Competition and Patent Term Restoration Act of 1984 (Public Law 98–417) (the 1984 amendments), which authorized the approval of duplicate versions of drug products approved under an ANDA procedure. ANDA sponsors must, with certain exceptions, show that the drug for which they are seeking approval contains the same active ingredient in the same strength and dosage form as the ''listed drug,'' which is a version of the drug that was previously approved under a new drug application (NDA). Sponsors of ANDAs do not have to repeat the extensive clinical testing otherwise necessary to gain approval of an NDA. The only clinical data required in an ANDA are data to show that the drug that is the subject of the ANDA is bioequivalent to the listed drug.

The 1984 amendments include what is now section 505(j)(7) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355(j)(7)), which requires FDA to publish a list of all approved drugs. FDA publishes this list as part of the ''Approved Drug Products with Therapeutic Equivalence Evaluations,'' which is generally known as the ''Orange Book.'' Under FDA regulations, drugs are withdrawn from the list if the agency withdraws or suspends approval of the drug's NDA or ANDA for reasons of safety or effectiveness or if FDA determines that the listed drug was withdrawn from sale for reasons of safety or effectiveness (21 CFR 314.162).

Regulations also provide that the agency must make a determination as to whether a listed drug was withdrawn from sale for reasons of safety or effectiveness before an ANDA that refers to that listed drug may be approved (21 CFR 314.161(a)(1)). FDA may not approve an ANDA that does not refer to a listed drug.

Cyanocobalamin injection (Rubramin PC), 1mg/mL in a 10 mL vial is the subject of NDA 6–799. On November 28, 1951, Bristol-Myers Squibb Co. received approval to market cyanocobalamin injection. Cyanocobalamin is vitamin B_{12}. Subsequently, Bristol-Meyers Squibb Co. withdrew cyanocobalamin injection from sale.

On November 29, 2001, PharmaForce, Inc., submitted a citizen petition (Docket No. 01P–0533) under 21 CFR 10.30 to FDA requesting that the agency determine whether cyanocobalamin injection was withdrawn from sale for reasons of safety or effectiveness. FDA has reviewed its records and determined that cyanocobalamin injection was not withdrawn from the market for safety or efficacy reasons. Accordingly, the agency will list cyanocobalamin injection in the ''Discontinued Drug Product List'' section of the Orange Book. The ''Discontinued Drug Product List'' delineates, among other items, drug products that have been discontinued from marketing for reasons other than safety or effectiveness. ANDAs that refer to cyanocobalamin injection may be approved by the agency.

Dated: July 17, 2002.

Margaret M. Dotzel,

Associate Commissioner for Policy.

[FR Doc. 02–18976 Filed 7–25–02; 8:45 am]

BILLING CODE 4160–01–S

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. 02E–0023]

Determination of Regulatory Review Period for Purposes of Patent Extension; Definity

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) has determined the regulatory review period for Definity and is publishing this notice of that determination as required by law. FDA has made the determination because of the submission of an application to the Director of Patents and Trademarks, Department of Commerce, for the extension of a patent that claims that human drug product.

ADDRESSES: Submit written comments and petitions to the Dockets Management Branch (HFA–305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. Submit electronic comments to http://www.fda.gov/dockets/ecomments.

FOR FURTHER INFORMATION CONTACT: Claudia Grillo, Office of Regulatory Policy (HFD–007), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301–827–3460.

SUPPLEMENTARY INFORMATION: The Drug Price Competition and Patent Term Restoration Act of 1984 (Public Law 98–417) and the Generic Animal Drug and Patent Term Restoration Act (Public Law 100–670) generally provide that a patent may be extended for a period of up to 5 years so long as the patented item (human drug product, animal drug product, medical device, food additive, or color additive) was subject to regulatory review by FDA before the item was marketed. Under these acts, a product's regulatory review period forms the basis for determining the amount of extension an applicant may receive.

A regulatory review period consists of two periods of time: A testing phase and an approval phase. For human drug products, the testing phase begins when the exemption to permit the clinical investigations of the drug becomes effective and runs until the approval phase begins. The approval phase starts with the initial submission of an application to market the human drug product and continues until FDA grants permission to market the drug product. Although only a portion of a regulatory review period may count toward the actual amount of extension that the Director of Patents and Trademarks may award (for example, half the testing phase must be subtracted as well as any time that may have occurred before the patent was issued), FDA's determination of the length of a regulatory review period for a human drug product will include all of the testing phase and approval phase as specified in 35 U.S.C. 156(g)(1)(B).

FDA recently approved for marketing the human drug product Definity (perflutren lipid microspheres). Definity is indicated for use in patients with suboptimal echocardiograms to opacify the left ventricular chamber and to improve the delineation of the left ventricular endocardial border. Subsequent to this approval, the Patent and Trademark Office received a patent term restoration application for Definity (U.S. Patent No. 5,527,521) from Dupont Contrast Imaging, Inc., and the Patent and Trademark Office requested FDA's assistance in determining this patent's eligibility for patent term restoration. In a letter dated February 14, 2002, FDA advised the Patent and Trademark Office that this human drug product had undergone a regulatory review period and that the approval of Definity represented the first permitted commercial marketing or use of the product. Shortly thereafter, the Patent and Trademark Office requested that FDA determine the product's regulatory review period.

