring protection in the interest of national security is properly classified and safeguarded.

(b) Overclassification and unnecessary classification are avoided.

(c) Information is classified as long as required by national security considerations.

(d) Unnecessary expense to the Department of Defense, industry, and the U.S. government, resulting from protection of information no longer requiring classification, is eliminated.

(e) Declassified information is made available to the public under 32 CFR Part 285.

(f) Classified inventories are reduced to the minimum necessary to meet operational requirements, thereby affording better protection to that which remains.

(g) DoD military and civilian personnel, who require access to classified information in the conduct of official business, are familiar with the requirements of DoD 5200.1-R and E.O. 12356 and 32 CFR Part 2001, and that they comply with those requirements.

§ 159.5 Responsibilities.

(a) The *Deputy Under Secretary of Defense (Policy)* shall:

(1) Direct and administer the DoD Information Security Program, establish policy, standards, criteria, and procedures to comply with E.O. 12356, except its section 3.4.

(2) Conduct an active oversight program to ensure effective implementation of DoD 5200.1-R, Executive Order 12356, and 32 CFR Part 2001, to include security education and training.

(3) Consider and take action on complaints and suggestions from persons within or outside the government regarding the DoD information Security Program.

(b) The *Assistant Secretary of Defense (Public Affairs)* shall direct and administer a DoD Mandatory Declassification Review Program under section 3.4., E.O. 12356, and establish policies and procedures for processing mandatory declassification review requests, including appeals, under section 3.4(d) of E.O. 12356 and section 2001.32(a)(2)(iii) of Information Security Oversight Office (ISOO) Directive No. 1 [1] that make maximum use of DoD Component resources and systems established to implement 32 CFR Part 285.

(c) The *Head of each DoD Component* shall:

(1) Designate a senior official who shall be responsible for the direction and administration of the Component's Information Security Program, to include

[1] Copies may be obtained, if needed, from the Director, Information Security Oversight, General Service Administration, Washington, DC 20405.