FREQUENTLY ASKED QUESTIONS
FOR
LICENSING OF EMERGING MEDICAL TECHNOLOGIES

The NRC developed these questions and answers as guidance to illustrate issues that may arise in licensing material under Part 35, Subpart K, Other Medical Uses of Byproduct Material or Radiation from Byproduct Material (i.e. 10 CFR 35.1000).

1. What is 10 CFR 35.1000 licensing?

The medical use of radioactive material is regulated in Title 10 of the Code of Federal Regulations (CFR), Part 35. Medical uses in 10 CFR Part 35 are divided into categories based on the type of material and the purpose of use. The categories are as follows:

- Use of unsealed byproduct material for uptake, dilution, and excretion studies for which a written directive is not required (10 CFR 35, Subpart D)
- Use of unsealed byproduct material for imaging and localization studies for which a written directive is not required (10 CFR 35, Subpart D)
- Use of unsealed byproduct material for which a written directive is required (Subpart E)
- Use of sealed sources for brachytherapy (10 CFR 35, Subpart F)
- Use of sealed sources and medical devices for diagnosis (10 CFR 35, Subpart G)
- Use of sealed sources in remote afterloader unit, teletherapy unit, or gamma stereotactic radiosurgery unit (10 CFR 35, Subpart H)
- Other medical uses of byproduct material or radiation from byproduct material (10 CFR 35, Subpart K)

10 CFR 35, Subpart K, or 10 CFR 35.1000, is a separate category to capture medical uses that are not addressed by the other categories described in 10 CFR Part 35 (i.e. 10 CFR 35 Subparts D through H) because of their unique use or other radiation safety properties. The regulations in 10 CFR 35.1000 are broadly construed to allow for the timely licensing of a wide range of new technologies that may become available in the future for patient treatment without the need for new rulemaking. 10 CFR 35.1000 use can consist of a new radionuclide in unsealed or sealed form, or a sealed source in a device that is unique or novel in its use for patient treatment.

Current regulations can be found at 10 CFR Part 35, Medical Use of Byproduct Material. More detail about the NRC oversight and licensing of medical use of byproduct material can be found at the Medical Uses Licensee Toolkit page and the Frequently Asked Questions About Licensing Medical Uses of Byproduct Material Under Revised 10 CFR Part 35 page, available at https://www.nrc.gov/materials/miau/med-use-toolkit/faqs-part35.html.

2. How is 10 CFR 35.1000 use regulated?

A new emerging medical technology (EMT) may be categorized in any of the categories listed in 10 CFR Part 35 (see Question no. 1) based on its design and the function. The NRC staff reviews a new EMT when there is a question about which category its medical use should be licensed under. If the NRC staff determines the use of the new EMT is not specifically addressed in 10 CFR Subparts D through H, it will be required to be licensed under Subpart K, 10 CFR 35.1000, and the staff will issue licensing guidance specific to the new EMT.

Licensing guidance contains acceptable means of satisfying the requirements in 10 CFR 30.33, General requirements for issuance of specific licenses; 10 CFR 35.12, Application for license, amendment or renewal; and a set of regulations and specific conditions which the Commission considers acceptable framework for the medical use of the EMT. However, the licensing guidance is not intended to be the only means of satisfying the NRC's requirements. The applicant may submit alternative information and commitments for the NRC staff to make a licensing determination. Examples of NRC-issued licensing guidance can be found at https://www.nrc.gov/materials/miau/med-use-toolkit/emerg-licensed-med-tech.html.

3. What topics are discussed in Licensing Guidance?

The following are topics commonly described in the licensing guidance. The topics for a specific guidance may be different depending on the characteristics of the EMT.

- Device Description
- Radionuclides, Form, Possession Limits, and Purpose of Use
- Training and Experience
- License Conditions
    - Procedures for Administration
    - Medical Event Reporting
    - Labeling
    - Surveys
    - Calibration
    - Contamination Control
    - Radiation Protection Program Changes
- Written Directives
- Patient Release
- Sealed Source and Device Registry

4. What information does NRC staff need to review a new EMT?

The NRC staff's Medical Safety and Events Assessment Branch (MSEB) will review available information and work with a vendor or manufacturer and early users, if available, to understand the radiation safety profile of the EMT. It is very helpful for the vendor or manufacturer to designate a point of contact for any additional questions the NRC staff may have regarding the EMT.

To begin a review of an EMT, the staff will review information available about the EMT such as the radionuclide involved, the activity, the physical form of the material, the type of radiopharmaceutical or source, delivery device or apparatus, and the business website with information about the product. Further, the NRC staff evaluates how the material is administered, planned administered activity or delivered dose, and the target organ or treatment site. Additionally, the staff may ask information pertaining to the radiation safety precautions and instructions, methodology for measurement of dosages or doses to be administered to patients, and the calibration, maintenance, and repair of instruments and equipment necessary for radiation safety. Most of this information is contained in the Vendor's Instructions for Use (IFU) product document and if applicable, the Device Description (DD).

