

immobilization of glucose isomerase enzyme preparations is safe. Therefore, FDA is amending the secondary direct food additive regulations to provide for the use of glutaraldehyde and DEAE-cellulose as set forth below.

In accordance with § 170.35(c)(2) (21 CFR 170.35(c)(2)), the petitions and the documents that FDA considered and relied upon in reaching its decision to approve the use of these secondary direct food additives are on public display and available for inspection at the dockets Management Branch (address above) between 9 a.m. and 4 p.m., Monday through Friday. The petitions and documents may also be inspected at the Bureau of Foods (address above) by appointment with the information contact person listed above.

FDA 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 therefore will not be prepared. The agency's findings of no significant impact and the evidence supporting this finding, contained in an environmental assessment (pursuant to 21 CFR 25.31, proposed December 11, 1979; 44 FR 71742) may be seen in the Dockets Management Branch (address above) between 9 a.m. and 4 p.m., Monday through Friday.

List of Subjects in 21 CFR Part 173

Food additives, Food processing aids.

Therefore, under the Federal Food, Drug, and Cosmetic Act (secs. 201(s), 409, 72 Stat. 1784-1788 as amended (21 U.S.C. 321(s), 348)) and under authority delegated to the Commissioner of Food and Drugs (21 CFR 5.10), Part 173 is amended by adding new § 173.357, to read as follows:

PART 173—SECONDARY DIRECT FOOD ADDITIVES PERMITTED IN FOOD FOR HUMAN CONSUMPTION

§ 173.357 Materials used as fixing agents in the immobilization of enzyme preparations.

Fixing agents may be safely used in the immobilization of enzyme preparations in accordance with the following conditions:

(a) The materials consist of one or more of the following:

(1) Substances generally recognized as safe in food.

(2) Substances identified in this subparagraph and subject to such limitations as are provided:

Substances	Limitations
Diethylaminoethyl-cellulose.	May be used as a fixing material in the immobilization of glucose isomerase enzyme preparations for use in the manufacture of high fructose corn syrup, in accordance with § 184.1372 of this chapter.
Glutaraldehyde.....	Do.

(b) The fixed enzyme preparation is washed to remove residues of the fixing materials.

Any person who will be adversely affected by the foregoing regulation may at any time on or before March 10, 1983 submit to the Dockets Management Branch (address above) written objections thereto and may make a written request for a public hearing on the stated objections. Each objection shall be separately numbered and each numbered objection shall specify with particularity the provision of the regulation to which objection is made. Each numbered objection on which a hearing is requested shall specifically so state; failure to request a hearing for any particular objection shall constitute a waiver of the right to a hearing on that objection. Each numbered objection for which a hearing is requested shall include a detailed description and analysis of the specific factual information intended to be presented in support of the objection in the event that a hearing is held; failure to include such a description and analysis for any particular objection shall constitute a waiver of the right to a hearing on the objection. Three copies of all documents found in brackets in the heading of this regulation. Received objections may be seen in the office above between 9 a.m. and 4 p.m., Monday through Friday.

Effective date: This regulation shall become effective February 8, 1983.

(Secs. 201(s), 409, 72 Stat. 1784-1788 as amended (21 U.S.C. 321(s), 348))

Dated: January 19, 1983.

William F. Randolph,
Acting Associate Commissioner for
Regulatory Affairs.

[FR Doc. 83-3214 Filed 2-7-83; 8:45 am]

BILLING CODE 4160-01-M

21 CFR Parts 182 and 184

[Docket Nos. 76G-0073, 76G-0445, 77G-0049, 77G-0099, 81G-0048, and 82G-0148]

Substances Generally Recognized as Safe; High Fructose Corn Syrup and Insoluble Glucose Isomerase Enzyme Preparations

AGENCY: Food and Drug Administration.

ACTION: Final rule.

SUMMARY: The Food and Drug Administration (FDA) is listing high fructose corn syrup as generally recognized as safe (GRAS) for use in food in Part 182 (21 CFR Part 182). In addition, the agency is affirming that certain insoluble glucose isomerase enzyme preparations are GRAS for use in the manufacture of high fructose corn syrup. Elsewhere in this issue of the Federal Register, the agency is also approving the secondary direct food additive use of diethylaminoethylcellulose (DEAE-cellulose) and glutaraldehyde as fixing agents in the immobilization of glucose isomerase enzyme preparations. FDA is taking these actions in response to GRAS petitions submitted by Standard Brands, Anheuser-Busch, Miles Laboratories, CPC International, Novo Laboratories, and GB Fermentation Industries.

DATES: Effective February 8, 1983. The Director of the Federal Register approves the incorporation by reference of certain publications in 21 CFR 184.1372 effective February 8, 1983.

