4164-01-P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2015-D-2306]

Testicular Toxicity: Evaluation During Drug Development; Draft Guidance for Industry; Availability

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA or Agency) is announcing the availability of a draft guidance for industry entitled "Testicular Toxicity: Evaluation During Drug Development." The draft guidance addresses nonclinical findings that may raise concerns of a drug-related adverse effect on the testes, clinical monitoring of adverse testicular effects early in clinical development, and the design and conduct of a safety clinical trial assessing drug-related testicular toxicity. The draft guidance is intended to assist sponsors developing drugs to identify nonclinical signals of testicular toxicity and to evaluate the potential for such toxicity in humans.

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comment on any guidance at any time (see 21 CFR 10.115(g)(5)), to ensure that the Agency considers your comment on this draft guidance before it begins work

on the final version of the guidance, submit either electronic or written comments on the draft guidance by [INSERT DATE 90 DAYS AFTER DATE OF PUBLICATION IN THE FEDERAL REGISTER].

ADDRESSES: Submit written requests for single copies of the draft guidance to the Division of Drug Information, Center for Drug Evaluation and Research, Food and Drug Administration, 10001 New Hampshire Ave., Hillandale Building, 4th Floor, Silver Spring, MD 20993-0002. Send one self-addressed adhesive label to assist that office in processing your requests. See the SUPPLEMENTARY INFORMATION section for electronic access to the draft guidance document.

Submit electronic comments on the draft guidance to http://www.regulations.gov.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: Eufrecina Deguia, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 22, rm. 5348, Silver Spring, MD 20993-0002, 301-796-0881.

SUPPLEMENTARY INFORMATION:

I. Background

FDA is announcing the availability of a draft guidance for industry entitled "Testicular Toxicity: Evaluation During Drug Development." This draft guidance is intended to help sponsors identify nonclinical signals that raise concern regarding the potential for human testicular toxicity and to evaluate those signals appropriately in human studies.

The draft guidance describes the standard battery of nonclinical studies that are used to assess the effects of pharmaceuticals on the male reproductive system. The draft guidance discusses findings in nonclinical studies that may increase the level of concern for drug-related testicular toxicity. Examples of nonclinical studies that could be used to further evaluate initial signals of testicular toxicity are also described. The draft guidance then provides a general approach on how to weigh the relevance of nonclinical findings, taking into account factors that can confound the interpretation of these findings.

If a concerning nonclinical signal is identified, the draft guidance presents suggestions for clinical monitoring when the drug is initially administered to humans. These suggestions aim to minimize the hazards to men while making possible the collection of data that will assist in evaluating the potential toxicity of the drug in the target population. These early studies, however, are not intended to be a definitive evaluation of the potential for testicular toxicity of the drug. Rather, they can provide clinical information that, together with the nonclinical information, will support a judgment as to whether the testicular toxicity signal warrants indepth evaluation in a dedicated safety study.

If a reasonable basis for concern of human testicular toxicity exists, a dedicated clinical safety trial with a primary objective of evaluating drug-related testicular toxicity may be warranted. The draft guidance provides recommendations for the design of such a trial, including conduct, endpoints, and presentation of results. These are general recommendations for the purpose of defining the role of drugs in testicular injury; however,

the specific details of an individual trial may vary depending on the context of use of the drug product.

This 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 current thinking of FDA on the evaluation of testicular toxicity during drug development. It does not establish rights for any person and is not binding on FDA or the public. You can use an alternative approach if it satisfies the requirements of the applicable statutes and regulations.

II. The Paperwork Reduction Act of 1995

This draft guidance refers to previously approved collections of information found in FDA regulations. These collections of information 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 collections of information in 21 CFR part 312 have been approved under OMB control number 0910-0014.

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 or http://www.regulations.gov.

Dated: July 13, 2015.

Leslie Kux,

Associate Commissioner for Policy.

[FR Doc. 2015-17557 Filed: 7/16/2015 08:45 am; Publication Date: 7/17/2015]