

safety or effectiveness (21 CFR 314.162). FDA may be called upon to make such a finding when petitioned by a potential ANDA applicant (§ 314.161 (21 CFR 314.161)).

On March 19, 1996, Richard Hamer Associates, Inc., submitted a citizen petition (Docket No. 96P-0090/CP1), under 21 CFR 10.25(a), 10.30, and 314.161(b), requesting that the agency determine whether testosterone propionate 2% ointment was discontinued from sale for reasons of safety or effectiveness and, if the agency determines that the drug was not discontinued from sale for reasons of safety or effectiveness, to relist the drug in the Orange Book. Testosterone propionate 2% ointment (Perandren Ointment) was the subject of NDA 0-0499 held by Ciba Pharmaceutical Co. This NDA was submitted to FDA on January 24, 1939, and under the procedures of the act at that time, the NDA "became effective" (the statutory equivalent of "approval" under the act as it appears now) on March 7, 1939, 23 years before passage of the 1962 amendments to the act. The significance of these dates is that from 1938 through 1962, FDA reviewed drugs only to pass upon their safety. The 1962 amendments to the act (Pub. L. 87-781 (October 10, 1962)) required FDA to review drugs not only for safety, but also for effectiveness. The effectiveness standard applied both prospectively to new drugs entering the market and retrospectively to drugs whose applications became effective between 1938 and 1962.

In the **Federal Register** of September 23, 1971 (36 FR 18885), FDA withdrew approval of NDA 0-0499 for Perandren Ointment based on the applicant's failure to submit required annual reports (section 505(e) of the act and 21 CFR 314.80 and 314.81).

In the **Federal Register** of December 6, 1996 (61 FR 64754), FDA in responding to the Hamer petition, announced its determination that testosterone propionate 2% ointment (Perandren Ointment) was not discontinued from sale for reasons of safety or effectiveness. In that same notice, FDA announced that this determination will allow FDA to approve ANDA's for testosterone propionate 2% ointment. Upon further investigation, however, FDA has determined that NDA 0-0499 for Perandren Ointment was never approved as effective for any of its labeled indications and, therefore, was never a "listed drug" such that it could be "relisted." As discussed previously, for a drug approved under section 505(c) of the act to be a "listed drug," it must have been approved for

effectiveness as well as safety. No information was ever submitted on the effectiveness of this product prior to its withdrawal of approval in 1971. So, while it remains true that NDA 0-0499 was not discontinued from sale for reasons of safety or effectiveness, it is not appropriate at this time to accept ANDA's for testosterone propionate 2% ointment.

The **Federal Register** notice of December 6, 1996, is amended insofar as it is inconsistent with the findings of this notice.

Dated: April 27, 1998.

William K. Hubbard,

Associate Commissioner for Policy Coordination.

[FR Doc. 98-11684 Filed 5-1-98; 8:45 am]

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DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. 96E-0189]

Determination of Regulatory Review Period for Purposes of Patent Extension; LIPOSORBER® LA-15 System

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) has determined the regulatory review period for LIPOSORBER® LA-15 System 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 Commissioner of Patents and Trademarks, Department of Commerce, for the extension of a patent which claims that medical device.

ADDRESSES: Written comments and petitions should be directed to the Dockets Management Branch (HFA-305), Food and Drug Administration, 12420 Parklawn Dr., rm. 1-23, Rockville, MD 20857.

FOR FURTHER INFORMATION CONTACT: Brian J. Malkin, Office of Health Affairs (HFY-20), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301-827-6620.

SUPPLEMENTARY INFORMATION: The Drug Price Competition and Patent Term Restoration Act of 1984 (Pub. L. 98-417) and the Generic Animal Drug and Patent Term Restoration Act (Pub. L. 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 medical devices, the testing phase begins with a clinical investigation of the device and runs until the approval phase begins. The approval phase starts with the initial submission of an application to market the device and continues until permission to market the device is granted. Although only a portion of a regulatory review period may count toward the actual amount of extension that the Commissioner of Patents and Trademarks may award (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 medical device will include all of the testing phase and approval phase as specified in 35 U.S.C. 156(g)(3)(B).

FDA recently approved for marketing the medical device LIPOSORBER® LA-15 System. LIPOSORBER® LA-15 System is indicated for use in performing low density lipoprotein cholesterol (LDL-C) apheresis to acutely remove LDL-C from the plasma of high risk patient populations for whom diet has been ineffective and maximum drug therapy has either been ineffective or not tolerated. Subsequent to this approval, the Patent and Trademark Office received a patent term restoration application for LIPOSORBER® LA-15 System (U.S. Patent No. 4,637,994) from Kanegafuchi Kagaku Kogyo Kabushiki Kaisha, and the Patent and Trademark Office requested FDA's assistance in determining this patent's eligibility for patent term restoration. In a letter dated August 7, 1996, FDA advised the Patent and Trademark Office that this medical device had undergone a regulatory review period and that the approval of LIPOSORBER® LA-15 System 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 LIPOSORBER® LA-15 System is 3,598 days. Of this time, 1,995 days occurred during the testing phase of the regulatory review period, while 1,603 days occurred during the approval

phase. These periods of time were derived from the following dates:

1. *The date a clinical investigation involving this device was begun:* April 18, 1986. FDA has verified the applicant's claim that the date the investigational device exemption (IDE) required under section 520(g) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 360j(g)) for human tests to begin became effective April 18, 1996, the date that the IDE for a similar, related product, LIPOSORBER® LA-40 System, was approved.

