

VII. Submission Requirements

The original and five copies of the completed Grant Application Form PHS 398 (Rev. 5/95) or the original and two copies of the PHS 5161 (Rev. 7/92) for State and local governments, with copies of the appendices for each of the copies, should be delivered to Robert L. Robins (address above). State and local governments may choose to use the PHS 398 application form in lieu of the PHS 5161. The application receipt date is June 18, 1998. If the receipt date falls on a weekend, it will be extended to Monday; if the date falls on a holiday, it will be extended to the following workday. No supplemental or addendum material will be accepted after the receipt date.

The outside of the mailing package and item 2 of the application face page should be labeled "Response to RFA-FDA-CFSAN-98-1."

VIII. Method of Application

A. Submission Instructions

Applications will be accepted during working hours, 8 a.m. to 4:30 p.m., Monday through Friday, on or before the established receipt date.

Applications will be considered received on time if sent or mailed on or before the receipt date as evidenced by a legible U.S. Postal Service dated postmark or a legible date receipt from a commercial carrier, unless they arrive too late for orderly processing. Private metered postmarks shall not be acceptable as proof of timely mailing. Applications not received on time will not be considered for review and will be returned to the applicant. Applicants should note that the U.S. Postal Service does not uniformly provide dated postmarks. Before relying on this method, applicants should check with their local post office.

Do not send applications to the Center for Scientific Research (CSR), NIH. Any application that is sent to NIH, that is then forwarded to FDA and not received in time for orderly processing, will be deemed unresponsive and returned to the applicant. Instructions for completing the application forms can be found on the NIH home page on the Internet (address: <http://www.nih.gov/grants/funding/phs398/phs398.html>); the forms can be found at http://www.nih.gov/grants/funding/phs398/forms_toc.html). However, as noted previously, applications are not to be mailed to NIH. Applications must be submitted via mail delivery as stated previously. FDA is unable to receive applications via Internet.

B. Format for Application

Submission of the application must be on Grant Application Form PHS 398 (Rev. 5/95). All "General Instructions" and "Specific Instructions" in the application kit should be followed with the exception of the receipt dates and the mailing label address. Applicants are also advised that FDA does not adhere to the page limitations or the type size and line spacing requirements imposed by NIH on its applications. Do not send applications to CSR, NIH. Applications from State and local governments may be submitted on Form PHS 5161 (Rev. 7/92) or Form PHS 398 (Rev. 5/95).

The face page of the application should reflect RFA's number RFA-FDA-CFSAN-98-1.

Data included in the application, if restricted with the legend specified below, may be entitled to confidential treatment as trade secret or confidential commercial information within the meaning of the Freedom of Information Act (FOIA) (5 U.S.C. 552(b)(4)) and FDA's implementing regulations (21 CFR 20.61).

Information collection requirements requested on Form PHS 398 and the instructions have been submitted by PHS to the Office of Management and Budget (OMB) and were approved and assigned OMB control number 0925-0001.

C. Legend

Unless disclosure is required by FOIA as amended (5 U.S.C. 552), as determined by the freedom of information officials of DHHS or by a court, data contained in the portions of this application which have been specifically identified by page number, paragraph, etc., by the applicant as containing restricted and/or proprietary information shall not be used or disclosed except for evaluation purposes.

Dated: April 3, 1998.

William K. Hubbard,

Associate Commissioner for Policy Coordination.

[FR Doc. 98-11743 Filed 5-1-98; 8:45 am]

BILLING CODE 4160-01-F

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. 96P-0090]

Determination That Testosterone Propionate 2% Ointment Was Not Withdrawn From Sale for Reasons of Safety or Effectiveness; Amendment

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is amending a previous determination regarding the fact that testosterone propionate 2% ointment (Perandren Ointment) was not withdrawn from sale for reasons of safety or effectiveness. FDA has determined that it is not appropriate at this time to accept abbreviated new drug applications (ANDA's) for testosterone propionate 2% ointment.

FOR FURTHER INFORMATION CONTACT:

David T. Read, Center for Drug Evaluation and Research (HFD-7), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20855, 301-594-2041.

SUPPLEMENTARY INFORMATION: 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 a "listed drug." A listed drug is one that has an effective approval, either under section 505(c) of the Federal Food, Drug, and Cosmetic Act (the act) (21 U.S.C. 355(c)) for safety and effectiveness or under section 505(j) of the act, which has not been withdrawn for reasons of safety or effectiveness (21 CFR 314.3, see also 21 U.S.C. 355(j)(6)). Neither at the time of ANDA submission nor at the time of ANDA approval is it essential that a listed drug be currently marketed.

FDA's "Approved Drug Products with Therapeutic Equivalence Evaluations" (popularly referred to as the "Orange Book") contains the official register of listed drugs, and a drug is removed from this register in either of two ways. First, a listed drug is removed if the agency withdraws or suspends approval of the drug's new drug application (NDA) or ANDA for reasons of safety or effectiveness. Second, in the case of a listed drug that was discontinued from sale but did not have its approval withdrawn or had its approval withdrawn for reasons other than safety or effectiveness, the drug is removed if FDA determines that it was discontinued from sale for reasons of

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