FDA has determined that the applicable regulatory review period for Definity is 2,160 days. Of this time, 1,193 days occurred during the testing phase of the regulatory review period, while 967 days occurred during the approval phase. These periods of time were derived from the following dates:

1. *The date an exemption under section 505(i) of the Federal Food, Drug, and Cosmetic Act (the act) (21 U.S.C. 355(i)) became effective*: September 3, 1995. The applicant claims September 13, 1995, as the date the investigational new drug application (IND) became

effective. However, FDA records indicate that the IND effective date was September 3, 1995, which was 30 days after FDA receipt of the IND.

2. *The date the application was initially submitted with respect to the human drug product under section 505(b) of the act*: December 8, 1998. FDA has verified the applicant's claim that the new drug application (NDA) for Definity (NDA 21–064) was initially submitted on December 8, 1998.

3. *The date the application was approved*: July 31, 2001. FDA has verified the applicant's claim that NDA 21–064 was approved on July 31, 2001.

This determination of the regulatory review period establishes the maximum potential length of a patent extension. However, the U.S. Patent and Trademark Office applies several statutory limitations in its calculations of the actual period for patent extension. In its application for patent extension, this applicant seeks 1,418 days of patent term extension.

Anyone with knowledge that any of the dates as published are incorrect may submit to the Dockets Management Branch (see **ADDRESSES**) written or electronic comments and ask for a redetermination by September 24, 2002. Furthermore, any interested person may petition FDA for a determination regarding whether the applicant for extension acted with due diligence during the regulatory review period by January 22, 2003. To meet its burden, the petition must contain sufficient facts to merit an FDA investigation. (See H. Rept. 857, part 1, 98th Cong., 2d sess., pp. 41–42, 1984.) Petitions should be in the format specified in 21 CFR 10.30.

Comments and petitions should be submitted to the Dockets Management Branch. Three copies of any information are to be submitted, except that individuals may submit a single copy. Comments are to be identified with the docket number found in brackets in the heading of this document. Comments and petitions may be seen in the Dockets Management Branch between 9 a.m. and 4 p.m., Monday through Friday.

Dated: April 22, 2002.

Jane A. Axelrad,

Associate Director for Policy, Center for Drug Evaluation and Research.

[FR Doc. 02–18975 Filed 7–25–02; 8:45 am]

BILLING CODE 4160–01–S

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. 02D–0254]

Draft Guidance for Industry on Inhalation Drug Products Packaged in Semipermeable Container Closure Systems; Availability

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is announcing the availability of a draft guidance for industry entitled ''Inhalation Drug Products Packaged in Semipermeable Container Closure Systems.'' This draft guidance is intended to provide guidance for industry on inhalation drug products that are packaged in semipermeable primary container closure systems. This draft guidance also covers related chemistry, manufacturing, and controls (CMC) considerations. FDA is issuing this draft guidance to address public health concerns raised by the possible leaching and entry of chemical contaminants into inhalation drug products packaged in semipermeable primary container closure systems.

DATES: Submit written or electronic comments on the draft guidance by October 24, 2002. General comments on agency guidance documents are welcome at any time.

ADDRESSES: Submit written requests for single copies of the draft guidance to the Division of Drug Information (HFD–240), Center for Drug Evaluation and Research, Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857. Send one self-addressed adhesive label to assist that office in processing your requests. Submit written comments on the draft guidance to the Dockets Management Branch (HFA–305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. Submit electronic comments to *http://www.fda.gov/dockets/ecomments*. *See* the **SUPPLEMENTARY INFORMATION** section for electronic access to the draft guidance document.

FOR FURTHER INFORMATION CONTACT: Badrul Chowdhury or Guirag Poochikian, Center for Drug Evaluation and Research (HFD–570), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301–827–1050.

SUPPLEMENTARY INFORMATION:

I. Background

FDA is announcing the availability of a draft guidance for industry entitled ''Inhalation Drug Products Packaged in Semipermeable Container Closure Systems.'' Inhalation drug products used in the treatment of patients with asthma or chronic obstructive pulmonary disease may be packaged in semipermeable primary container closure systems, such as low-density polyethylene. Over time, chemical impurities can accumulate in an inhalation drug product packaged in semipermeable primary container closure systems as a result of the degradation of formulation components, leaching from the container closure system, and/or entry from the local environment. Volatile chemical components from the local environment, including the secondary packaging, can react with the drug product formulation to form different impurities. The clinical consequences of chemical contamination of inhalation drug products are uncertain; however, given the known sensitivity of patients using these products to respiratory irritants and sensitizers, it is possible that these chemical contaminates may induce bronchospasm. Because bronchospasm is also the indication for which the inhalation drug product is used, it is difficult in the clinical setting to establish whether bronchospasm after the use of a drug product may be due to chemical contaminants or to a patient's underlying disease. Since it is possible that chemical contaminants in the inhalation drug products used to treat critically ill patients could adversely affect such patients, FDA is issuing this draft guidance to provide recommendations for inhalation drug products packaged in semipermeable primary container closure systems. This draft guidance provides recommendations on: (1) Appropriate protective secondary packaging, (2) embossing and/or debossing of the primary container in lieu of paper labels, and (3) general guidance on the number of unit-dose containers to be contained within each protective secondary package. These recommendations apply to drug products, both those in development and those already approved and marketed in the United States.

This draft guidance is being issued consistent with FDA's good guidance practices regulation (21 CFR 10.115). The draft guidance represents the agency's current thinking on inhalation drug products packaged in semipermeable container closure systems. It does not create or confer any