The NRC staff will use this information to determine if the EMT is addressed in a Subpart D through H. If it is, the NRC staff will recommend the traditional subpart for licensing and may issue supplemental licensing guidance to be used with NUREG 1556, Volume 9 as necessary. However, if the EMT is not addressed in one of those subparts, the NRC will recommend licensing under 10 CFR 35.1000 and begin developing licensing guidance.

If it is determined that licensing under 10 CFR 35.1000 is necessary, the NRC staff will inquire about pertinent information about the product, which includes items required by 10 CFR 35.12(d). Specifically, the NRC staff will inquire about any additional aspects of the medical use of the material that are applicable to radiation safety that are not addressed in, or differ from, Subparts A through C, L and M in 10 CFR Part 35, and a recommended set of regulations and commitments for licensee use. These will include the applicable radiation safety program requirements in Subparts D through H, which are appropriate to the specific EMT.

If the product consists of a sealed source in a device, the NRC staff will review how the device works during normal operating conditions, and if there are any additional safety features and procedures to follow during emergencies. Please review Question no. 8 pertaining to sealed source and device registration.

Any radiopharmaceutical or medical device used for patient treatments must be reviewed by the U.S. Food and Drug Administration (FDA) prior to material administration to humans. The NRC staff will coordinate with the FDA as necessary. Please review Question no. 10 pertaining to FDA review.

5. What is the NRC contact if I have a new EMT and would like the NRC staff to review to determine medical users licensing pathway?

For any new inquiries, please contact MSEB at medicalquestions.resource@nrc.gov.

6. My clinical site would like to use an EMT for medical purposes, how do I get started?

For instructions on how to apply for an NRC license for the medical use of an EMT, please review Licensing of Medical, Industrial, and Academic Uses of Nuclear Materials as well as NRC guidance, NUREG 1556, Volume 9, Revision 3, Program-Specific Guidance About Medical Use Licenses. For questions regarding licensing the medical use of an EMT, please

contact your licensing authority. NRC regional contact information may be found here and Agreement State contact information may be found here.

7. What is the NRC process for review of a new EMT?

The NRC medical radiation safety program staff will work with the vendor or manufacturer and early users to gather and review information described in Question no. 4. The NRC medical radiation safety program staff may also coordinate with NRC or Agreement State sealed source and device reviewers. Once information has been gathered and reviewed, the NRC staff will make a licensing pathway recommendation, either under a traditional subpart (i.e. Subpart D through H) or Subpart K, 10 CFR 35.1000. This recommendation is then reviewed and agreed upon by the Standing Committee for Reviewing Emerging Medical Technologies (SCREMT). SCREMT consists of NRC technical staff, legal staff, and Agreement State representatives.

If SCREMT determines the EMT should be licensed under 10 CFR 35.1000, the NRC staff will draft 10 CFR 35.1000 licensing guidance containing one set of acceptable regulations and specific conditions for use. This draft licensing guidance is then reviewed by SCREMT. Once SCREMT concurs on the draft licensing guidance, the document is usually provided to the Advisory Committee on Medical Use of Isotopes (ACMUI) and the Organization of Agreement States. After all comments have been resolved, the final licensing guidance is issued if the product has FDA approval for either research or clinical use and a Sealed Source and Device (SS&D) certificate, as appropriate. The process takes approximately 8 months assuming NRC staff are able to gather the information needed to review the EMT and FDA approval and SS&D certificate have been issued.

8. What is Sealed Source and Device Registry (SSDR)?

The Sealed Source and Device Registry (SSDR) is an NRC database of completed radiation safety evaluations by the NRC or Agreement States for specific devices containing a radioactive sealed source. The evaluation review responsibility depends on where the device will be distributed from (i.e. an Agreement State or non-Agreement Sate). If the distribution will be from a non-Agreement State, the NRC staff generates the Sealed Source and Device (SS&D) certificate for the device/sealed source. If the distribution will be from an Agreement State, vendors should contact the Agreement State to discuss sealed source and device registration. The NRC may still generate the SS&D certificate if the Agreement State does not perform SS&D reviews. Vendors should still contact the NRC as described in Question no. 4 to review the licensing for the future medical users of the EMT.

Devices designed for medical treatments undergo a rigorous review in accordance with 10 CFR 32.210. The NRC staff or Agreement State staff evaluates the design and proposed use, manufacture and prototype testing, quality control program, labeling, leak testing, installation, service and maintenance, operating and safety instructions, and potential hazards to ensure that the radiation safety properties of the source or device are adequate to minimize undue radiation exposures. Once a specific medical device is approved in the SSDR and a certificate issued, the device must be used in accordance with the radiation safety conditions and limitations described in the SS&D certificate, and as required in 10 CFR 35.400, 35.500, and

35.600, or as described in the medical use licensing guidance under 10 CFR 35.1000. Additional information about Sealed Sources and Devices can be found at https://www.nrc.gov/materials/miau/sealed-source.html.