FOR FURTHER INFORMATION CONTACT: Mary C. Custer, Bureau of Foods (HFF-335, Food and Drug Administration, 200 C St., SW., Washington, DC 20204, 202-426-9463.

SUPPLEMENTARY INFORMATION: Under the procedures described in § 170.35 (21 CFR 170.35), Standard Brands, Inc., 625 Madison Ave., New York, NY 10022; Anheuser-Busch, Inc., St. Louis, MO 63118; Miles Laboratories, Inc., Elkhart, IN 46514; CPC International, Inc., International Plaza, Englewood Cliffs, NJ 07632; Novo Laboratories, Inc., 59 Danbury Rd., Wilton, CT 06897; and GB Fermentation Industries, Inc., One North Broadway, Des Plaines, IL 60018, submitted GRAS petitions (GRASP) 4G0042 (Docket No. 82G-0148), 6G0080 (Docket No. 76G-0073), 7G0080 (Docket No. 76G-0445), 7G0084 (Docket No. 77G-0049), 7G0088 (Docket No. 77G-0099), and 1G0271 (Docket No. 81G-0048), respectively. Each of the petitions requested affirmation that a specific glucose isomerase enzyme preparation, derived from a specific microorganism and rendered insoluble (fixed) with specific materials, is GRAS for use in the production of high fructose corn syrup from corn syrup glucose. The microorganisms named in the petitions are *Streptomyces rubiginosus* (GRASP 4G0042), *Actinoplanes missouriensis* (GRASP 6G0080 and 1G0271), *Streptomyces olivaceus* (GRASP 7G0080), *Streptomyces*

multigeneration reproduction studies in the rat.

The petitions also include specifications with supporting analytical data that indicate that the enzyme preparations, produced and fixed as indicated above, meet the general requirements and specifications for enzyme preparations set forth in the Food Chemicals Codex, 3d Ed.

In response to the notice of filing of GRASP 4G0042, published in the Federal Register on August 6, 1974, the agency received a comment from a law firm stating that glucose isomerase enzyme, from whatever source derived, possesses the same basic physical and chemical properties and activity. The comment suggested that GRAS status should not be confined to the use of the enzyme prepared from the particular source named by the petitioner, but rather that the use of glucose isomerase enzyme, as such, in the manufacture of high fructose corn syrup should be affirmed as GRAS.

The agency does not agree with this comment. Although the agency acknowledges that, by definition, a glucose isomerase enzyme from any source will convert glucose to fructose, the agency concludes that this fact alone is inadequate to establish the safety of the use of the final enzyme preparation. As indicated by the data provided in these petitions, an assessment of the safety and suitability of a glucose isomerase-enzyme preparation must include consideration of the safety of the organism from which the enzyme preparation is derived, as well as consideration of the safety of the enzyme preparation itself, including such factors as the presence of additional cellular material and residual processing materials in the enzyme preparation and the level of enzyme preparation in the final food product.

After evaluating the petitions, the agency has made the following conclusions:

1. Data from the petitions establish that insoluble glucose isomerase enzyme preparations have no history of common use in food in the United States before January 1, 1958. Consequently, these enzyme preparations are not GRAS based on history of common use in food.

However, after evaluating the petitions, the agency concludes that insoluble glucose isomerase enzyme preparations derived from safe and suitable microorganisms, such as *S. rubiginosus*, *A. missouriensis*, *S. olivaceus*, *S. olivochromogenes*, and *B. coagulans*, and rendered insoluble (fixed) with GRAS ingredients or approved materials, are GRAS for use in the manufacture of high fructose corn

syrup based on scientific procedures. The published scientific literature demonstrates that the microbial sources are well known and available to the scientific community and contains no reports of toxicity or pathogenicity problems associated with their use. In addition, the animal feeding studies contained in one of the petitions were presented at annual conferences of the American Association of Cereal Chemists (1971) and the American Chemical Society (1973). In addition, a substantial amount of manufacturing data for glucose isomerase enzyme preparations has been published in several publications and also was presented at the annual meetings mentioned above. The manufacturing data indicate that the use of immobilized enzyme preparations results in virtually nil levels of enzymatic processing materials entering the final food product. The conclusion that these preparations are GRAS is corroborated by analytical data and unpublished animal studies contained in the petitions that confirm the safety of the use of these enzyme preparations and the safety of the organisms from which they are derived.

The agency has further concluded that insoluble glucose isomerase enzyme preparations derived from microorganisms other than those listed above may also be GRAS, provided that the selection of the microorganism adheres to the criteria established during this review and reflected above in the discussion entitled, "Source of Glucose Isomerase Enzyme." Under these criteria, GRAS status is limited to enzyme preparations that are derived from microorganisms that are precisely classified, nonpathogenic, nontoxicogenic, and generally available to the scientific community. Furthermore, the published scientific literature should contain studies in which these microorganisms were utilized without any evidence of pathogenicity of toxicogenicity being associated with their use.

