impact statement is not required and this petition results in a regulation, the notice of availability of the agency's finding of no significant impact and the evidence supporting that finding will be published with the regulation in the **Federal Register** in accordance with 21 CFR 25.40(c) (proposed December 11, 1979; 44 FR 71742).

Dated: March 18, 1983.

Sanford A. Miller,

Director, Bureau of Foods.

[FR Doc. 83-7936 Filed 3-28-83; 8:45 am]

BILLING CODE 4160-01-M

[Docket No. 82D-0350]

General Principles of Process Validation; Current Good Manufacturing Practice Draft Guideline

AGENCY: Food and Drug Administration.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is announcing the availability of a draft guideline entitled "Guideline on General Principles of Process Validation," which outlines general principles of process validation the agency views as acceptable parts of a process validation program for preparing humam and animal drug products and medical devices. The draft guideline, which is being made available for public comment to provide the agency with views to be considered in its development of a final guideline, is intended to inform interested persons of these acceptable principles to facilitate compliance with the current good manufacturing practice (CGMP) regulations and to help assure the quality of human and animal drug products and medical devices. The guideline was prepared by FDA's National Center for Drugs and Biologics and National Center for Devices and Radiological Health.

DATE: Comments by May 31, 1983.

ADDRESS: Requests for a copy of the draft guideline and written comments regarding the draft guideline to the Dockets Management Branch (HFA-305), Food and Drug Administration, Rm. 4-62, 5600 Fishers Lane, Rockville, MD 20857.

FOR FURTHER INFORMATION CONTACT:

For Human and Animal Drug Products: Clifford G. Broker, National Center for Drugs and Biologics (HFN-323), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301-443-5307.

For Medical Devices: Edward J. McDonnell, National Center for Devices and Radiological Health (HFK-130), Food and Drug Administration, 8757 Georgia Ave., Silver Spring, MD 20910, 301-427-7122.

SUPPLEMENTARY INFORMATION: The draft guideline is intended to inform interested persons of process validation principles that FDA believes constitute acceptable ways of compliance with applicable CGMP regulations. FDA notes that because of the great variety of products, processes, and manufacturing facilities it is impossible to state comprehensively all the specific validation elements applicable to every situation. However, several broad process validation concepts presented in the draft guideline have general applicability and provide an acceptable framework for building a comprehensive approach to process validation.

The draft guideline is being made available for public comment before being issued as the formal position of the agency. If, following the receipt of comments, the agency concludes that the guideline reflects acceptable process validation principles for compliance with applicable CGMP regulations, the guideline will be made final, and the availability will be announced under § 10.90(b) (21 CFR 10.90(b)). That section provides for the use of guidelines to establish procedures of general applicability that are not legal requirements but are acceptable to the agency. A person who follows a guideline is assured that his or her conduct will be acceptable to the agency. A person may also choose to use alternative procedures even though they are not provided for in the guideline. A person who chooses to do so may discuss the matter further with the agency to prevent an expenditure of money and effort for work that the agency may later determine to be unacceptable. Therefore, manufacturers are encouraged to use this opportunity to submit comments on the draft guideline if they have suggestions for its revision.

Interested persons may, on or before May 31, 1981, submit written comments on the draft guideline to the Dockets Management Branch (address above). These comments will be considered in determining whether further amendments to, or revisions of, the draft guideline are warranted. Comments should be in two copies (except that individuals may submit single copies), identified with the docket number found in brackets in the heading of this document. The draft guideline and received comments may be seen in the Dockets Management Branch between 9 a.m. and 4 p.m., Monday through Friday. Requests for a single copy of the draft guideline should be sent to the Dockets Management Branch.

Dated: March 23, 1983.

Joseph P. Hile,

Associate Commissioner for Regulatory Affairs.

