Historical Background of the U.S. Nuclear Regulatory Commission's Training and Experience Requirements for Radiopharmaceuticals Requiring a Written Directive

Introduction*:*

To address the Commission's directions in Staff Requirements Memorandum (SRM) SRM-M170817,[1] the U.S. Nuclear Regulatory Commission (NRC) staff conducted an evaluation of the training and experience (T&E) requirements for authorized users (AUs) of radiopharmaceuticals under Title 10 of the *Code of Federal Regulations* (10 CFR) Part 35, "Medical Use of Byproduct Material," Subpart E, "Unsealed Byproduct Material—Written Directive Required." To support its evaluation,[2] the staff has summarized the timeline of relevant rule changes related to training for radiopharmaceuticals requiring a written directive.

Historical Background and Timeline of Changes:

1956

The NRC's (then the Atomic Energy Commission [AEC]) medical use regulations were first included in 10 CFR Part 30, "Rules of General Applicability to Domestic Licensing of Byproduct Material," under 10 CFR 30.24, "Special requirements for issuance of specific licenses," in 1956 (Volume 21 of the *Federal Register* page 214 [21 FR 214]; January 11, 1956). At that time, specific licenses were issued to individual physicians for human use of byproduct material and the requirements for T&E were general. The regulations used words such as "substantial experience," "extensive experience," and "specialized training" to describe the T&E that was required for human use of radioactive material. Specific information describing the extent of the T&E that was acceptable was detailed in several AEC guidance documents, some of which the staff no longer has access to. The AEC evaluated each proposed individual's T&E on a case-by-case basis and completed the evaluations using worksheets.

The regulations in 10 CFR 30.24 required, in part, that –

> — For human use in institutions – an application by an institution for a specific license for human use will be approved if the physician designated on the application as the individual user has substantial experience in the proposed use, the handling and administration of radioisotopes and, where applicable, the clinical management of radioactive patients." [10 CFR 30.24(a)(4)]
>
> — For licensing of individual physicians for human use – an application by an individual physician for a specific license for human use will be approved if the applicant has extensive experience in the proposed use, the handling and administration of radioisotopes and, where applicable, the clinical management of radioactive patients. (The physician shall furnish suitable evidence of such experience with his application. A

[1] SRM-M170817, "Staff Requirements – Affirmation Session, 10:30 A.M., Thursday, August 17, 2017, Commissioners' Conference Room, One White Flint North, Rockville, Maryland (Open to Public Attendance)," dated August 16, 2017, available at Agencywide Documents Access and Management System (ADAMS) Accession No. ML17229B283.

[2] The staff's evaluation is documented in SECY-18-0084, "Staff Evaluation of Training and Experience Requirements for Administering Different Categories of Radiopharmaceuticals in Response to SRM-M170817," dated August 28, 2019 and available at ADAMS Accession No. ML18135A276; and SECY-20-0005, "Rulemaking Plan for Training and Experience Requirements for Unsealed Byproduct Material," dated January 13, 2020, and available at ADAMS Accession No. ML19321E358.

statement from the medical isotope committee in the institution where he acquired his experience, indicating its amount and nature, may be submitted as evidence of such experience). [10 CFR 30.24(b)(3)]

— For human use of sealed sources – an application for a specific license for use of a sealed source for human use will be approved if the applicant (or if the application is made by an institution, the individual user) has specialized training in the therapeutic use of the radioactive device considered (teletherapy unit, beta applicator, etc.) or has experience equivalent to such training; and is a physician. [10 CFR 30.24(c)(4)]

1965

In 1965, the regulations in 10 CFR Part 30 were re-codified (30 FR 8185; June 26, 1965), and the medical use requirements were relocated into the newly created 10 CFR Part 35, titled "Human Uses of Byproduct Material." This part included special requirements under specific licenses for (1) licensing of individual physicians for human use of byproduct material; (2) licensing of human use of byproduct material in sealed sources; and (3) licensing of human use of byproduct material in institutions. It also included a general license for medical use of certain quantities of byproduct materials. The regulations stayed general and language from the former Part 30, as described earlier, remained the same and was transitioned over.