2. FDA currently considers the use of food-grade gelatin and diatomaceous earth in the production of high fructose corn syrup to be GRAS. A 1963 FDA advisory opinion letter concluded that diatomaceous earth of a suitable purity is GRAS for use as a filtering aid. The use of diatomaceous earth as a fixing agent for enzymes is very similar to its use as a filtering aid. FDA would classify both of these uses as processing aids as defined in § 170.3(o)(24) (21 CFR 170.3(o)(24)), and both uses would result in the same level of contact with food. Finally, in both of these uses, the diatomaceous earth is removed from the

final food product. Therefore, the agency considers the use of diatomaceous earth as a fixing agent for enzymes to be GRAS. The agency intends to publish a proposal addressing the GRAS status of the food use of diatomaceous earth, including its use as a fixing agent for enzymes, in the near future.

The agency has traditionally considered materials such as ceramics, glass, and stainless steel as GRAS for food-contact use, based on their safe history of common use as food-contact materials before 1958. However, because the use of these materials has been so widespread, the agency has never considered it necessary to list these materials as GRAS. Therefore, the agency is noting that the use of these materials in the production of high fructose corn syrup is GRAS but is continuing its traditional practice of not specifically listing them as GRAS.

3. Glutaraldehyde and DEAE-cellulose, when used in the immobilization of glucose isomerase enzyme preparations, although not GRAS, are safe secondary direct food additives under section 409 of the Federal Food, Drug, and Cosmetic Act. There is no evidence that these substances were commonly used in food for these purposes in the United States before 1958. In addition, the agency has determined that the potential toxicity of crosslinking agents, including glutaraldehyde, and resins, including DEAE-cellulose, that could be used to fix glucose isomerase enzyme preparations establishes a basis for assuring limited consumer exposure to these substances. Consequently, the agency has concluded that the most appropriate way of regulating this group of substances and of ensuring their continued safe use in food is to provide for the use of fixing agents in a food additive regulation.

4. High fructose corn syrup as defined below in new § 182.1866 (21 CFR 182.1866) is GRAS for use in food. The agency has concluded that high fructose corn syrup is as safe for use in food as sucrose, corn sugar, corn syrup, and invert sugar. FDA bases this conclusion on the saccharide composition of this product and the safety of the insoluble glucose isomerase enzyme preparations used in its manufacture. High fructose corn syrup contains approximately the same glucose to fructose ratio as honey, invert sugar, and the disaccharide sucrose. In addition, the minor saccharides contained in high fructose corn syrup are the same, and present at similar levels, as the nonglucose saccharides that are present in corn syrup and corn sugar. Sucrose is

**DEPARTMENT OF HEALTH AND
HUMAN SERVICES**
Food and Drug Administration
21 CFR Part 179

[Docket No. 81N-0004]

**Irradiation in the Production,
Processing, and Handling of Food**
AGENCY: Food and Drug Administration.

ACTION: Final rule.

SUMMARY: The Food and Drug Administration (FDA) is amending its regulations to permit additional uses of ionizing radiation for the treatment of food. These regulations: (1) Permit manufacturers to use irradiation at doses not to exceed 1 kiloGray (kGy) to inhibit the growth and maturation of fresh foods and to disinfect food of arthropod pests, (2) permit manufacturers to use irradiation at doses not to exceed 30 kGy to disinfect dry or dehydrated aromatic vegetable substances (such as spices and herbs) of microorganisms, (3) require that foods that are irradiated be labeled to show this fact both at the wholesale and at the retail level, and (4) require that manufacturers maintain process records of irradiation for a specified period and make such records available for FDA inspection. These regulations are promulgated on the agency's initiative and are necessary to permit the safe use of ionizing radiation. This document responds to comments on the February 14, 1984, proposed rule (49 FR 5714).

DATES: Effective April 18, 1986; objections by May 19, 1986.

ADDRESS: Written objections and request for a hearing to the Dockets Management Branch (HFA-305), Food and Drug Administration, Rm. 4-62, 5600 Fishers Lane, Rockville, MD 20857.

FOR FURTHER INFORMATION CONTACT: Clyde A. Takeguchi, Center for Food Safety and Applied Nutrition (HFF-330), Food and Drug Administration, 200 C St. SW., Washington, DC 20204, 202-472-5740.

