

**MEMORANDUM OF UNDERSTANDING
BETWEEN THE
U.S. NUCLEAR REGULATORY COMMISSION
AND THE
U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION**

The Nuclear Regulatory Commission (NRC) and the Food and Drug Administration (FDA), Department of Health and Human Services (DHHS), have regulatory responsibilities concerning medical devices, drugs, and biological products utilizing byproduct, source, or special nuclear material. The organizations in FDA that are principally responsible for these products are the Center for Devices and Radiological Health (CDRH), the Center for Drug Evaluation and Research (CDER), and the Center for Biologics Evaluation and Research (CBER). The organizations in NRC that are principally responsible for these products are the Office of Nuclear Material Safety and Safeguards (NMSS), the Office of Nuclear Reactor Regulation (NRR), and the Office of State and Tribal Programs (OSTP). For their respective authorities, the agencies hereby agree as follows:

I. Purpose and Scope

- A. The purpose of this Memorandum of Understanding (MOU) is to coordinate existing NRC and FDA regulatory programs for (1) medical devices, drugs, and biological products utilizing byproduct, source, or special nuclear material; and (2) the use of potassium iodide (KI) in response to events involving accidental release of radioactive iodine. These regulatory programs include activities for evaluating and authorizing the manufacture, sale, distribution, licensing, and labeled intended use of such products.
- B. This MOU covers (1) medical devices, drugs, and biological products utilizing byproduct, source, or special nuclear material regulated under the Atomic Energy Act of 1954, as amended; and (2) the use of potassium iodide (KI) in response to events involving accidental release of radioactive iodine. The terms "drug" and "device" are defined in the Federal Food, Drug, and Cosmetic Act, as amended (21 USC 321(g) and (h)), and "biological product" is defined in the Public Health Service Act (42 USC 262). A biological product may be either a drug or device and is described in Part II, FDA, of this MOU. The terms "byproduct material," "source material," and "special nuclear material" are defined in Section 11(e), (z), and (aa) of the Atomic Energy Act of 1954, as amended, and described in Part II, NRC, of this MOU.

Medical devices affected by this MOU include, but are not limited to: in vitro diagnostic kits (radioimmunoassay); utilization facilities licensed to perform medical therapy; and teletherapy and brachytherapy sources, systems, and accessory devices. Biologics affected by this MOU include, but are not limited to: licensed in vitro diagnostic kits (radioimmunoassay), and radiolabeled biologics. Drugs affected by this MOU include all those that contain byproduct,

source, or special nuclear material and potassium iodide.

II Authority and Regulatory Program

A. FDA

FDA is responsible for assuring the safety, effectiveness, and proper labeling of medical products, i.e., drugs, devices, and biological products.

1. FDA/CDRH

The principal statute under which FDA/CDRH regulates devices is the Federal Food, Drug, and Cosmetic Act, as amended by the Medical Device Amendments of 1976; the Safe Medical Devices Act of 1990; the Medical Devices Act of 1992; the Food, Drug Modernization Act of 1997; and the Medical Device User Fee and Modernization Act of 2002.

Section 201(h) of the Federal Food, Drug, and Cosmetic Act, as amended, defines "device" as follows:

"The term "device" means an instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article, including any component, part, or accessory, which is --

- 1) Recognized in the official National Formulary, or the United States Pharmacopeia, or any supplement to them;
- 2) Intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease, in man or other animals;
- 3) Intended to affect the structure or any function of the body of man or other animals, and which does not achieve its primary intended purposes through chemical action within or on the body of man or other animals, and which is not dependent upon being metabolized for the achievement of its primary intended purposes.

FDA/CDRH programs intended to ensure the safety and effectiveness of devices include, but are not limited to, the following:

- 1) Review of investigational device exemptions, premarket notification (510(k)), premarket approval (PMA);
- 2) Review of voluntary and mandatory medical device reports; and
- 3) Enforcement activities such as routine and directed inspections, and enforcement activities such as product removal, recall, warning letters, and

case actions such as seizure, injunction, prosecution, and civil penalties.

2. FDA/CDER

The principal statute under which FDA/CDER regulates drugs for human use is the Federal Food, Drug, and Cosmetic Act, as amended.