1974 – 1987

Between 1974 and 1987, there were several rule changes that introduced the use of "Groups I to VI" to describe specific medical uses. The groups (see Table 1) later evolved into the current medical modalities under 10 CFR 35.100 to 35.600. Regarding the T&E of physicians, the regulations continued to use the terms "substantial experience," "extensive experience," and "specialized training."

Medical use regulations in the late 1970s and early 1980s separated the use of radiopharmaceuticals into different categories to allow different uses to be regulated appropriately:

Group Number	Use
I	Use of prepared radiopharmaceuticals for certain diagnostic studies involving measurements of uptake, dilution, and excretion (I-131 for thyroid uptake, etc.)
II	Use of prepared radiopharmaceuticals for diagnostic studies involving imaging and tumor localizations (I-131 for thyroid imaging, etc.)
III	Use of generators and reagent kits for preparation and use of radiopharmaceuticals containing byproduct material for certain diagnostic uses (Mo-99/Tc-99 generators for brain, thyroid, salivary gland, blood pool imaging, etc.)
IV	Use of prepared radiopharmaceuticals for certain therapeutic uses that do not normally require hospitalization for purpose of radiation safety (I-131 for hyperthyroidism and cardiac dysfunction, P-32 for treatment of polycythemia vera, leukemia and bone metastases, etc.)
V	Use of prepared radiopharmaceuticals for certain therapeutic uses that normally require hospitalization for purpose of radiation safety (I-131 for thyroid carcinoma, etc.)
VI	Use of sources and devices containing byproduct material for certain medical uses (Am-241 for bone mineral analysis, Sr-90 for superficial eye treatment)

1979

In January 1979, there was a major revision to NRC's medical use licensing guidance and the first version of the NRC Regulatory Guide (RG) 10.8, "Guide for the Preparation of Applications for Medical Programs" was issued (ADAM Accession No. ML13350A208). This was the first time that specific information on acceptable T&E for medical uses was consolidated into one guidance document. The regulations in 10 CFR Part 35 remained general and physicians' T&E were examined individually per the licensing documentation and based on the criteria contained in the RG. The guidance included in the RG began to delineate T&E based on hours.

The RG stated that if a physician had been previously authorized to use radioactive material, only the previous license number or copy of the license needed to be submitted. If the physician had not been previously authorized to use the requested radionuclide, the physician had to state where he or she was licensed to practice medicine and to submit a complete description of his T&E via NRC Form 313M. The NRC examined the licensee's submittal on a case-by-case basis. If the physician did not include the T&E described in the RG, the physician could state their specific qualifications and the submittal would be reviewed by the Commission with assistance from the Advisory Committee on the Medical Uses of Isotopes (ACMUI). The RG contained criteria for acceptable T&E in Appendix A, "Acceptable Training and Experience for Medical Uses of Byproduct Material."

Section 3, "Training Requirements for Therapy Procedures involving Radiopharmaceuticals," in RG 10.8, Appendix A describes the training criteria needed to use or supervise the use of byproduct for either Group IV or Group V:

Training Criteria to use or directly supervise the use of byproduct material listed in Group IV	**Hours**
Training in basic radioisotope handling techniques including: • Radiation physics and instrumentation (25 hours) • Radiation protection (25 hours) • Mathematics pertaining to the use and measurement of radioactivity (10 hours) • Radiation biology (20 hours)	80
Clinical training in specific therapy procedures: • Iodine-131 for treatment of hyperthyroidism and/or cardiac conditions: o Clinical experiences in the diagnosis of thyroid function and active participation in the treatment of ten patients. • Phosphorus-32 for treatment of polycythemia vera, leukemia, and/or bone metastases: o Treatment of three patients with any combination of these three conditions. • Colloidal phosphorus-32 intracavitary treatment: o Active participation in the treatment of three patients	N/A