SUPPLEMENTARY INFORMATION:
Table of Contents

- I. Introduction
- II. Comments
 - A. Safety
 - 1. Radiolytic products
 - 2. Spices
 - 3. Other minor foods
 - 4. Destruction of nutrients
 - 5. Selective destruction of microorganisms
 - 6. Toxicological studies
 - 7. Alleged adverse effects
 - B. Labeling Issues
 - C. Current Good Manufacturing Practice
 - D. Other Technical Effects

- E. Packaging
- F. Public Education
- G. Impact Analyses
- III. Objections
- IV. References
- V. Agency Action

I. Introduction

Under section 409 (b) and (d) of the Federal Food, Drug, and Cosmetic Act (the act), the Secretary may approve a food additive petition from an interested person or may propose the issuance of a food additive regulation upon the Secretary's own initiative (21 U.S.C. 348 (b) and (d)). It is less common for FDA, acting as the Secretary's delegate, to propose and then establish a regulation itself, than to respond to a sponsor's petition. In the case of food irradiation, FDA had, before 1981, approved several food additive petitions for the use of various sources of radiation on certain foods and food-packaging materials (21 CFR Part 179). Subsequent to these approvals, an FDA committee evaluated testing criteria that would be necessary to support the safety of food irradiation for various uses.

In the *Federal Register* of March 27, 1981 (46 FR 18992), FDA published an advance notice of proposed rulemaking that announced the availability of the Bureau of Foods' (now the Center for Food Safety and Applied Nutrition) Irradiated Food Committee (BFIFC) Report (Ref. 1), which outlined a course of action for assuring the safety of irradiated foods, and requested comments on the overall approach.

In the *Federal Register* of February 14, 1984 (49 FR 5714), FDA published a proposed rule that would: (1) Establish general provisions for food irradiation, (2) permit the use of food irradiation at doses not exceeding 1 kiloGray (kGy) (100 kilorads; 100 krad)¹ for inhibiting the growth and maturation of fruits and vegetables and for insect disinfection of food, (3) allow irradiation to be used for microbial disinfection of certain dried spices and dried vegetable seasonings at a dose not to exceed 30 kGy (3 Mrad), (4) eliminate the current irradiated food labeling requirements for retail labeling, and (5) replace the current sections (21 CFR 179.22 and 179.24) dealing with the irradiation of food with new §§ 179.25 and 179.26 (21 CFR 179.25 and 179.26). The proposal

¹ The Systeme Internationale (SI) unit for expressing the amount of absorbed radiation dose is the Gray (joules/kilogram, abbreviated Gy). An older unit commonly used is the rad. The equivalent value in rads (100 rad = 1 Gy) will be enclosed in parentheses when referring to the amount of absorbed radiation. The prefixes kilo (k) and mega (M) represent a thousandfold and a millionfold, respectively. Thus, kilorad means a thousand rads and a megarad means a million rads.

responded to comments on the advance notice of proposed rulemaking.

Apart from that ongoing rulemaking, FDA has approved a number of food additive petitions to provide for the safe use of gamma radiation at doses up to 10 kGy (1 Mrad) to control insect infestation and microbial contamination in dried herbs, spices, and vegetable seasonings (48 FR 30613, July 5, 1983; 48 FR 46022, October 11, 1983; 49 FR 24988, June 19, 1984; 50 FR 15415, April 18, 1985) and in dry enzyme preparations (50 FR 24190, June 10, 1985). FDA also issued a final rule on July 22, 1985 (50 FR 29858) which amended 21 CFR 179.22(b) in response to a petition to provide for the safe use of gamma radiation at doses up to 1 kGy (100 krad) to control *Trichinella spiralis* in pork.

The act requires that a food additive, including a source of radiation used to process food, be shown to be safe under the proposed conditions of use before use of the food additive can be approved. That is, the agency must be assured with reasonable certainty that no harm will result from irradiation of food. A source of radiation is specifically defined as a food additive in section 201(s) of the act (21 U.S.C. 321(s)). The Senate report on the Food Additives Amendment of 1958 made clear that "[s]ources of radiation (including radioactive isotopes, particle accelerators and X-ray machines) intended for use in processing food are included in the term 'food additive' as defined in this legislation." S. Rept. 2422, 85th Cong., 2d Sess. 63 (1958).

Section 409 of the act lists the criteria which must be considered by the agency before a food additive regulation is issued. The statute does not prescribe what safety tests should be performed but leaves that determination to the discretion of scientists. The definition of safety, as drawn from the legislative history of the Food Additives Amendment of 1958, has been codified in 21 CFR 170.3(i) as follows:

(i) "Safe" or "safety" means that there is a reasonable certainty in the minds of competent scientists that the substance is not harmful under the intended condition of use. It is impossible in the present state of scientific knowledge to establish with complete certainty the absolute harmlessness of the use of any substance. Safety may be determined by scientific procedures or by general recognition of safety. In determining safety, the following factors shall be considered:

(1) The probable consumption of the substance and of any substance formed in or on food because of its use.

