

**DEPARTMENT OF HEALTH AND HUMAN SERVICES****Food and Drug Administration**

[Docket No. 2005D-0203]

**Draft Guidance for Industry on Safety Testing of Drug Metabolites; Availability****AGENCY:** Food and Drug Administration, HHS.**ACTION:** Notice.

**SUMMARY:** The Food and Drug Administration (FDA) is announcing the availability of a draft guidance for industry entitled "Safety Testing of Drug Metabolites." This draft guidance provides recommendations on the safety assessment of unique or major human metabolites of small molecule (nonbiologic) therapeutic products under development. This draft guidance is intended to serve as a resource for general testing considerations as well as provide recommendations on the timing of these studies in relation to the clinical development.

**DATES:** Submit written or electronic comments on the draft guidance by August 5, 2005. General comments on agency guidance documents are welcome at any time.

**ADDRESSES:** Submit written requests for single copies of the draft guidance to the Division of Drug Information (HFD-240), Center for Drug Evaluation and Research, Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857.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 Submit written comments on the draft guidance to the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852.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://www.fda.gov/dockets/ecomments>. See the **SUPPLEMENTARY INFORMATION** section for electronic access to the draft guidance document.

**FOR FURTHER INFORMATION CONTACT:**

Aisar Atrakchi, Center for Drug Evaluation and Research (HFD-120), Food and Drug Administration, 1451 Rockville Pike, Rockville, MD 20852, 301-594-2850.

**SUPPLEMENTARY INFORMATION:****I. Background**

FDA is announcing the availability of a draft guidance for industry entitled "Safety Testing of Drug Metabolites." There are quantitative and qualitative differences in metabolic profiles across species. These differences become

important when exposure parameters of a drug in a nonclinical species are used to assess safety in humans during risk assessment. In the past, contribution of metabolites to the overall toxicological potential of the parent drug was generally unknown or not considered; analytical technologies to identify and measure metabolites have only become available over the past decade.

Although in general there is adequate correlation in metabolic profiles between humans and those obtained in standard nonclinical safety studies, there are, however, cases when these studies do not adequately evaluate clinically relevant and/or biologically active metabolites. This may be due to such metabolites being unique to humans or present at very low levels in the animal species used in the standard toxicity studies. As a result, FDA has developed a draft guidance to provide recommendations on the safety assessment of unique or major human metabolites of small molecule (nonbiologic) therapeutic products. These recommendations should help applicants conduct adequate safety assessments of metabolites.

This draft guidance provides general testing considerations for unique or major drug metabolites including study design, identification of metabolites, structure activity relationship, and types of nonclinical studies needed to assess metabolite toxicity. It also addresses the timing of these studies in relation to the clinical development.

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 agency's current thinking on 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 the 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.

**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>.

Dated: May 27, 2005.

**Jeffrey Shuren,***Assistant Commissioner for Policy.*

[FR Doc. 05-11205 Filed 6-3-05; 8:45 am]

**BILLING CODE 4160-01-S****DEPARTMENT OF HOMELAND SECURITY****Coast Guard**

[USCG-2005-21322]

**Collection of Information Under Review by Office of Management and Budget (OMB): OMB Control Number: 1625-0015****AGENCY:** Coast Guard, DHS.**ACTION:** Request for comments.

**SUMMARY:** In compliance with the Paperwork Reduction Act of 1995, the Coast Guard intends to seek the approval of OMB for the renewal of one Information Collection Request (ICR). The ICR is for 1625-0015, Bridge Permit Application Guide. Before submitting the ICR to OMB, the Coast Guard is inviting comments on it as described below.

**DATES:** Comments must reach the Coast Guard on or before August 5, 2005.

**ADDRESSES:** To make sure that your comments and related material do not enter the docket [USCG-2005-21322] more than once, please submit them by only one of the following means:

(1) By mail to the Docket Management Facility, U.S. Department of Transportation (DOT), room PL-401, 400 Seventh Street, SW., Washington, DC 20590-0001.

(2) By delivery to room PL-401 on the Plaza level of the Nassif Building, 400 Seventh Street SW., Washington, DC, between 9 a.m. and 5 p.m., Monday through Friday, except Federal holidays. The telephone number is 202-366-9329.

(3) By fax to the Docket Management Facility at 202-493-2251.

(4) Electronically through the Web site for the Docket Management System at <http://dms.dot.gov>.

The Docket Management Facility maintains the public docket for this notice. Comments and material received from the public, as well as documents mentioned in this notice as being available in the docket, will become part

of this docket and will be available for inspection or copying at room PL-401 on the Plaza level of the Nassif Building, 400 Seventh Street, SW., Washington, DC, between 9 a.m. and 5 p.m., Monday through Friday, except Federal holidays. You may also find this docket on the Internet at <http://dms.dot.gov>.

Copies of the complete ICR are available through this docket on the Internet at <http://dms.dot.gov>, and also from Commandant (CG-611), U.S. Coast Guard Headquarters, room 6106 (Attn: Ms. Barbara Davis), 2100 Second Street, SW., Washington, DC 20593-0001. The telephone number is 202-267-2326.

**FOR FURTHER INFORMATION CONTACT:** Ms. Barbara Davis, Office of Information Management, telephone 202-267-2326, or fax 202-267-4814, for questions on these documents; or telephone Ms. Andrea M. Jenkins, Program Manager, Docket Operations, 202-366-0271, for questions on the docket.