[FR Doc. 83-7933 Filed 3-28-83; 8:45 am]

BILLING CODE 4160-01-M

[Docket No. 79D-0465]

Human, Biological, and Animal Drugs and Medical Devices; Availability of Draft Guideline for Use of the Limulus Amebocyte Lysate (LAL) Test

AGENCY: Food and Drug Administration.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is announcing the availability of a draft guideline for use of the Limulus Amebocyte Lysate (LAL) test as an end product endotoxin test for human, biological, and animal injectable drugs and medical devices. The draft guideline, which is being made available for public comment to provide the agency with views to be considered in its development of a final guideline, is intended to inform manufacturers of acceptable methods of validating the LAL test before using it as an alternative to the official rabbit pyrogen test. Manufacturers of human, biological, and animal injectable drugs and medical devices may start using the LAL test following the procedures set forth in the draft guideline. For human, biological, and animal injectable drugs that are subject to requirements of submission of applications to the agency, FDA will accept and approve, as appropriate, supplements to applications for approval that describe use of the LAL test. Manufacturers of medical devices are not required to submit applications or supplemental applications for premarket approval or premarket notification submissions to describe use of the LAL test, unless the LAL test procedures used by such manufacturer deviate significantly from the procedures in the draft guideline.

DATES: Comments by June 27, 1983.

ADDRESS: Requests for a copy of the draft guideline and written comments regarding the draft guideline to the Dockets Management Branch (HFA-305), Food and Drug Administration, Rm. 4-62, 5600 Fishers Lane, Rockville, MD 20857.

FOR FURTHER INFORMATION CONTACT:

Human Drugs: Terry E. Munson, National Center for Drugs and Biologics (HFN-325), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301-443-6007.

Biological Products: Michael L. Hooton, National Center for Drugs and Biologics (HFN–813), Food and Drug Administration, 8800 Rockville Pike, Bethesda, MD 20205, 301–443–1306.
Animal Drugs: Patricia Cushing, Bureau of Veterinary Medicine (HFV–143), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301–443–1788.
Medical Devices: Virginia C. Ross, National Center for Devices and Radiological Health (HFK–430), Food and Drug Administration, 8757 Georgia Ave., Silver Spring, MD 20910, 301–427–7226.

SUPPLEMENTARY INFORMATION: In the **Federal Register** of January 12, 1973 (38 FR 1404), FDA announced that LAL intended to measure bacterial endotoxins in blood and drugs for human use is a biological product subject to licensing under section 351 of the Public Health Service Act (42 U.S.C. 262). LAL is prepared from the circulating blood cells (amebocytes) of the horseshoe crab (*Limulus polyphemus*). Since 1973, LAL has been used in a test procedure that has proved to be both a sensitive indicator of the presence of bacterial endotoxins (pyrogens) and valuable in enabling manufacturers to withhold from the market human drugs and other products which, if they contain bacterial endotoxins and are administered to humans, may produce fever, shock, and death.

When FDA published the January 12, 1973 **Federal Register** notice, the available data on and experience with the LAL test did not support its use as an end product test for endotoxins and, thus, it was not then considered a suitable alternative to the official United States Pharmacopeia (USP) rabbit pyrogen test. However, the LAL test was considered suitable as an inprocess endotoxin test, i.e., a preliminary test conducted only for informational purposes, but could not serve as a basis for the release of particular lots of blood or drug products. Accordingly, the January 12, 1973 notice permitted marketing of the LAL test without a biological product license if its use was limited to the inprocess testing of human drugs and if its labeling stated that the test was not suitable as a replacement for the official rabbit pyrogen test.

Since 1973, production techniques for the LAL test have been standardized, consistently yielding LAL test results with an endotoxin sensitivity over 100 times greater than that previoulsy possible. Moreover, the LAL test is faster and more economical and can be tested on a smaller volume of product than the rabbit pyrogen test. In addition, one individual can perform many LAL tests in 1 day.

In a notice published in the **Federal Register** of November 4, 1977 (42 FR 57749), FDA announced conditions under which the LAL test could be used as an end product endotoxin test for licensed biological products and medical devices. On March 26, 1979, the then Bureau of Medical Devices (now the Office of Medical Devices (OMD) in FDA's National Center for Devices and Radiological Health) made available to interested persons a draft guideline setting forth conditions for using the LAL test for medical devices.