(2) The cumulative effect of the substance in the diet, taking into account any

and which may be subjected to incidental irradiation during the radiation treatment of prepackaged foods. This regulation was issued in response to petitions for packaging materials used with food during irradiation in anticipation of expanded uses of food irradiation in the 1960's. Therefore, the agency disagrees with the comment that § 179.45 is unnecessary.

Section 179.45, however, does not list packaging materials that are generally recognized as safe (e.g., glass, wood, natural fibers) but which may exhibit different characteristics of migration to food during irradiation. FDA knows of no information on such materials during irradiation by which they could be generally recognized as safe. Therefore, FDA does not consider such materials to be generally recognized as safe when used in packaging that is irradiated in contact with food. The agency invites petitions to amend § 179.45 to include generally recognized as safe packaging materials and other packaging materials not currently in § 179.45.

The agency agrees that the failure to address packaging in the proposal may cause confusion. Because of the possible confusion, FDA is adding a new paragraph in § 179.26 clarifying the intended requirement that packaging materials containing food during irradiation must comply with § 179.45.

F. Public Education

66. Many comments stated that a need exists for a public education campaign supported by the government and industry.

The agency agrees that there is a need for public education in this area. However, the agency is responsible for ensuring that food additives including a source of radiation are safe; FDA has no proper role as a promoter of a specific food additive or food process. The agency believes that the primary responsibility for such educational activities remains with industry in this instance.

G. Impact Analyses

The agency stated in the proposed rule that existing safeguards in regulations issued by the Occupational Safety and Health Administration (OSHA), the Nuclear Regulatory Commission (NRC), the Department of Transportation (DOT), and FDA are adequate to ensure that there will be no adverse environmental effect. However, many comments expressed concerns about the environmental impact of this regulation. These comments can be separated into three categories: (1) Radiation safety within the facility (worker safety), (2) waste storage and

disposal, and (3) transportation. FDA requested a response to these comments from OSHA (Ref. 71), NRC (Ref. 72), and DOT (Ref. 73) and has summarized their responses below.

67. Several comments were concerned with worker exposure and with plant safety and claimed that current safety standards are inadequate to protect workers employed in industries handling radioactive materials.

A facility using radioactive material must first obtain a license from NRC or the corresponding agency in an agreement State. NRC has informed FDA that in order for a firm to be licensed to possess and use radioactive material in an irradiator, the firm must file an application with NRC or the corresponding State agency. The information that needs to be submitted includes the training and experience of individuals responsible for the radiation safety programs, the training provided to persons who will work under the supervision of the responsible individuals, a description of the facility, the safety systems designed to protect personnel from exposure to radiation, and the radiation protection program.

NRC states that the regulatory "Guide for the Preparation of Applications for Licenses for the Use of Panoramic Dry Source-Storage Irradiators, Self-contained Wet Source-Storage Irradiators, and Panoramic Wet Source-Storage Irradiators" (Ref. 74) provides guidance to potential applicants about specific details needed in an application for possession and use of radioactive material in an irradiator. The NRC staff reviews the application to determine that (1) the applicant's proposed equipment and facilities are adequate to protect health and minimize danger to life and property, (2) the applicant is qualified by training and experience to use the radioactive material for the purpose requested and in such a manner as to protect health and minimize danger to life and property, and (3) the program described will result in compliance with NRC's regulatory requirements. If the information provided in an application is satisfactory, a license is issued. After issuance, NRC conducts periodic inspections of irradiator facilities. In 1978 and 1979, NRC collected exposure data from all licensees. The average annual measurable dose for persons engaged in irradiation operations was 160 millirems. (The maximum permissible ionizing radiation dose for workers is 5,000 millirems per year.)

68. One comment stated that OSHA's ionizing radiation standard (29 CFR 1910.96) would apply to worker exposures from machine-produced

radiations, but questioned the organization's ability to ensure worker safety.

In response to this comment, OSHA confirmed that its current ionizing radiation standard (29 CFR 1910.96) would apply to worker exposures to radiation from machine-produced sources. As in the past, OSHA will concentrate its inspectional resources on high priority problems, and will consider additional action should information develop indicating a need for concern.

69. Many comments were concerned about the safety of transporting radioactive materials, in general, and also argued that implementation of this regulation would lead to increased amounts of radioactive materials being transported.

Both DOT and NRC have responded to this comment. They stated that the transportation of radioactive materials is an activity which is highly regulated by both the Federal and State governments. Both DOT and NRC have regulatory requirements that govern all aspects of transportation in detail, from quality assurance in packaging to requirements for posting information that is clearly visible on transporting vehicles.

The overall safety of transporting radioactive materials was evaluated in the NRC report entitled "Final Environmental Statement on the Transportation of Radioactive Material by Air and Other Modes" (NUREG-0170) (Ref. 75). The report concluded that the total risk from all transportation of such materials was acceptably low. NRC has concluded, after review of the subject, that the regulations are adequate to protect the public against unreasonable risks from the transport of radioactive materials (46 FR 21619; April 13, 1981). NRC believes such shipments can be made safely because licensees shipping radioactive material for use in food irradiators are required to comply with an NRC regulatory program.

