DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA–2009–D–0007]

Product Development Under the Animal Rule, Revised Draft Guidance for Industry; Availability

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is announcing the availability of a revised draft guidance for industry entitled ''Product Development Under the Animal Rule.'' When human efficacy studies are neither ethical nor feasible, FDA may rely on adequate and well-controlled animal efficacy studies to support approval of a drug or licensure of a biological product under the Animal Rule. This revised draft guidance replaces the 2009 draft guidance for industry entitled ''Animal Models—Essential Elements to Address Efficacy Under the Animal Rule'' and addresses a broader scope of issues for products developed under the Animal Rule. Once finalized, this guidance is intended to help potential sponsors (industry, academia, and government) understand FDA's expectations for product development under the Animal Rule.

DATES: Although you can comment on any guidance at any time (see 21 CFR 10.115(g)(5)), to ensure that the Agency considers your comment on this revised draft guidance before it begins work on the final version of the guidance, submit either electronic or written comments on the draft guidance by August 4, 2014.

ADDRESSES: Submit written requests for single copies of the revised draft guidance to the Division of Drug Information, Center for Drug Evaluation and Research, Food and Drug Administration, 10001 New Hampshire Ave., Hillandale Building, rm. 4147, Silver Spring, MD 20993–0002; or Office of Communication, Outreach and Development, Center for Biologics Evaluation and Research (CBER), Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 71, rm. 3128, Silver Spring, MD 20993–0022. Send one self-addressed adhesive label to assist that office in processing your requests. The revised draft guidance may also be obtained by mail by calling CBER at 1–800–835–4709 or 240–402–7800. See the **SUPPLEMENTARY INFORMATION** section for electronic access to the draft guidance document.

Submit electronic comments on the revised draft guidance to *http://www.regulations.gov*. Submit written comments to the Division of Dockets Management (HFA–305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852.

FOR FURTHER INFORMATION CONTACT: Rosemary Roberts, Office of Counter-Terrorism and Emergency Coordination, Center for Drug Evaluation and Research, Food and Drug Administration, 10001 New Hampshire Ave., Hillandale Building, Mailstop 2163, Silver Spring, MD 20993–0002, 301–796–2210; or Cynthia Kelley, Office of the Director, Center for Biologics Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 71, rm. 7204, Silver Spring, MD 20993–0002, 240–402–8089.

SUPPLEMENTARY INFORMATION:

I. Background

In the **Federal Register** of January 21, 2009 (74 FR 3610), FDA announced the availability of a draft guidance for industry entitled ''Animal Models—Essential Elements to Address Efficacy Under the Animal Rule,'' which identified the critical characteristics (essential data elements) of an animal model to be addressed when developing drug or biological products for approval or licensure under the Animal Rule. The 2009 draft guidance is available to the public on FDA's Web site at *http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/default.htm*.

This notice announces the availability of a revision to that draft guidance. The revised draft addresses a broader scope of issues for products developed under the Animal Rule. Based on written comments to the 2009 draft guidance and comments expressed at the related FDA public meeting held on November 5, 2010, FDA broadened the scope of the guidance to discuss product development under the Animal Rule. The revised draft guidance is intended to help potential sponsors understand FDA's expectations for product development under the Animal Rule.

The revised draft guidance has been placed in a new category/subject area, Animal Rule, and can be found under Guidances (Drugs) at the following Web link: *http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/default.htm*.

New information addressing FDA's current thinking for studies related to the development of products under the Animal Rule is included in the revised draft guidance. Section III discusses regulatory considerations, including product development plans, access to investigational drugs during a public health emergency, communications with FDA, and animal model qualification program. General expectations for Animal Rule-specific studies are discussed in section IV, including a discussion of ensuring data quality and integrity. Additional information regarding the selection of an effective dose of the investigational drug for humans is discussed in section V. Design considerations for adequate and well-controlled efficacy studies in animals are described in section VI, which includes a discussion on general principles and dose selection in animals. Special considerations for vaccines and for cellular and gene therapies are outlined in sections VII.A and B, respectively. An additional checklist for the elements of an adequate and well-controlled animal efficacy study protocol is provided in section X. General principles for the care and use of animals in biomedical research and types of animal care interventions are explained in Appendices A and B, respectively. Finally, general expectations for natural history studies are described in Appendix C.

This revised draft guidance is being issued consistent with FDA's good guidance practices regulation (21 CFR 10.115). The draft guidance, when finalized, will represent the Agency's current thinking on product development under the Animal Rule. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. An alternative approach may be used if such approach satisfies the requirements of the applicable statutes and regulations.