9. How do I apply to have a device approved in the SSDR?

Certain States have entered into agreements with the NRC that give the individual States the authority to regulate byproduct material, including performing safety evaluations of sealed sources and/or devices, within their borders. If the applicant resides within the Agreement State's borders for a State that performs SS&D reviews, the applicant wishing to apply for a SS&D registration must apply with the Agreement State. If the applicant resides within the NRC jurisdiction or in an Agreement State which does not perform SS&D reviews, the applicant must apply with the NRC.

The Agreement State Program, including the listing of Agreement States and their point of contact, is described in more detail at https://www.nrc.gov/about-nrc/state-tribal/agreement-states.html.

Instructions and guidance regarding applications for SS&D registrations can be found in the NRC guidance, NUREG 1556, Volume 3, Revision 2, "Consolidated Guidance About Materials Licenses: Applications for Sealed Source and Device Evaluation and Registration," available at https://www.nrc.gov/reading-rm/doc-collections/nuregs/staff/sr1556/v3/index.html.

Applications to the NRC for SS&D registrations must be submitted to LBLicensingAssistant.Resource@nrc.gov. The NRC review and approval process takes 180 days. Agreement State review times vary, and it is recommended that vendors reach out to the Agreement States early in the process to discuss timelines.

10. What is the role of the U.S. Food and Drug Administration (FDA) during review and approval of 10 CFR 35.1000 use?

The NRC and the FDA have distinct but complementary roles in regulating the medical use of radioactive material. The NRC's role is to ensure the radiation safety associated with the use of the material by ensuring the safety of the public, workers, patients, and environment. In contrast, the FDA ensures the EMT is safe and effective for use in patient care. Both the NRC and the FDA work together as described in a Memorandum of Understanding (MOU), which delineates the responsibilities of each Agency concerning the use of radioactive material. The MOU between the NRC and the FDA can be found at MOU 225-22-017 | FDA.

Before any radioactive material is licensed for medical use, the NRC will verify it can be used in accordance with FDA regulations. Vendors should not assume the NRC knows when they begin talks with the FDA for approval or the status of FDA reviews; due to their distinct roles, the NRC and the FDA may not be able to share information. It is recommended that vendors or manufacturers reach out to the NRC as described in Question no. 5 when they start discussions with the FDA to ensure that the NRC has sufficient time to develop 10 CFR 35.1000 licensing guidance as necessary or receive an SS&D certification.

For additional information, please review the FDA website at www.fda.gov.

11. What license does a vendor need to ship a radioactive device or material from an international location?

If the device or material is imported, general import license requirements apply in 10 CFR Part 110 to U.S. persons, not foreign vendors. Specifically, a general license is issued to any person (in the U.S.) to import byproduct, source, or special nuclear material if the U.S. consignee is authorized to receive and possess the material under the relevant NRC or Agreement State regulations. See the regulations at 10 CFR 110.27 -- General license for imports.

A general license is a paperless authorization, meaning a physical license is not obtained from the NRC. So, there is no "issuance" to the importer. The importer would be responsible for ensuring that the receiving facility holds a license for the possession, use, and/or distribution of the radioactive material prior to the actual import of the referenced material.

12. Can vendors ship a device directly to a medical use licensee (i.e. hospital) from an international location?

As described in Question no. 8, all sealed sources or devices containing sealed sources must be registered in the Sealed Source and Device Registry. Then, the device and/or sealed source can be imported under a general license as described in Question no. 11 to a U.S. consignee who is authorized for possession, use, and/or distribution of the device and/or sealed source.

Usually, a foreign vendor will send the device and/or sealed source to a radiopharmacy or a manufacturer who is licensed under 10 CFR 32.74. Radiopharmacies or manufacturers authorized for device and/or sealed source distribution in accordance with 10 CFR 32.74 can import the product and then distribute it to medical use licensees.

13. Can a foreign vendor import a radiopharmaceutical directly to the hospital for patient treatment or does the pharmaceutical need to be sent to a radiopharmacy first?

As indicated in question no. 11, the material can be imported to a licensee who is authorized for possession, use, and/or distribution of the radioactive material. Regulations in 10 CFR 35.100, 35.200 and 35.300 specify where a licensee must obtain radioactive material from for medical use and these regulations do not permit use of material obtained directly from an international company without an NRC license.

The most common path is for a foreign vendor to send the material through a licensed radiopharmacy who is licensed under 10 CFR 32.72. Radiopharmacies are authorized for possession and distribution of radiopharmaceuticals in accordance with 10 CFR 32.72 and/or 32.74; and thus, can import material and then distribute it to medical use licensees.

14. Is the NRC considering developing regulations for uses licensed under 10 CFR 35.1000?

The NRC is considering revising 10 CFR Part 35, “Medical Use of Byproduct Material,” to add requirements that address calibration and dosage measurement for strontium-82/rubidium-82 generators and to establish risk-informed, performance-based requirements for existing and future EMTs. The NRC is also considering additional changes to 10 CFR Part 35 to accommodate developments in the medical field related to new radiopharmaceuticals and EMTs.