

## DEPARTMENT OF HEALTH AND HUMAN SERVICES

### Food and Drug Administration

[Docket No. 2005D–0033]

### Draft Guidance for Industry on Internal Radioactive Contamination— Development of Decorporation Agents; Availability

**AGENCY:** Food and Drug Administration, HHS.

**ACTION:** Notice.

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**SUMMARY:** The Food and Drug Administration (FDA) is announcing the availability of a draft guidance for industry entitled “Internal Radioactive Contamination—Development of Decorporation Agents.” This draft document provides guidance to industry on the development of decorporation agents for the treatment of internal radioactive contamination when evidence is needed to demonstrate the effectiveness of the agents, but human efficacy studies are unethical or infeasible. In such instances, the Animal Efficacy Rule may be invoked to approve new medical products not previously marketed or new indications for previously marketed products. Specifically, this draft guidance addresses chemistry, manufacturing and controls (CMC) information; animal efficacy, safety pharmacology, and toxicology studies; clinical pharmacology, biopharmaceutics, and human safety studies; and postapproval commitments.

**DATES:** Submit written or electronic comments on the draft guidance by [*insert date 90 days after date of publication in the **Federal Register***]. General comments on agency guidance documents are welcome at any time.

**ADDRESSES:** Submit written requests for single copies of this draft guidance to the Division of Drug Information (HFD–240), Center for Drug Evaluation and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 Submit written comments on the draft guidance to the Division of Dockets Management (HFA–305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852.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 guidance document.

**FOR FURTHER INFORMATION CONTACT:** Patricia A. Stewart, Center for Drug Evaluation and Research (HFD–160), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301–827–7510.

**SUPPLEMENTARY INFORMATION:**

**I. Background**

FDA is announcing the availability of a draft guidance for industry entitled “Internal Radioactive Contamination—Development of Decorporation Agents.” This draft guidance is being issued to facilitate the development of new decorporation agents or new uses of previously marketed medical products for the treatment of internal radioactive contamination.

Internal radioactive contamination can arise from accidents involving nuclear reactors, industrial sources, or medical sources. The potential for such accidents has been present for many years. Recent events also have highlighted the potential for nonaccidental radioactive contamination as a result of malicious, criminal, or terrorist actions. Internal contamination occurs when radioactive material is ingested, inhaled, or absorbed from a contaminated wound. As long as these radioactive contaminants remain in the body, they may pose significant health risks. Long-term health concerns include the potential for the development of cancers of the lung, liver, thyroid, stomach,

and bone and, when a radioactive contaminant is inhaled, for the development of fibrotic changes in the lung that may lead to restrictive lung disease. The only effective method of reducing these risks is removal of the radioactive contaminants from the body.

“Decorporation agents” refer to medical products that increase the rate of elimination or excretion of inhaled, ingested, or absorbed radioactive contaminants. The effectiveness of most decorporation agents for the treatment of internal radioactive contamination cannot be tested in humans because the occurrence of accidental or nonaccidental radioactive contamination is rare, and it would be unethical to deliberately contaminate human volunteers with potentially harmful amounts of radioactive materials for investigational purposes.

FDA is issuing this draft guidance to facilitate the development of new decorporation agents or new indications for previously marketed medical products that may be eligible for approval under the Animal Efficacy Rule (21 CFR part 314, subpart I and 21 CFR part 601, subpart H). As set forth in this rule, under certain circumstances animal studies can be relied on to provide substantial evidence of effectiveness of a product. Evaluation of the product for safety in humans is still required, and cannot be addressed by animal studies alone. The adequacy of human safety data will need to be assessed from clinical pharmacology and safety studies conducted in humans. This draft guidance addresses the design and conduct of the requisite CMC, animal efficacy, safety pharmacology, toxicology, clinical pharmacology, biopharmaceutics, and human safety studies needed to support approval of new decorporation agents or new uses of previously marketed medical products for the treatment of internal radioactive contamination.

In addition, approval under the Animal Efficacy Rule is subject to certain postapproval commitments, including submission of a plan for conducting postmarketing studies that would be feasible should an accidental or intentional release of radiation occur, postmarketing restrictions to ensure safe use, if deemed necessary, and product labeling information intended for the patient advising that, among other things, the product's approval was based on effectiveness studies conducted in animals alone. This draft guidance addresses the postapproval commitments that would be needed for approval of a new decorporation agent or for a new indication for a previously approved agent under the Animal Efficacy Rule.

This draft 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 development of decorporation agents for the treatment of internal radioactive contamination. 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 on the guidance at any time. Two copies of mailed comments are to be submitted, except that individuals may submit one copy. Comments are to be identified with the docket number found in brackets in the heading of this document. The draft guidance and received comments are available for public examination 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: February 4, 2005.

**Jeffrey Shuren,**

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