This notice and the new draft guideline change certain provisions in the 1979 draft guideline, based upon the device industry's substantial expertise in using the LAL test since the 1979 draft guideline was made available. FDA no longer believes it necessary for manufacturers to submit to OMD data establishing that the LAL test that the manufacturer proposes to use is at least equivalent to the official USP rabbit pyrogen test. If a manufacturer follows the draft guideline now being made available, OMD need not grant written approval to use the LAL test. A device manufacturer that plans to use LAL test procedures deviating significantly from the test procedures in the draft guideline is required to obtain written approval from the Director of OMD through submission of a premarket notification (see section 510(k) of the Federal Food, Drug, and Cosmetic Act (the act) (21 U.S.C. 360) and FDA's regulations governing premarket notification procedures (21 CFR 807.81(a)(3))), or a premarket approval application or supplement (see section 515 of the act (21 U.S.C. 360(e))).

The November 4, 1977 notice stated that the use of LAL for drug products other than biological would be the subject of a future **Federal Register** publication. Accordingly, in the **Federal Register** of January 18, 1980 (45 FR 3668), FDA published a notice announcing the availability of a draft guideline that described the conditions for validating the LAL test before using it as a final end product endotoxin test for human and veterinary injectionable drug products. The January 18, 1980 notice also requested that manufacturers submit comments and information to FDA that might be helpful in preparing the final guideline.

After reviewing the comments received on the 1979 and 1980 drafts, FDA is combining the drafts into a single draft agency guideline which differs in two significant ways from the earlier drafts. Because of these changes, FDA has decided to make the agency draft guideline available for comment, but at the same time, to permit firms to start using the LAL test following the procedures set forth in the draft guideline.

Because of different applicable statutory provisions and regulations and the nature of some products, the draft guideline sets forth somewhat different procedures for performing the LAL test as an end product test for the various categories of products regulated by FDA. For human, biological, and animal injectable drugs that are subject to the requirements of submission of applications to the agency, FDA will accept and approve, when appropriate, supplements to applications for approval that describe use of the LAL test. As discussed above, manufacturers of medical devices are not required to submit applications or supplemental applications for premarket approval or premarket notification submissions to describe use of the LAL test, unless the LAL test procedures to be used by a manufacturer would deviate significantly from the procedures in the draft guideline.

One of the two significant changes in the draft guideline involves the method of expressing the endotoxin limits for human and animal drug products. In the 1980 draft guideline, the endotoxin limit for parenteral drug product was 0.25 endotoxin unit per milliliter (EU/mL) of drug product. This limit applied to parenteral drugs without regard to the dose administered. Comments objected to this method of expressing the endotoxin limit. The comments said that the effects of endotoxin are related to the amount of endotoxin contained in the dose administered to a patient rather than the amount of endotoxin contained in 1 mL of the product.

FDA agrees with the comments. FDA is changing the endotoxin limit so that the amount of endotoxin permitted in the product is related to the dose. Because the dose varies from product to product, the endotoxin limit is expressed as K/M. K is 5.0 EU/kilogram (kg), which represents the approximate threshold pyrogen dose for humans and rabbits. M represents the rabbit pyrogen dose or the maximum human dose per kg that would be administered in a 1-hour period, whichever, is larger. Thus, a product that has a maximum human dose of 10 mL/kg could contain no more than 0.5 EU/mL of the product.

The second significant change in the draft guideline is the deletion of the section of the 1980 draft guideline entitled "Absence of Non-endotoxin Pyrogenic Substances." The agency

believes that the testing described in this section would be of value only if a large number of batches were tested, and that requiring so much batch testing would be unreasonable and expensive. Therefore, FDA has determined that such testing is inappropriate and unnecessary.