Although the device was subsequently modified, the results of the initial clinical investigations on the earlier model, LIPOSORBER® LA-40 System were included in FDA's analysis of the approved product's safety and effectiveness. The test on the earlier model is, therefore, part of the testing phase.

Additionally, the product is of a type which, under present regulations, would require IDE approval prior to the start of clinical investigations, and normally the initiation of the testing phase for a medical device is determined by reference to the approval phase of the relevant IDE.

2. *The date an application was initially submitted with respect to the device under section 515 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 360e):* October 3, 1991. The applicant claims March 24, 1988, as the date the premarket approval application (PMA) for the LIPOSORBER® LA-40 System (PMA 880019) was initially submitted, which applicant argues should be used in place of the PMA for LIPOSORBER® LA-15 System (PMA 910018). FDA records indicate that PMA 880019 was received by the agency on March 25, 1998, but this PMA was never filed, and it was withdrawn by the applicant on April 3, 1996. The applicant claims that PMA 910018 was submitted on March 26, 1991, but FDA records indicate that it was submitted on October 3, 1991.

The applicant argues that the PMA for the LA-40 device should be used as the start of the approval phase for the LA-15 device, because its liposorber technology and adsorbent are identical to those described in the patent for which applicant is requesting extension, U.S. Patent No. 4,637,994. The LA-15 device contains additional components of a plasma separator, the tubing system for plasmaphereses and the apheresis unit.

However, the patent term restoration regulations define the approval phase of medical device in terms of the actual approved product, not an earlier tested product. For example, while the patent term restoration statute does define drug

product as the active ingredient of a new drug, "product" for "medical devices" has been defined as "[a]ny medical device * * * subject to regulation under the Federal Food, Drug, and Cosmetic Act" (35 U.S.C. 156(f)). Given that the LA-40 device was withdrawn by applicant from further regulatory consideration, the LA-15 device is the only applicable medical device subject to FDA regulations.

Regarding the definition of regulatory review period for the start of the approval phase of a medical device, the regulations state " * * * the period beginning on the date the application was initially submitted with respect to the device under section 515 and ending on the date such application was approved under such Act * * * " 35 U.S.C. 156(g)(3)(B); see also 21 CFR 60.22(c)(2)(i). In this case, the only PMA which submitted, filed, and approved under section 515 of the Federal Food, Drug, and Cosmetic Act was PMA P910018, which was submitted on October 3, 1991, and is, therefore, the appropriate date the approval application was initially submitted for LIPOSORBER® LA-15 System.

3. *The date the application was approved:* February 21, 1996. FDA has verified the applicant's claim that PMA P910018 was approved on February 21, 1996.

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 1,825 days of patent term extension.

Anyone with knowledge that any of the dates as published is incorrect may, on or before July 6, 1998, submit to the Dockets Management Branch (address above) written comments and ask for a redetermination. Furthermore, any interested person may petition FDA, on or before November 2, 1998, for a determination regarding whether the applicant for extension acted with due diligence during the regulatory review period. 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 (address above) in three copies (except that individuals may submit single copies) and 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: March 31, 1998.

Thomas J. McGinnis,

Deputy Associate Commissioner for Health Affairs.

[FR Doc. 98-11682 Filed 5-1-98; 8:45 am]

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DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

Dental Plaque Subcommittee of the Nonprescription Drugs Advisory Committee; Notice of Meeting

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

This notice announces a forthcoming meeting of a public advisory committee of the Food and Drug Administration (FDA). The meeting will be open to the public.

Name of Committee: Dental Plaque Subcommittee of the Nonprescription Drugs Advisory Committee.

General Function of the Committee: To provide advice and recommendations to the agency on FDA's regulatory issues.

Date and Time: The meeting will be held on May 27, 28, and 29, 1998, 8:30 a.m. to 5 p.m.

Location: Holiday Inn, Two Montgomery Village Ave., Gaithersburg, MD.

Contact Person: Robert L. Sherman or Stephanie A. Mason, Center for Drug Evaluation and Research (HFD-560), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD, 301-827-5191, or FDA Advisory Committee Information Line, 1-800-741-8138 (301-443-0572 in the Washington, DC area), code 12541. Please call the Information Line for up-to-date information on this meeting.

Agenda: On May 27, 1998, the subcommittee will discuss: (1) The safety and effectiveness of the combination of stannous pyrophosphate and zinc citrate; (2) the effectiveness of the combination of hydrogen peroxide, sodium lauryl sulfate, sodium citrate and zinc chloride; (3) the safety and effectiveness of hexetidine, soluble pyrophosphate, nonsaponifiable fraction of corn oil, bromchlorophene and chlorhexidine digluconate; and (4) final formulation testing. On May 28, 1998, the subcommittee will discuss labeling