II. Paperwork Reduction Act

This revised draft guidance refers to previously approved collections of information that are subject to review by the Office of Management and Budget (OMB) under the Paperwork Reduction Act of 1995 (44 U.S.C. 3501–3520). The collection of information in 21 CFR part 312 (investigational new drug applications) has been approved under OMB control number 0910–0014. The collection of information in 21 CFR part 314 (new drug applications) has been approved under OMB control number 0910–0001. The collection of information resulting from special protocol assessments has been approved under OMB control number 0910–0470. The collection of information resulting from formal meetings between applicants and FDA has been approved under OMB control number 0910–0429. The collection of information resulting

from Good Laboratory Practices has been approved under OMB control number 0910–0119. The collection of information resulting from current good manufacturing practices has been approved under OMB control number 0910–0139.

III. Comments

Interested persons may submit either electronic comments regarding this document to *http://www.regulations.gov* or written comments to the Division of Dockets Management (see **ADDRESSES**). It is only necessary to send one set of comments. Identify comments with the docket number found in brackets in the heading of this document. Received comments may be seen in the Division of Dockets Management between 9 a.m. and 4 p.m., Monday through Friday, and will be posted to the docket at *http://www.regulations.gov*.

IV. Electronic Access

Persons with access to the Internet may obtain the document at either *http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/default.htm, http://www.fda.gov/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/Guidances/default.htm*, or *http://www.regulations.gov*.

Dated: May 29, 2014.

Leslie Kux,

Assistant Commissioner for Policy.

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DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA–2012–E–0594]

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

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) has determined the regulatory review period for XIAFLEX 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 which claims that human biological product.

ADDRESSES: Submit electronic comments to *http://www.regulations.gov.* Submit written petitions (two copies are required) and written comments to the Division of Dockets Management (HFA–305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. Submit petitions electronically to *http://www.regulations.gov* at Docket No. FDA–2013–S–0610.

FOR FURTHER INFORMATION CONTACT: Beverly Friedman, Office of Management, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 51, Rm. 6257, Silver Spring, MD 20993–0002, 301–796–7900.

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 biological products, the testing phase begins when the exemption to permit the clinical investigations of the biological becomes effective and runs until the approval phase begins. The approval phase starts with the initial submission of an application to market the human biological product and continues until FDA grants permission to market the biological product. Although only a portion of a regulatory review period may count toward the actual amount of extension that the Director of U.S. 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 biological product will include all of the testing phase and approval phase as specified in 35 U.S.C. 156(g)(1)(B).

FDA has approved for marketing the human biologic product XIAFLEX (collagenase clostridium histolyticum). XIAFLEX is indicated for treatment of adult patients with Dupuytren's contracture with a palpable cord. Subsequent to this approval, the U.S. Patent and Trademark Office received a patent term restoration application for XIAFLEX (U.S. Patent No. RE39941) from Auxilium Pharmaceuticals, Inc., and the U.S. Patent and Trademark Office requested FDA's assistance in determining this patent's eligibility for patent term restoration. In a letter dated March 11, 2013, FDA advised the U.S. Patent and Trademark Office that this human biological product had undergone a regulatory review period and that the approval of XIAFLEX represented the first permitted commercial marketing or use of the product. Thereafter, the U.S. Patent and Trademark Office requested that FDA determine the product's regulatory review period.

FDA has determined that the applicable regulatory review period for XIAFLEX is 5,278 days. Of this time, 4,937 days occurred during the testing phase of the regulatory review period, while 341 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 (21 U.S.C. 355(i)) became effective:* August 24, 1995. FDA has verified the applicant's claim that the date the investigational new drug application became effective was on August 24, 1995.

2. *The date the application was initially submitted with respect to the human biological product under section 351 of the Public Health Service Act (42 U.S.C. 262*): February 27, 2009. FDA has verified the applicant's claim that the biologics license application (BLA) for XIAFLEX (BLA 125338) was initially submitted on February 27, 2009.

3. *The date the application was approved:* February 2, 2010. FDA has verified the applicant's claim that BLA 125338 was approved on February 2, 2010.

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 1,806 days of patent term extension.

Anyone with knowledge that any of the dates as published are incorrect may submit to the Division of Dockets Management (see **ADDRESSES**) either electronic or written comments and ask for a redetermination by August 4, 2014. 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 December 1, 2014. To meet its burden,