This draft guideline is being made available for public comment before its issuance by FDA as its formal position. FDA invites interested persons to comment on any provision of the draft LAL guideline. However, the agency especially invites comments and data concerning the use of the turbidimetric technique for testing products covered by this guideline. If, after considering the comments and making appropriate changes, FDA concludes that the guideline reflects acceptable procedures for decisionmaking on LAL tests, the guideline will be made final, and its availability will be announced under § 10.90(b) of FDA's regulations (21 CFR 10.90(b)). That section provides for use of guidelines to establish procedures of general applicability that are not legal requirements but are acceptable to the agency. A person who follows a guideline is assured that his or her conduct will be acceptable to the agency. A person may also choose to use alternative procedures or standards even though they are not provided for in the guideline. A person who chooses to do so may discuss the matter further with the agency to prevent expenditure of money and effort for work that the agency may later determine to be unacceptable.

Interested persons may submit written comments to the Dockets Management Branch by June 27, 1983. Two copies of all comments are to be submitted, except that individuals may submit one copy. Comments are to be identified with the docket number found in brackets in the heading of this document. The draft guideline and received comments may be seen in the office above between (9 a.m. and 4 p.m., Monday through Friday. Requests for a single copy of the draft guideline should be sent to the Dockets Management Branch.

Dated: March 21, 1983.

Mark Novitch,

Deputy Commissioner of Food and Drugs.

[FR Doc. 83-7934 Filed 3-24-83; 11:30 am]

BILLING CODE 4160-01-M

[Docket No. 83G-0062]

Pfizer, Inc.; Filing of Petition for Affirmation of GRAS Status

AGENCY: Food and Drug Administration.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is announcing that Pfizer, Inc., has filed a petition (GRASP 2G0282) proposing affirmation that lactase enzyme from *Candida pseudotropicalis* used in hydrolyzing lactose in milk and milk products is generally recognized as sfe (GRAS) as a direct human food ingredient.

DATE: Comments by May 31, 1983.

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

FOR FURTHER INFORMATION CONTACT: Vivian Prunier, Bureau of Foods (HFF-335), Food and Drug Administration, 200 C St. SW., Washington, D.C. 20204, 202-426-5487.

SUPPLEMENTARY INFORMATION: Under the Federal Food, Drug, and Cosmetic Act (sec. 409(b)(5), 72 Stat. 1786 (21 U.S.C. 348(b)(5))) and the regulations for affirmation of GRAS status in § 170.35 (21 CFR 170.35), notice is given that a petition (GRASP 2G0282) has been filed by Pfizer, Inc., 235 E. 42d St., New York, NY 10017, proposing affirmation that lactase enzyme from *Candida pseudotropicalis* used to hydrolyze lactose in milk and milk products is GRAS as a direct human food ingredient.

The petition has been placed on display at the Dockets Management Branch (address above).

Any petition that meets the format requirements outlined in § 170.35 is filed by the agency. There is no prefiling review of the adequacy of data to support a GRAS conclusion. Thus, the filing of a petition for GRAS affirmation should not be interpreted as preliminary indication of suitability for affirmation.

Interested persons may, on or before May 31, 1983, review the petition and/or file comments (two copies, identified with the docket number found in brackets in the heading of this document) with the Dockets Management Branch (address above). Comments should include any available information that would be helpful in determining whether the substance is, or is not, GRAS. A copy of the petition and received comments may be seen in the Dockets Management Branch, between 9 a.m. and 4 p.m., Monday through Friday.

Dated: March 18, 1983.

Sanford A. Miller,

Director, Bureau of Foods.

[FR Doc. 83-7939 Filed 3-28-83; 8:45 am]

BILLING CODE 4160-01-M

[Docket No. 83F-0049]

Union Carbide Corp.; Filing of Food Additive Petition

AGENCY: Food and Drug Administration.

ACTION: Notice

SUMMARY: The Food and Drug Administration (FDA) is announcing that Union Carbide Corp. has filed a petition proposing that the food additive regulations be amended to provide for the safe use of fluorine treated polyethylene as a component of food-contact surfaces.