Training Criteria to use or directly supervise the use of byproduct material listed in Group V	Hours
Training in basic radioisotope handling techniques including: • Radiation physics and instrumentation (25 hours) • Radiation protection (25 hours) • Mathematics pertaining to the use and measurement of radioactivity (10 hours) • Radiation biology (20 hours)	80
Clinical training in specific therapy procedures; • Iodine-131 for treatment of thyroid carcinoma: o Clinical experience in diagnosis of thyroid function and treatment of hyperthyroidism and/or cardiac dysfunction and active participation in the treatment of three patients with thyroid carcinoma. • Colloidal gold-198 for intracavitary treatment: o Active participation in the treatment of three patients.	N/A

1987

A major T&E rule change was issued (51 FR 36951) on October 16, 1986 and became effective on April 1, 1987. The rule change included specific information on acceptable T&E and specific hours were designated for classroom and laboratory training and supervised clinical experience. These requirements were included in a section specifically for T&E requirements: Subpart J – 10 CFR 35.900 through 35.972. The T&E requirements were specific with detailed criteria. The NRC listed certain specialty board certifications as part of the T&E requirements for authorized individuals. The non-board certification path (now referred to as the "alternate pathway") included criteria for hours of classroom and laboratory training and hours of supervised clinical experience, or a training program in nuclear medicine that includes all the specified classroom and lab training, work experience, and supervised clinical experience.

Subpart J, "Training and Experience Requirements," was laid out by task. It also contained several clauses that grandfathered individuals who received training prior to the new rule.

1987 Subpart J, "Training and Experience Requirements"	Title
35.900	Radiation Safety Officer
35.901	Training for experienced Radiation Safety Officer*
35.910	Training for uptake, dilution, and excretion studies
35.920	Training for imaging and localization studies
35.930	Training for therapeutic use of radiopharmaceuticals
35.932	Training for treatment of hyperthyroidism
35.934	Training for treatment of thyroid carcinoma
35.940	Training for use of brachytherapy sources
35.941	Training for ophthalmic use of strontium-90
35.950	Training for use of sealed sources for diagnosis
35.960	Training for teletherapy
35.961	Training for teletherapy physicist
35.970	Training for experienced authorized users*
35.971	Physician training in a three-month program*
35.972	Recentness of training

*These requirements grandfathered individuals who had received training prior to the new rule.

The 1987 requirements for a physician training for therapeutic use of radiopharmaceuticals are provided below:

> 10 CFR 35.930, "Training for therapeutic use of radiopharmaceuticals"
>
> Except as provided in 35.970, the licensee shall require the authorized user of radiopharmaceuticals in 35.300 to be a physician who:
>
> (a) Is certified by:
>
> (1) The American Board of Nuclear Medicine; or
>
> (2) The American Board of Radiology in radiology or therapeutic radiology; or
>
> (b) Has had classroom and laboratory training in basic radioisotope handling techniques applicable to the use of therapeutic radiopharmaceuticals, and supervised clinical experience as follows:
>
> (1) 80 hours of classroom and laboratory training that includes:
>
> (i.) Radiation physics and instrumentation;
>
> (ii.) Radiation protection;
>
> (iii.) Mathematics pertaining to the use and measurement of radioactivity; and
>
> (iv.) Radiation biology; and
>
> (2) Supervised clinical experience under the supervision of an authorized user at a medical institution that includes:
>
> (i.) Use of iodine-131 for diagnosis of thyroid function and the treatment of hyperthyroidism or cardiac dysfunction in ten individuals; and
>
> (ii.) Use of iodine-131 for treatment of thyroid carcinoma in three individuals.

2002

On April 24, 2002 (effective October 24, 2002; 67 FR 20249), 10 CFR Part 35 was amended in its entirety and addressed, among other things, new T&E requirements and the requirements for recognition of medical and other specialty boards whose certifications may be used to demonstrate the adequacy of the radiation safety officer (RSO), authorized medical physicist (AMP), authorized nuclear pharmacist (ANP), and authorized user (AU). In addition, the NRC retained the existing T&E requirements designated as Subpart J in Part 35 for a two-year period—the old regulations, Subpart J – 10 CFR 35.900 through 35.972, remained effective until October 2004. The new T&E requirements were included in 10 CFR 35.190, 35.290, 35.390, 35.490, 35.590, and 35.690.