Food irradiation sources are held in the form of welded, sealed sources and are transported in accident-resistant packaging. There has never been a release of radioactive materials from one of these packages in the United States as a result of a transportation accident, even when transporting powders, liquids, or gases. The transportation of sealed sources would make a release even more unlikely.

70. One comment stated that DOT, NRC, and the States are ineffective in their regulation of transportation of radioactive materials.

ADDRESS: Federal Energy Regulatory Commission, Office of the Secretary, Room 3110, 825 North Capitol Street NE., Washington, DC 20426.

FOR FURTHER INFORMATION CONTACT: Peter J. Roidakis, Federal Energy Regulatory Commission, Office of the General Counsel, 825 North Capitol Street NE., Washington, DC 20426, (202) 357-8213.

Order Granting Extension of Time for Responses to Take-or-Pay Date Request

Before Commissioners: Martha O. Hesse, Chairman; Anthony G. Sousa, Charles G. Stalon, Charles A. Trabandt and C.M. Naeve.

I. Introduction

On August 7, 1987, the Commission issued Order No. 500¹ which promulgated interim regulations in response to the decision of the United States Court of Appeals for the District of Columbia Circuit in *Associated Gas Distributors v. FERC*.² On August 26, 1987, the Commission served 45 interstate natural gas pipelines with data requests regarding the take-or-pay obligations in their gas purchase contracts. The responses to these data requests are intended to provide an accurate and current data base for a studied response to the Court's decision in *Associated Gas Distributors*.

II. Discussion

Numerous pipelines and their trade associations have filed for extensions of time to respond to the take-or-pay data request.³ Upon consideration, the Commission hereby grants in part the pipelines' requests for additional time in which to respond to the take-or-pay data requests, and extends the date responses are due to November 2, 1987.

The Commission is aware that the interim regulations also provide for certain operative dates integral to their implementation and operation. Specifically, the suspension of § 284.10 of the Commission's regulations was

removed effective November 1, 1987; and, as of November 1, 1987, natural gas that was being transported by interstate pipelines would continue to be eligible for transportation by the interstate pipelines only if the pipeline and the shipper agree, or an affidavit offering certain take-or-pay credits has been submitted to the pipeline. While the Commission is not adjusting these operative dates at this time, the Commission may, upon further consideration, adjust those dates, if it finds such action necessary. Finally, the Commission notes the numerous substantive issues that have been raised in various rehearing requests, clarification motions, and comments received to date. These issues may also be treated in a subsequent order where necessary, or by other responsive means, as appropriate.

The purpose of this order is solely to extend the date by which responses to the take-or-pay date requests are due, and is not intended to constitute a final order on rehearing.

III. Administrative findings

The Commission is extending a data request response date integral to the implementation of Order No. 500. The Commission finds that the public interest would be served and that good cause exists to make this extension effective immediately pursuant to sections 553(b)(B) and 553(d)(3) of the Administrative Procedure Act.

IV. Order

The date for response to the Order No. 500 take-or-pay data request is extended to November 2, 1987.

By the Commission,
Kenneth F. Plumb,
Secretary.
[FR Doc. 87-24494 Filed 10-21-87; 8:45 am]
BILLING CODE 5717-01-M

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Part 173

[Docket No. 81G-0282]

Secondary Direct Food Additives Permitted in Food for Human Consumption; Polyethylenimine

AGENCY: Food and Drug Administration.
ACTION: Final rule.

SUMMARY: The Food and Drug Administration (FDA) is amending the food additive regulations to provide for

the safe use of polyethylenimine as a fixing agent for the immobilization of microbial enzyme preparations used as sources of glucose isomerase. This action is in response to a petition filed by UOP, Inc.

DATES: Effective October 22, 1987; objections by November 23, 1987. The Director of the Office of the Federal Register approves the incorporation by references of certain publications at 21 CFR 173.357, effective October 22, 1987.

ADDRESS: Written objections to the Dockets Management Branch (HFA-305), Food and Drug Administration, Rm. 4-62, 5600 Fishers Lane, Rockville, MD 20857.

FOR FURTHER INFORMATION CONTACT: James H. Maryanski, Center for Food Safety and Applied Nutrition (HFF-334), Food and Drug Administration, 200 C Street SW., Washington, DC 20204, 202-426-8950.