FOR FURTHER INFORMATION CONTACT: Julius Smith, Bureau of Foods (HFF-334), Food and Drug Administration, 200 C St. SW., Washington, DC 20204, 202-472-5690.

SUPPLEMENTARY INFORMATION: Under the Federal Food, Drug and Cosmetic Act (sec. 409(b)(5), 72 Stat. 1786 (21 U.S.C. 348(b)(5))), notice is given that a petition (FAP 8B3394) has been filed by Union Carbide Corp., Old Saw Mill River Rd., Tarrytown, NY 10591, proposing that Part 177 (21 CFR Part 177) be amended to provide for the safe use of fluorine treated polyethylene as a component of food-contact surfaces.

The potential environmental impact of this action is being reviewed. If the agency finds that an environmental impact statement is not required and this petition results in a regulation, the notice of availability of the agency's finding of no significant impact and the evidence supporting that finding will be published with the regulation in the **Federal Register** in accordance with 21 CFR 25.40(c) (proposed December 11, 1979; 44 FR 71742).

Dated: March 18, 1983.

Sanford A. Miller,

Director, Bureau of Foods.

[FR Doc. 83-7937 Filed 3-28-83; 8:45 am]

BILLING CODE 4160-01-M

[Docket No. 83C-0012]

American Cyanamid Co.; Filing of Color Additive Petition

AGENCY: Food and Drug Administration.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is announcing that American Cyanamid Co. has filed a petition proposing that the color additive regulations be amended to provide for an increase in the current use levels of D&C Green No. 6 for coloring polyglycolic acid surgical sutures.

FOR FURTHER INFORMATION CONTACT: Garnett R. Higginbotham, Bureau of Foods (HHF–334), Food and Drug Administration, 200 C St. SW., Washington, DC 20204, 202–472–5690.

SUPPLEMENTARY INFORMATION: Under the Federal Food, Drug, and Cosmetic Act (sec. 706(b)(1), 74 Stat. 399–402 as amended (21 U.S.C. 376(b)(1))), notice is given that a petition, CAP 3C0170, has been filed by American Cyanamid Co., Pearl River, NY 10965, proposing that § 74.1206(c)(1)(i) (21 CFR 74.1206(c)(1)(i)) of the color additive regulations be amended to provide for an increase to 0.5 percent of D&C Green No. 6 by weight for coloring polyglycolic acid sutures.

The potential environmental impact of this action is being reviewed. If the agency finds that an environmental impact statement is not required and this petition results in a regulation, the notice of availability of the agency's finding of no significant impact and the evidence supporting that finding will be published with the regulation in the **Federal Register** in accordance with 21 CFR 25.40(c) (proposed December 11, 1979; 44 FR 71742).

Dated: March 17, 1983.

Sanford A. Miller,

Director, Bureau of Foods.

[FR Doc. 83-7828 Filed 3-28-83; 8:45 am]

BILLING CODE 4160-01-M

[Docket No. 83F-0027]

E.I. duPont de Nemours & Co., Inc.; Filing of Food Additive Petition

AGENCY: Food and Drug Administration.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is announcing that E.I. duPont de Nemours & Co., Inc., has filed a petition proposing that the food additive regulations be amended to provide for the safe use of perfluorocarbon elastomers as articles or components of articles intended for repeated use in contact with food.

FOR FURTHER INFORMATION CONTACT: Marvin D. Mack, Bureau of Foods (HFF–334), Food and Drug Administration, 200 C St. SW., Washington, DC 20204, 202–472–5740

SUPPLEMENTARY INFORMATION: Under the Federal Food, Drug, and Cosmetic Act (sec. 409(b)(5), 72 Stat. 1786 (21 U.S.C. 348(b)(5))), notice is given that a petition (FAP 3B3683) has been filed by E.I. duPont de Nemours & Co., Inc., Wilmington, DE 19898, proposing that Part 177 (21 CFT Part 177) be amended to provide for the safe use of perfluorocarbon elastomers as articles or components of articles intended for repeated use in contact with food.