Section 201(g)(1) of the Federal Food, Drug, and Cosmetic Act, as amended, defines "drug" as follows:

The term "drug" means:

- 1) Articles recognized in the official United States Pharmacopeia, official Homeopathic Pharmacopeia of the United States, or official National Formulary, or any supplement to any of them; and
- 2) Articles intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease in man or other animals; and
- 3) Articles (other than food) intended to affect the structure or any function of the body of man or other animals; and
- 4) Articles intended for use as a component of any articles specified in clause (1), (2), or (3).

FDA/CDER functions intended to ensure the effectiveness, safety, and quality of drugs for human use include, but are not limited to, the following:

- 1) Review of clinical and bioavailability studies, manufacturing processes, and testing methods;
- 2) Review of voluntary and mandatory adverse reaction reports and drug product defect reports; and
- 3) Enforcement activities such as routine and directed inspections, product removal, recall, warning letters, and case actions such as seizure, injunction, prosecution, and civil penalties.
- 4) Issuance of guidance to other federal agencies, and state and local governments, regarding the safe and effective use of potassium iodide (KI), for use in the development of emergency response plans for events involving accidental release of radioactive iodine.

3. FDA/CBER

The principal statute under which FDA/CBER regulates biological products is the Public Health Service Act.

However, biological products also meet the definition of either a drug or device under the

Federal Food, Drug, and Cosmetic Act, as amended.

Section 351(I) of the Public Health Service Act defines a biological product as, "a virus, therapeutic serum, toxin, or antitoxin, vaccine, blood, blood component or derivative or arsphenamine (or any other trivalent organic arsenic compound), applicable to the prevention, treatment or cure, of a disease or condition of human beings."

FDA/CBER functions intended to ensure the effectiveness, safety, and quality of biological products for human use include, but are not limited to, the following:

- 1) Review of clinical and bioavailability studies, manufacturing processes, and testing methods;
- 2) Review of voluntary and mandatory adverse reaction reports and biological product deviation reporting; and
- 3) Enforcement activities such as routine and directed inspections, and enforcement activities such as product removal, recall, warning letters, and case actions such as seizure, injunction, prosecution, license revocation and suspension, and civil penalties.

B. NRC

NRC is responsible for licensing and regulating nuclear facilities and material and for conducting research in support of the licensing and regulatory process, as mandated by the Atomic Energy Act of 1954, as amended; the Energy Reorganization Act of 1974, as amended; and in accordance with the National Environmental Policy Act of 1969, as amended, and other applicable statutes. NRC responsibilities include protecting public health and safety, protecting the environment, and safeguarding materials in the interest of national security.

1. NRC/NMSS

NMSS's responsibilities for the medical use of byproduct, source, and special nuclear material include, but are not limited to:

- 1) Licensing and inspection of medical, industrial, academic and commercial uses of byproduct material;
- 2) Development and implementation of NRC policy for the regulation of activities involving safety, quality, approval, and inspection and enforcement regarding the use and handling of byproduct, source, or special nuclear materials;
- 3) Reviewing of sealed sources or devices to provide reasonable assurances that the radiation safety properties of the source or device are adequate to protect health and minimize danger to life and property; and
- 4) Monitoring and investigation, as necessary, of medical events as defined

in 10 CFR 35.2, which occur during the intentional internal or external administration of byproduct, source, special nuclear material, or radiation therefrom, to human beings in the practice of medicine.

2. NRC/OSTP

OSTP's responsibilities for the medical use of byproduct, source, and special nuclear materials include, but are not limited to:

- 1) Negotiation of Agreements with States under section 274 of the Atomic Energy Act of 1954, as amended;
- 2) Evaluation of the program of a new Agreement State to determine if it is adequate to protect the public health and safety, and if it is compatible with the NRC program;
- 3) Periodic evaluation of the Agreement State programs to determine continued adequacy and compatibility;
- 4) Training of, and consultation with, Agreement States on radiological public health and safety issues.

3. NRC/NRR

NRR=s responsibilities include, but are not limited to:

- 1) Licensing and inspection of utilization facilities for medical therapy, pursuant to 10 CFR 50.21 and 10 CFR 50.41;
- 2) Development and implementation of NRC policy for the regulation of activities involving safety, quality, approval, and inspection and enforcement regarding the use of utilization facilities for medical therapy;
- 3) Oversight of production of byproduct materials at facilities licensed under 10 CFR Part 50; and
- 4) Development of policy and requirements for emergency planning, which reflect FDA guidance on the use of potassium iodide, for events involving the accidental release of radioactive iodine.