SUPPLEMENTARY INFORMATION:

I. Introduction

In a notice published in the *Federal Register* of November 17, 1981 (46 FR 56505), FDA announced that a GRAS affirmation petition (GRASP 1G0277) had been filed by a law firm on behalf of UOP, Inc., 20 UOP Plaza, Des Plaines, IL 60016, proposing affirmation that high fructose corn syrup prepared from corn syrup glucose by the action of a glucose isomerase-enzyme preparation derived from *Streptomyces olivochromogenes* (*S. olivochromogenes*) and immobilized with polyethylenimine cross-linked with glutaraldehyde is generally recognized as safe (GRAS) as a direct human food ingredient.

In the *Federal Register* of February 8, 1983 (48 FR 5715), FDA listed high fructose corn syrup as GRAS (21 CFR 182.1866) for use in food as a nutritive carbohydrate sweetener when prepared from high dextrose equivalent corn starch hydrolysate by the action of insoluble glucose isomerase enzyme preparations as described in 21 CFR 184.1372. In that document, FDA recognized that the safety of the glucose isomerase enzyme preparations, and therefore of high fructose corn syrup, depends on several factors. Among these factors are the nature of the microorganism used as the source of the glucose isomerase enzyme preparation and the presence of residues of the enzyme, of additional cellular material, and of residues of processing materials in the final food ingredient (high fructose corn syrup).

¹ 52 FR 30334 (Aug. 14 1987). The interim regulations became effective on September 15, 1987.

² 624 F.2d 981 (D.C. Cir. 1987).

³ See, e.g., petition of Interstate Natural Gas Association of America (INGAA) filed September 21, 1987, in Docket No. RM87-34-000 at 1 ("INGAA strongly urges that the Commission extend the time for responding to the data requests until December 15, 1987"); see also petitions of Valley Gas Transmission, Inc., Northwest Pipeline Corporation, Williams Natural Gas Company, Transcontinental Gas Pipe Line Corporation, Williston Basin Interstate Pipeline Company, Valero Interstate Transmission Company, Carnegie Natural Gas Company, Western Gas Interstate Company, Equitable Resources, Inc., United Gas Pipe Line Company, American Gas Association, Kentucky West Virginia Gas Company, Northern Natural Gas Company, Division of Enron Corp., ANR Pipeline Company and Colorado Interstate Gas Company.

II. The Petition

The petition submitted by UOP, Inc., describes the microbial enzyme preparation used to produce high fructose corn syrup as a partially purified extract derived from *S. olivochromogenes* that is free of viable cells and that is immobilized (fixed or rendered insoluble) with glutaraldehyde and polyethylenimine on a ceramic carrier. In evaluating the data in the petition, FDA considered whether each component of the fixed enzyme preparation is currently approved for the proposed use.

FDA has affirmed that enzyme preparations derived from *S. olivochromogenes* are GRAS (21 CFR 184.1372) for use as sources of glucose isomerase. Glutaraldehyde is listed in 21 CFR 173.357 as a fixing agent in the immobilization of glucose isomerase enzyme preparations for use in the manufacture of high fructose corn syrup. In the Federal Register document that listed high fructose corn syrup as GRAS (48 FR 5715), FDA stated that materials such as ceramics, glass, and stainless steel are GRAS for food-contact use based on a history of widespread use.

Therefore, FDA finds that the ingredients of UOP, Inc.'s, fixed enzyme preparation, except polyethylenimine, are either regulated food additives or GRAS food ingredients. This final rule addresses the proposed use of polyethylenimine as a fixing agent for microbial enzymes used as sources of glucose isomerase.

III. Requirements for GRAS Status

In accordance with 21 CFR 170.30, an ingredient may be GRAS either (1) on the basis of experience based on common use in food prior to January 1, 1958, or (2) of scientific procedures. Because the information that UOP, Inc., submitted in support of its petition did not establish that polyethylenimine was in common use in food before 1958, FDA considered whether the petition contained evidence from scientific procedures that established that this use of polyethylenimine is GRAS.

FDA reviewed the data on the safety of both polyethylenimine and the starting materials used to manufacture the ingredient. Although polyethylenimine has not been found to cause cancer, it may contain minute amounts of ethylenimine and 1,2-dichloroethane as impurities. These chemicals have been shown to cause cancer in test animals. Residual amounts of reactants and manufacturing aids, such as these chemicals, are commonly found as contaminants in

chemical products, including food additives.

Based on its evaluation, the agency finds that polyethylenimine is not GRAS based upon scientific procedures because the potential toxicity of ethylenimine and of 1,2-dichloroethane requires that consumer exposure to these impurities be limited. Therefore, the agency has concluded that polyethylenimine, when used to immobilize glucose isomerase enzyme preparations, is a food additive subject to section 409 of the Federal Food, Drug, and Cosmetic Act (the act), and that the additive, if found to be safe, should be listed with other enzyme fixing agents as a secondary direct food additive in Part 173. This conclusion is consistent with the agency's previous action (48 FR 5715) that listed fixing agents used in the immobilization of glucose isomerase enzyme preparations in § 173.357.

