

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2008-D-0065 (formerly Docket No. 2005D-0203)]

Guidance for Industry on Safety Testing of Drug Metabolites; 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 "Safety Testing of Drug Metabolites." This guidance provides recommendations to industry on when and how to identify and characterize drug metabolites whose nonclinical toxicity needs to be evaluated. It also provides recommendations on the timing and type of nonclinical studies that should be conducted to investigate the potential for clinical toxicity of drug metabolites. This guidance applies to small molecule nonbiologic drug products under development. This guidance finalizes the draft guidance published on June 6, 2005.

DATES: Submit written or electronic comments on agency guidances at any time.

ADDRESSES: Submit written requests for single copies of this guidance to the Division of Drug Information (HFD-240), 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 Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. Submit electronic comments to <http://>

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Certifier D. Hawkins

/www.regulations.gov. See the **SUPPLEMENTARY INFORMATION** section for electronic access to the guidance document.

FOR FURTHER INFORMATION CONTACT: Aisar Atrakchi, Center for Drug Evaluation and Research (HFD-130), Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 22, rm. 4384, Silver Spring, MD 20993-0002, 301-796-1036.

SUPPLEMENTARY INFORMATION:

I. Background

FDA is announcing the availability of a guidance for industry entitled “Safety Testing of Drug Metabolites.” This guidance addresses drug metabolites of small molecule nonbiologic drug products and does not apply to some cancer products. It applies to drug metabolites that are not adequately evaluated in standard toxicology testing with the parent drug. This can happen if the metabolite is present only in humans or if it is present at higher levels (referred to in the guidance as “disproportionate drug metabolite”) in humans than in any of the animal toxicology test species. The guidance provides recommendations on the timing and types of nonclinical safety studies that should be conducted for drug metabolites that are present at greater than 10 percent of the parent drug systemic exposure as measured in plasma.

A draft version of this guidance was made available for public comment in 2005 (70 FR 32839, June 6, 2005). All of the public comments we received have been considered and the guidance was revised as appropriate.

This guidance is being issued consistent with FDA’s good guidance practices regulation (21 CFR 10.115). The guidance represents the agency’s current thinking on the safety testing of drug metabolites. 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. Comments

Interested persons may submit to the Division of Dockets Management (see **ADDRESSES**) written or electronic comments regarding this document. Submit a single copy of electronic comments or two paper copies of any mailed comments, except that individuals may submit one paper copy. Comments are to be identified 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.

Please note that on January 15, 2008, the FDA Web site transitioned to the Federal Dockets Management System (FDMS). FDMS is a Government-wide, electronic docket management system. Electronic submissions will be accepted by FDA through FDMS only.

III. Electronic Access

Persons with access to the Internet may obtain the document at either <http://www.fda.gov/cder/guidance/index.htm> or <http://www.fda.gov/ohrms/dockets/default.htm>.

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JS
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Jeffrey Shuren,
Assistant Commissioner for Policy.

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