

ADDRESSES: Written comments and petitions should be directed to the Dockets Management Branch (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852.

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 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 Commissioner 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 *Xeloda*TM (capecitabine). *Xeloda*TM is indicated for the treatment of patients with metastatic breast cancer resistant to both paclitaxel and an anthracycline-containing chemotherapy regimen or resistant to paclitaxel and for whom further anthracycline therapy is not indicated. Subsequent to this approval, the Patent and Trademark Office received a patent term restoration application for *Xeloda*TM (U.S. Patent No. 4,966,891) from Hoffmann-La Roche, 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 December 10, 1998, FDA advised the Patent and Trademark Office that this human drug product had undergone a regulatory review period and that the approval of *Xeloda*TM 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 *Xeloda*TM is 1,410 days. Of this time, 1,228 days occurred during the testing phase of the regulatory review period, while 182 days occurred during the approval phase. These periods of time were derived from the following dates:

1. The date an exemption under section 505 of the Federal Food, Drug, and Cosmetic Act (the act) (21 U.S.C. 355) became effective: June 22, 1994. The applicant claims June 19, 1994, as the date the investigational new drug application (IND) became effective. However, FDA records indicate that the IND effective date was June 22, 1994, 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 of the act: October 31, 1997. The applicant claims October 28, 1997, as the date the new drug application (NDA) for *Xeloda*TM (NDA 20-896) was initially submitted. However, FDA records indicate that NDA 20-896 was submitted on October 31, 1997.

3. The date the application was approved: April 30, 1998. FDA has verified the applicant's claim that NDA 20-896 was approved on April 30, 1998.

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 799 days of patent term extension.

Anyone with knowledge that any of the dates as published is incorrect may, on or before March 29, 1999, 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 July 26, 1999, 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: January 18, 1999.

Thomas J. McGinnis,

Deputy Associate Commissioner for Health Affairs.

[FR Doc. 99-1851 Filed 1-26-99; 8:45 am]

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DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. 98E-0783]

Determination of Regulatory Review Period for Purposes of Patent Extension; *Emadine*TM

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) has determined the regulatory review period for *Emadine*TM 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 human drug product.

ADDRESSES: Written comments and petitions should be directed to the Dockets Management Branch (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852.

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 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 Commissioner 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 Emadine™ (emedastine difumarate). Emadine™ is indicated for the temporary relief of the signs and symptoms of allergic conjunctivitis. Subsequent to this approval, the Patent and Trademark Office received a patent term restoration application for Emadine™ (U.S. Patent No. 4,430,343) from Kanebo, Ltd., and the Patent and Trademark Office requested FDA's assistance in determining this patent's eligibility for patent term restoration. In a letter dated December 10, 1998, FDA advised the Patent and Trademark Office that this human drug product had undergone a regulatory review period and that the approval of Emadine™ 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 Emadine™ is 1,410 days. Of this time, 766 days occurred during the testing phase of the regulatory review period, while 644 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:* February 20, 1994. FDA has verified the applicant's claim that the date the investigational

new drug application became effective was on February 20, 1994.

2. *The date the application was initially submitted with respect to the human drug product under section 505 of the act:* March 26, 1996. The applicant claims March 22, 1996, as the date the new drug application (NDA) for Emadine™ (NDA 20-706) was initially submitted. However, FDA records indicate that NDA 20-706 was submitted on March 26, 1996.

3. *The date the application was approved:* December 29, 1997. FDA has verified the applicant's claim that NDA 20-706 was approved on December 29, 1997.

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 1,028 days of patent term extension.

Anyone with knowledge that any of the dates as published is incorrect may, on or before March 29, 1999, 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 July 26, 1999, 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.

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Dated: January 18, 1999.

Thomas J. McGinnis,

Deputy Associate Commissioner for Health Affairs.

[FR Doc. 99-1792 Filed 1-26-99; 8:45 am]

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DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. 98D-1268]

Guidance for Industry on Variations in Drug Products That May Be Included in a Single Abbreviated New Drug Application; Availability

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is announcing the availability of a guidance for industry entitled "Variations in Drug Products That May Be Included in a Single ANDA." This guidance was developed by the Office of Generic Drugs (OGD) in the Center for Drug Evaluation and Research to provide information to applicants on certain specific variations of a drug product that should be included in a single abbreviated new drug application (ANDA) and describe the general factors to be considered when determining whether single or multiple ANDA's should be submitted. It is intended to reduce the burden on industry for submitting and maintaining separate applications for certain variations of the same drug product.

DATES: Written comments may be submitted on the guidance by April 27, 1999. General comments on agency guidances are welcome at any time.

ADDRESSES: Copies of this guidance for industry are available on the Internet at "http://www.fda.gov/cder/guidance/index.htm". Submit written requests for single copies of "Variations in Drug Products That May Be Included in a Single ANDA" to the Drug Information Branch (HFD-210), 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 guidance to the Dockets Management Branch (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852.

FOR FURTHER INFORMATION CONTACT: Robert L. West, Center for Drug Evaluation and Research (HFD-600), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301-827-5846.

SUPPLEMENTARY INFORMATION: FDA is announcing the availability of a guidance for industry entitled "Variation in Drug Products That May Be Included in a Single ANDA." Prior