The agency has evaluated polyethylenimine as a food additive in accordance with 21 CFR 170.38(c) and 171.1.

IV. Determination of Safety

Under section 409(c)(3)(A) of the act (21 U.S.C. 348(c)(3)(A)), the so-called "general safety clause" of the statute, a food additive cannot be approved for a particular use unless a fair evaluation of the data available to FDA establishes that the additive is safe for that use. The concept of safety embodied in the Food Additives Amendment of 1958 is explained in the legislative history of the provision: "Safety requires proof of a reasonable certainty that no harm will result from the proposed use of an additive. It does not—and cannot—require proof beyond any possible doubt that no harm will result under any conceivable circumstances." H. Rept. 2284, 85th Cong., 2d Sess. 4 (1958). This concept of safety has been incorporated into FDA's food additive regulations (21 CFR 170.3(i)). The anticancer or Delaney clause of the Food Additives Amendment of 1958 (section 409(c)(3)(A) of the act (21 U.S.C. 348(c)(3)(A))) provides further that no food additive shall be deemed to be safe if it is found to induce cancer when ingested by man or animal.

In the past, FDA has often refused to approve a use of an additive that contained or was suspected of containing even minor amounts of a carcinogenic chemical, even though the additive as a whole had not been shown to cause cancer. The agency now believes, however, that developments in scientific technology and experience with risk assessment procedures make it possible for FDA to establish the safety of additives that contain a carcinogenic

chemical but that have not themselves been shown to cause cancer.

In the preamble to the final rule permanently listing D&C Green No. 6 published in the Federal Register of April 2, 1982 (47 FR 14138), FDA explained the basis for approving the use of a color additive that had not been shown to cause cancer, even though it contains a carcinogenic constituent. Since that decision, FDA has approved the use of other color additives and food additives on the same basis.

An additive that has not been shown to cause cancer, but that contains a carcinogenic constituent, may properly be evaluated under the general safety clause of the statute using risk assessment procedures to determine whether there is a reasonable certainty that no harm will result from the proposed use of the additive.

The agency's position is supported by *Scott v. FDA*, 728 F.2d 322 (6th Cir. 1984). That case involved a challenge to FDA's decision to approve the use of D&C Green No. 5, which contains a carcinogenic chemical but has itself not been shown to cause cancer. Relying heavily on the reasoning in the agency's decision to list this color additive, the United States Court of Appeals for the Sixth Circuit rejected the challenge to FDA's action and affirmed the listing regulation.

V. Safety of the Petitioned Use

FDA finds that the petitioned use of polyethylenimine will result in extremely low levels of exposure to this additive. Data submitted in support of the petition showed that polyethylenimine has never been detected in the final commercial product (high fructose corn syrup). Based on the limit of detection (0.2 part per million (ppm)) of the analytical method used in analyzing the commercial product and on considerations such as migration of the additive under the most severe intended conditions of use and the probable concentration in the daily diet, the agency has calculated the estimated daily intake of polyethylenimine from the petitioned use to be 11 micrograms per day (4 parts per billion (ppb) in the diet) for a 60-kilogram person. FDA does not ordinarily consider chronic testing to be necessary to determine the safety of additives whose use will result in such low exposure levels (Refs. 1 and 2).

To establish that polyethylenimine is safe for use as a fixing agent for glucose isomerase enzyme preparations, the petitioner submitted mutagenicity studies, acute oral toxicity studies in the rat, acute dermal toxicity studies, skin and eye irritation studies in the rabbit,

DEPARTMENT OF
HEALTH, EDUCATION, AND WELFARE
FOOD AND DRUG ADMINISTRATION
WASHINGTON 25, D. C.

FDA

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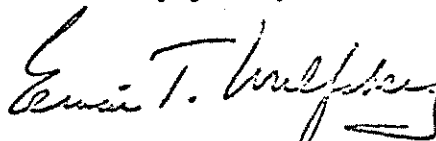
Mr. H. W. Kuni
Glass Containers Manufacturers Institute
99 Park Avenue
New York, New York

Dear Mr. Kuni:

Reference is made to our meeting this date with Messrs. Barnby, Lyon, Farmer and Smart.

Based on the data which you submitted together with other information available to us, we have had an opportunity to draw a conclusion concerning soda lime glass containers. We are of the opinion that glass containers of the soda-lime-alumina-silicate complex, clear or flint, and those colored amber, green, opal, blue, and yellow, with mineral colorants, are not food additives on the basis that they may not reasonably be expected to become a component of food or otherwise affect the characteristics of food and beverages under their intended conditions of use. This opinion is predicated on the assumption that such glass is produced under the controls which are characteristic of good manufacturing practice.

Sincerely yours,



Einar T. Wulfsberg
Food and Drug Officer