4. NRC/NSIR

NSIR=s responsibilities include, but are not limited to:

- 1) Developing overall NRC policy and providing management direction for evaluation and assessment of technical issues involving security at nuclear facilities;
- 2) NRC safeguards and security interface with the Office of Homeland Security and other agencies;
- 3) Directs the NRC program for response to incidents; and

- 4) NRC interface with the Federal Emergency Management Agency, FDA, and other Federal agencies on incidents involving nuclear materials.

1. Agreement States

Under section 274 of the Atomic Energy Act of 1954, as amended, the Commission is authorized to discontinue its regulatory authority for certain radioactive materials if a State has a program that is adequate to protect the public health and safety and compatible with NRC's program. The transfer of this regulatory authority is executed through an Agreement between the NRC and the Governor of a State. Agreement States use their own authority to regulate these materials.

III. Elements of Coordination

- A. Notification of Product Complaints, Medical Events, or Emergency Situations

Both agencies agree to promptly inform each other whenever they receive a report or otherwise become aware of a potential public health problem such as a malfunction, failure, or a medical event involving products of mutual regulatory concern. Each agency will assign one or more contact persons in order to ensure that such information is promptly exchanged and that appropriate FDA and/or NRC actions are initiated on the basis of any necessary compliance or follow-up objectives. Each agency will promptly notify the other when there is a change in an assigned contact person.

- B. Coordination of Investigations

Upon request, FDA and NRC will assist each other, to the fullest extent possible, in the investigation of incidents or complaints involving products of mutual regulatory concern.

For the purposes of this MOU, investigations will be considered to include inspections in response to incidents or events, as well as, formal investigations initiated in accordance with each agency's internal procedures, (Agreement States will be involved as appropriate to the specific situation). During the term of this agreement, joint inspections or observer invitations can be requested or extended by either agency, when deemed necessary, to ensure that information obtained from an investigation is collected, shared and acted upon in a timely and coordinated manner. Both agencies will make every reasonable effort to accommodate joint inspection or observer requests depending upon availability of personnel and current FDA or NRC priorities. Each agency will assign one or more persons to assure that investigations are coordinated in a manner that maximizes regulatory efficiency and minimizes duplication of effort. Each agency will promptly notify the other when there is a change in an assigned contact person.

1. Investigation Information Exchange

Both agencies agree to an exchange of information with respect to investigations and inspections. The purpose of these exchanges is to provide expert technical assistance to either agency and to assist either agency by reducing or eliminating any duplication of effort. The sharing of information between FDA and NRC (and Agreement States as appropriate) will be exercised to the extent authorized by law, and by NRC and FDA directives, statutes, and regulations, and will be consistent with the respective agency's mission.

Both agencies recognize the need to protect from public disclosure, data and information that are exchanged between the agencies and that fall within the definition of trade secret, or confidential commercial or financial information. Both agencies agree to exchange proprietary information in accordance with applicable regulations. If FDA provides NRC with trade secret information, there shall be an additional written agreement in the form of an exchange of letters between the appropriate liaison officers in accordance with 21 CFR 20.90. If a request calls for a disclosure determination regarding proprietary information such as a Freedom of Information Act request, response to a Congressional inquiry, or in cases where either agency must comply with various regulatory or public information responsibilities, for any such information obtained from the other agency, that agency will be notified of the request. The notified agency will be responsible for making any needed contact with the submitter of the protected information and accept the responsibility for evaluating the submitter's comments prior to rendering the disclosure determination.

To reserve the right of maximum control over actual disclosure of its own records, each agency shall retain legal authority and the commensurate responsibility over disclosure of those documents provided to the other agency.

Upon request, FDA and NRC will:

- 1) provide copies of Establishment or User Site Inspection Reports;
- 2) provide copies of all analytical data and correspondence of significance related to investigations or activities associated with an area of mutual regulatory concern;
- 3) provide copies of official legal or compliance actions taken against firms or licensees of mutual interest; and
- 4) participate in meetings with regulated industry covering issues of mutual regulatory concern.

2. NRC Licensee and Agreement State Notifications

Upon request, NRC will promptly notify NRC licensees and Agreement State Program Directors of any public health issues or other important user communications initiated by FDA as the result of joint investigations or other activities involving products of mutual regulatory concern.