The potential environmental impact of this action is being reviewed. If the agency finds that an environmental impact statement is not required and this petition results in a regulation, the notice of availability of the agency's finding of no significant impact and the evidence supporting that finding will be published with the regulation in the **Federal Register** in accordance with 21 CFR 25.40(c) (proposed December 11, 1979; 44 FR 71742).

Dated: March 17, 1983.

Sanford A. Miller,

Director, Bureau of Foods.

[FR Doc. 83-7830 Filed 3-28-83; 8:45 am]

BILLING CODE 4160-01-M

[Docket No. 83F-0064]

Monsanto Co.; Filing of Food Additive Petition

AGENCY: Food and Drug Administration.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is announcing that Monsanto Co. has filed a petition proposing that the food additive regulations be amended to consolidate the current listings for polyamine-epichlorohydrin wet strength resins.

FOR FURTHER INFORMATION CONTACT: Mary W. Lipien, Bureau of Foods (HFF–334), Food and Drug Administration, 200 C St. SW., Washington, DC 20204, 202–472–5740.

SUPPLEMENTARY INFORMATION: Under the Federal Food, Drug, and Cosmetic Act (sec. 409(b)(5), 72 Stat. 1786 (21 U.S.C. 348(b)(5))), notice is given that a petition (FAP 2B3606) has been filed by Monsanto Co., 800 N. Lindbergh Blvd., St. Louis, MO 63166, proposing that § 176.170 *Components of paper and paperboard in contact with aqueous and fatty foods* (21 CFR 176.170) be amended to consolidate the current listings for polyamine-epichlorohydrin wet strength resins.

The potential environmental impact of this action is being reviewed. If the agency finds that an environmental impact statement is not required and this petition results in a regulation, the notice of availability of the agency's finding of no significant impact and the evidence supporting that finding will be published with the regulation in the **Federal Register** in accordance with 21 CFR 25.40(c) (proposed December 11, 1979; 44 FR 71742).

Dated: March 17, 1983.

Sanford A. Miller,

Director, Bureau of Foods.

[FR Doc. 83-7829 Filed 3-28-83; 8:45 am]

BILLING CODE 4160-01-M

DEPARTMENT OF THE INTERIOR

Bureau of Land Management

[A-5321 and A-7730]

Arizona: Realty Action Competitive Sale of Public Land in Graham County; Correction

FR Doc. 83–2238 appearing on pages 3874 and 3875 in the issue of Thursday, January 27, 1983 is corrected by changing the closure date for acceptance of sealed bids from March 28, 1983 to April 18, 1983 and the date of the public sale from March 31, 1983 to April 19, 1983.

Dated: March 17, 1983.

Lester K. Rosenkrance,

District Manager.

[FR Doc. 83-7954 Filed 3-28-83; 8:45 am]

BILLING CODE 4310-84-M

Montana; Lewistown District Advisory Council; Meeting

AGENCY: Bureau of Land Management, Lewistown District Advisory Council, Interior.

ACTION: Notice of meeting.

SUMMARY: The Lewistown District Advisory Council will meet April 7, 1983. The agenda will be:

9:00 a.m. Committee Meetings: Land Sales and Exchanges, Carpenter Creek Change in Use, Ervin Ridge Wild Horses, Wilderness Study, Fire Management, and Billings Resource Area Management Plan Committees
12:00 p.m. Recess
1:00 p.m. Committee Reports (as above), Briefing on Square Butte Natural Area Access
5:00 p.m. Adjournment.

Public comment will be sought during subcommittee meetings and following each committee report.

DATE: April 7, 1983, 9:00 a.m. to 5:00 p.m.

ADDRESS: Lewistown District Office, Airport Road, Lewistown, Montana.

FOR FURTHER INFORMATION CONTACT: Glenn W. Freeman, District Manager, Bureau of Land Management, Lewistown, Montana 59457.

SUPPLEMENTARY INFORMATION: The Lewistown District Advisory Council is authorized under section 309 of the Federal Land Policy and Management Act of 1976 (43 U.S.C. 1739). The Council