10 CFR 35.390, "Training for use of unsealed byproduct material for which a written directive is required," was a new section. The T&E requirements for an AU for unsealed byproduct material for which a written directive is required were moved, with some modifications, from the old 10 CFR 35.930, "Training for therapeutic use of unsealed byproduct material." Three changes were made to this section during the rulemaking. First, the listing of specialty boards by name was deleted from the regulation; the regulatory text in 10 CFR Part 35 no longer incorporates a listing of specialty boards. In place of listing the boards, the final rule provides for NRC recognition of the boards. *Second, the new requirements require a total of 700 hours of T&E that must include classroom, laboratory, and supervised work experience.* Third, an individual must obtain written certification from a preceptor indicating that the individual has satisfactorily completed the requirements in this section and has achieved a level of competency sufficient to function independently as an AU.

The 2002 requirements for a physician training for the therapeutic use of radiopharmaceuticals are listed below:

> 10 CFR 35.390, “Training for use of unsealed byproduct material for which a written directive is required.”
>
> Except as provided in 10 CFR 35.57, the licensee shall require an authorized user of unsealed byproduct material for the uses authorized under 10 CFR 35.300 to be a physician who—
>
> (a) Is certified by a medical specialty board whose certification process includes all of the requirements in paragraph (b) of this section and whose certification has been recognized by the Commission or an Agreement State; or
>
> (b) (1) Has completed 700 hours of training and experience in basic radionuclide handling techniques applicable to the medical use of unsealed byproduct material requiring a written directive. The training and experience must include—
>
> (i) Classroom and laboratory training in the following areas—
>
> (A) Radiation physics and instrumentation;
> (B) Radiation protection;
> (C) Mathematics pertaining to the use and measurement of radioactivity;
> (D) Chemistry of byproduct material for medical use; and
> (E) Radiation biology; and
>
> ii) Work experience, under the supervision of an authorized user who meets the requirements in 10 CFR 35.390(a), 10 CFR 35.390(b), or equivalent Agreement State requirements. A supervising authorized user, who meets the requirements in 10 CFR 35.390(b), must have experience in administering dosages in the same dosage category or categories (i.e., 10 CFR 35.390(b)(1)(ii)(G)(1), (2), (3), or (4)) as the individual requesting authorized user status. The work experience must involve—
>
> (A) Ordering, receiving, and unpacking radioactive materials safely and performing the related radiation surveys;
> (B) Calibrating instruments used to determine the activity of dosages, and performing checks for proper operation of survey meters;
> (C) Calculating, measuring, and safely preparing patient or human research subject dosages;
> (D) Using administrative controls to prevent a medical event involving the use of unsealed byproduct material;
> (E) Using procedures to contain spilled byproduct material safely and using proper decontamination procedures;
> (F) Eluting generator systems, measuring and testing the eluate for radionuclidic purity, and processing the eluate with reagent kits to prepare labeled radioactive drugs; and
> (G) Administering dosages of radioactive drugs to patients or human research subjects involving a minimum of three cases in each of the following categories for which the individual is requesting authorized user status—

(1) Oral administration of less than or equal to 1.22 Gigabecquerels (33 millicuries) of sodium iodide I–131;
(2) Oral administration of greater than 1.22 Gigabecquerels (33 millicuries) of sodium iodide I-1312;
(3) Parenteral administration of any beta emitter or a photon-emitting radionuclide with a photon energy less than 150 keV; and/or
(4) Parenteral administration of any other radionuclide; and

(2) Has obtained written certification that the individual has satisfactorily completed the requirements in paragraph (b)(1) of this section and has achieved a level of competency sufficient to function independently as an authorized user for the medical uses authorized under 10 CFR 35.300. The written certification must be signed by a preceptor authorized user who meets the requirements in 10 CFR 35.390(a), 10 CFR 35.390(b), or equivalent Agreement State requirements. The preceptor authorized user, who meets the requirements in 10 CFR 35.390(b), must have experience in administering dosages in the same dosage category or categories (i.e., 10 CFR 35.390(b)(1)(ii)(G)(1), (2), (3), or (4)) as the individual requesting authorized user status.