C. Product Premarketing and Prelicensing Information Exchange

To the extent practicable the two agencies will share information concerning new technology or methods under development or review, including devices, drugs, or biologics, for which regulations have not yet been developed, or which is related to the mission of the other agency. Both agencies agree to exchange proprietary information in accordance with applicable regulations. If FDA provides NRC with trade secret information, there shall be an additional written agreement in the form of an exchange of letters between the appropriate liaison officers in accordance with 21 CFR 20.90.

This information will include, but is not limited to:

- 1) design, chemical and physical form of the material or the device
- 2) manufacture/preparation
- 3) prototype testing
- 4) quality assurance and control
- 5) labeling per regulatory requirements
- 6) intended use
- 7) safety analysis
- 8) installation
- 9) servicing
- 10) leak testing
- 11) operating instructions;
- 12) emergency/safety instructions.

D. Sharing of Other Information

FDA and NRC will offer each other the opportunity to comment on notifications to manufacturers, operators, licensees, or patients. FDA and NRC will also offer each other the opportunity to comment on regulations, regulatory guides or other communications that refer to activities, policies, or regulations of the other agency. If practicable, the documents will be provided prior to issuance.

Either agency may request additional information when deemed necessary to complete its mission.

E. Advisory Committees

NRC and FDA will make the other agency aware of and, to the extent possible, allow participation by a representative from the other agency in any Advisory Committee which advises on issues related to this MOU.

IV Name and Mailing Address of Participating Agencies

Food and Drug Administration
5600 Fishers Lane
Rockville, MD 20857

and the

Nuclear Regulatory Commission
Washington, D.C. 20555-0001

V. Liaison Officers

Each liaison officer will establish and maintain a call list of responsible persons within his or her organization. These call lists will designate specific persons for day-to-day contact on matters related to this MOU. These lists with current work and home phone numbers will be exchanged among the liaison officers.

Liaison officers are as follows:

A. For the Food and Drug Administration

Center for Devices and Radiological Health
Director, Office of Compliance
2094 Gaither Road
Rockville, MD 20850
Telephone: 301-594-4692

Center for Drug Evaluation and Research
Director, Executive Operations
1451 Rockville Pike
Rockville, MD 20852
Telephone: 301-594-5400

Center for Biologic Evaluation and Research
Deputy Director for Medicine, Office of Compliance
1401 Rockville Pike

Rockville, MD 20852
Telephone: 301-827-3028

Center for Food Safety and Applied Nutrition
Director of Compliance, Office of Premarket Approval,
200 C Street, SW
Washington, D.C. 20204
Telephone: 202-418-3093

Center for Veterinary Medicine
Director
Office of Surveillance and Compliance
7500 Standish Place
Rockville, MD 20855
Telephone: 301-827-1168

B. For the Nuclear Regulatory Commission

Director, Office of Nuclear Material Safety
and Safeguards
11545 Rockville Pike
Rockville, MD 20852
Telephone: 301-415-7800

Director, Office of Nuclear Reactor Regulation
11545 Rockville Pike
Rockville, MD 20852
Telephone: 301-415-2223

Director, Office of Nuclear Security and
Incident Response
11545 Rockville Pike
Rockville, MD 20852
Telephone: 301-415-7476

VI. Annual Inter-Agency Meeting

The liaison officers shall meet at least annually to evaluate the activities related to this MOU. FDA and NRC will host the meeting on alternating years.

VII. Other Laws and Matters

Nothing in this Memorandum of Understanding shall be deemed to restrict, modify, or otherwise limit the application or enforcement of any laws of the United States with respect to matters specified herein, nor shall anything in the Memorandum be construed as modifying the existing authority of either agency.

VIII. Effective Date, Modification and Termination of MOU

This MOU will take effect when it has been signed by the authorized representatives of FDA and NRC. It may be modified by mutual written consent or terminated by either agency upon a sixty (60) day advance written notice to the other agency.

APPROVED AND ACCEPTED FOR THE
NUCLEAR REGULATORY COMMISSION

BY: William D. Travers

TITLE: Executive Director of Operations

DATE: William Travers 12/4/02

APPROVED AND ACCEPTED FOR THE
FOOD AND DRUG ADMINISTRATION

BY: Philip J. Frappalo

TITLE: Philip J. Frappalo
Director, Office of Compliance
(Acting)

DATE: November 19, 2002