



4164-01-P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2015-D-2001]

Assessment of Male-Mediated Developmental Risk for Pharmaceuticals; Draft Guidance for Industry; Availability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SUMMARY: The Food and Drug Administration (FDA or Agency) is announcing the availability of a draft guidance for industry entitled “Assessment of Male-Mediated Developmental Risk for Pharmaceuticals.” This draft guidance provides recommendations to sponsors for assessing risks to embryo/fetal development resulting from administration of an active pharmaceutical ingredient (API) to males either through an effect on the male germ cell or from fetal exposure following seminal transfer of a potentially developmental toxicant to pregnant females. The need for measures to mitigate the risk to embryo/fetal development posed by males participating in clinical trials is also addressed.

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on any guidance at any time (see 21 CFR 10.115(g)(5)), to ensure that the Agency considers your comment on this draft guidance before it begins work on

the final version of the guidance, submit either electronic or written comments on the draft guidance by [INSERT DATE 60 DAYS AFTER DATE OF PUBLICATION IN THE FEDERAL REGISTER].

ADDRESSES: Submit written requests for single copies of the draft guidance to the Division of Drug Information, Center for Drug Evaluation and Research, Food and Drug Administration, 10001 New Hampshire Ave., Hillandale Building, 4th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 See the SUPPLEMENTARY INFORMATION section for electronic access to the draft guidance document.

Submit electronic comments on the draft guidance to 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: Lynnda Reid, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 22, rm. 5388, Silver Spring, MD 20993-0002, 301-796-0984.

SUPPLEMENTARY INFORMATION:

## I. Background

FDA is announcing the availability of a draft guidance for industry entitled “Assessment of Male-Mediated Developmental Risk for Pharmaceuticals.” This guidance presents an overview of FDA’s current approach to assessing potential risks associated with pharmaceutical use in male patients. Current regulatory guidance exists regarding the need to assess the

genotoxic and embryo/fetal developmental toxicity potential of pharmaceuticals before their administration to pregnant women and females of reproductive potential. However, there is a lack of consistency in clinical trial protocol designs and labeling documents regarding pregnancy risk for sexual partners of men being administered an API. The conceptus of a female sexual partner may be subject to developmental risk associated with pre- or post-conception exposure of a male to an API. Such male-mediated developmental toxicity may result from an effect of the API on the male germ cell before conception or occur as a result of direct exposure of the conceptus to the pharmaceutical following seminal transfer and vaginal uptake in a pregnant partner.

This draft guidance provides recommendations for addressing the potential for male-mediated adverse effects on pregnancy outcome for sponsors developing an investigational drug. Topics covered include: (1) Factors that investigators should consider when testing a new API in males, (2) nonclinical studies relevant to the assessment of male-mediated developmental risks, and (3) measures to prevent pregnancy or seminal transfer to a pregnant sexual partner when risk is either unknown or anticipated.

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 assessment of male-mediated developmental risk for pharmaceuticals. It does not establish any 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 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 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: June 8, 2015.

Leslie Kux,

Associate Commissioner for Policy.

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