During the 2002 rulemaking effort, the T&E hours were increased from 80 hours to 700 hours in the revised 10 CFR 35.390, "Training for use of unsealed byproduct material that requires a written directive." The NRC agreed with stakeholder comments that the T&E requirements should be increased for non-board-certified individuals wishing to use byproduct material for which a written directive is required. The staff justified this increase because these physicians would be authorized to elute generators and prepare radioactive drugs, as well as to administer a wide variety of radionuclides requiring written directives. The 2002 rule did maintain an 80-hour training track for the oral administration of sodium iodide I-131.

The Supplemental Information section 67 FR 20249 should be referred to for additional information on the staff's decision to require 700 hours of T&E for therapeutic radiopharmaceuticals. The staff explained the decision to not require a competency examination and instead include a list of subject areas to be addressed in a training program. The staff wanted to rely on the duration of the training program and on the preceptor's written certification to ensure that a physician completed the required T&E. These two factors would demonstrate that the physician was competent to function independently as an AU. The NRC staff believed that the specified training periods would provide individuals with sufficient knowledge to handle byproduct material safely. The staff chose not to include any further breakdown to allow for flexibility in designing and implementing training programs.

2005

On March 30, 2005, the NRC published in the *Federal Register* (70 FR 16336), a final rule that amended its regulations again to revise the T&E requirements for the medical use of byproduct material. The rule amended the regulations to change requirements for recognition of certain specialty boards' certification processes. No changes were made to the minimum hours required for classroom and lab training or supervised work experience.

Attestations were separated from the board certifications. Most board-certified individuals (except board certification processes recognized under 10 CFR 35.392 and 35.394) must

provide documentation of clinical experience and attestations in addition to their board certifications. This is because, except for 10 CFR 35.392 and 35.394, the board certification processes did not require documentation of the clinical experience or the attestation required by NRC to sit for the board examinations.

2007

In August 2007, the NRC implemented additional changes to the T&E regulations (72 FR 45147) which included grandfathering sections modified to allow for supervising individuals and preceptors that did not meet the new requirements for T&E. The T&E hours were not modified.

2018

In July 2018, 10 CFR Part 35 was revised (83 FR 33046) in response to specific issues with the implementation of the 2002 rule raised by the public, petitioners, ACMUI, NRC and Agreement State licensees, and NRC staff. No changes were made to the prescriptive hours or topics in the T&E criteria. The rule change amended the T&E requirements to (1) remove the requirement to obtain a written attestation for an individual who is certified by a specialty board whose certification process has been recognized by the NRC or an Agreement State in multiple sections; and (2) address a request filed in a petition for rulemaking (PRM), PRM-35-20, to exempt certain board-certified individuals from certain T&E requirements (i.e., “grandfather” these individuals).

Summary:

The T&E requirements in 10 CFR 35.390 were initially general and became more specific as time progressed. The regulations began as qualitative with NRC licensing evaluations of individual physicians in the 1950s and 1960s. The NRC issued consolidated guidance in the 1979 which introduced quantifiers for training. The guidance document included set hours of T&E to help guide licensees on the amount of training that would be appropriate. In 1986, the regulations added hours as a quantifier of T&E—80 hours of classroom and laboratory training were required for the therapeutic use of radiopharmaceuticals as well as supervised clinical experience (without associated hours) using I-131. In 2002, 10 CFR Part 35 changed to include the 700 hours of T&E that are currently applicable to physicians who use unsealed byproduct material for which a written directive is required. The increase to 700 hours was in response to stakeholder feedback and accompanied the NRC’s decision to not include a written examination to determine competence.