**SUPPLEMENTARY INFORMATION:**

**Public Participation and Request for Comments**

We encourage you to respond to this request for comments by submitting comments and related materials. We will post all comments received, without change, to <http://dms.dot.gov>, and they will include any personal information you have provided. We have an agreement with DOT to use the Docket Management Facility. Please see the paragraph on DOT's "Privacy Act Policy" below.

**Submitting Comments**

If you submit a comment, please include your name and address, identify the docket number for this request for comment [USCG-2005-21322], indicate the specific section of this document to which each comment applies, and give the reason for each comment. You may submit your comments and material by electronic means, mail, fax, or delivery to the Docket Management Facility at the address under **ADDRESSES**; but please submit them by only one means. If you submit them by mail or delivery, submit them in an unbound format, no larger than 8½ by 11 inches, suitable for copying and electronic filing. If you submit them by mail and would like to know that they reached the Facility, please enclose a stamped, self-addressed postcard or envelope. We will consider all comments and material received during the comment period. We may change the documents supporting this collection of information or even the underlying requirements in view of them.

**Viewing Comments and Documents**

To view comments, as well as documents mentioned in this notice as being available in the docket, go to <http://dms.dot.gov> at any time and conduct a simple search using the docket number. You may also visit the Docket Management Facility in room PL-401 on the Plaza level of the Nassif Building, 400 Seventh Street, SW., Washington, DC, between 9 a.m. and 5 p.m., Monday through Friday, except Federal holidays.

**Privacy Act**

Anyone can search the electronic form of all comments received in dockets by the name of the individual submitting the comment (or signing the comment, if submitted on behalf of an association, business, labor union, etc.). You may review the Privacy Act Statement of DOT in the **Federal Register** published on April 11, 2000 (65 FR 19477), or you may visit <http://dms.dot.gov>.

**Information Collection Request**

*Title:* Bridge Permit Application Guide.

*OMB Control Number:* 1625-0015.

*Summary:* The collection of information is a request for a bridge permit submitted as an application for approval by the Coast Guard of any proposed bridge project. An applicant must submit to the Coast Guard a letter of application along with letter-size drawings (plans) and maps showing the proposed project and its location.

*Need:* 33 U.S.C. 401, 491, 525, and 535 authorize the Coast Guard to approve plans and locations for all bridges and causeways that go over navigable waters of the United States.

*Respondents:* Public and private owners of bridges over navigable waters of the United States.

*Frequency:* On occasion.

*Burden Estimate:* The estimated burden has been decreased from 4,000 hours to 2,240 hours a year.

Dated: May 26, 2005.

**Nathaniel Heiner,**

*Acting, Assistant Commandant for Command, Control, Communications, Computers and Information Technology.*

[FR Doc. 05-11169 Filed 6-3-05; 8:45 am]

**BILLING CODE 4910-15-P**

**DEPARTMENT OF THE INTERIOR**

**Office of the Secretary**

**Notice of Final Changes to Procedures**

**AGENCY:** Department of the Interior.

**ACTION:** Notice of final changes to procedures.

**SUMMARY:** These changes to procedures modify the Departmental Manual at 516 DM 2.5, Cooperating Agencies (40 CFR 1501.6). These procedures clarify the responsibility of managers to offer this status to qualified agencies and governments, and to respond to requests for this status. These procedures also make clear the role of cooperating agencies in the implementation of the Department's National Environmental Policy Act (NEPA) compliance process. With this publication of these procedures they will be added to the Electronic Library of Interior Policies (ELIPS). ELIPS is located at: <http://elips.doi.gov/>.

The changes to the procedures are necessary to emphasize the importance of working with Federal and State agencies and Tribal and local governments through cooperating agency relationships in preparing environmental impact statements under NEPA.

**FOR FURTHER INFORMATION CONTACT:** Vijai N. Rai, Team Leader, Natural Resources Management, Office of Environmental Policy and Compliance; 1849 C Street, NW., Washington, DC 20240.

Telephone: 202-208-6661. e-mail: [vijai\\_rai@ios.doi.gov](mailto:vijai_rai@ios.doi.gov). Persons who use a telecommunications device for the deaf (TDD) may call the Federal Information Relay Service (FIRS) at 1-800-877-8339, 24 hours a day, 7 days a week.

**SUPPLEMENTARY INFORMATION:** This section provides general information, background, a summary of comments and responses, and procedural requirements.

*General Information:* In an Executive Order (EO 13352) on Facilitation of Cooperative Conservation, the President seeks to ensure that certain Federal agencies, including the Department of the Interior, implement laws relating to the environment and natural resources in a manner that promotes cooperative conservation. The EO emphasizes appropriate local participation in Federal decision-making, in accordance with agencies' respective agency missions, policies, and regulations.

In an effort to carry out the intent of EO 13352, the Department of the Interior is strengthening its National Environmental Policy Act (NEPA) implementing procedures which appear in part 516 of the Departmental Manual (DM) at 516 DM 2.5 on Cooperating Agencies. Consistent with both EO 13352 and the Secretary of the Interior's "4C's" policy, that is, Conservation through Communication, Consultation, and Cooperation, these revised