Questionnaire on the Evaluation of Tailored Training and Experience Requirements for Different Categories of Radiopharmaceuticals

1. What is the fundamental knowledge that is necessary for a physician to administer any radiopharmaceutical under Title 10 of the *Code of Federal Regulations* (10 CFR) 35.390? Below is a draft list that the U.S. Nuclear Regulatory Commission (NRC) staff has developed. Please add/delete topics from this list.

    a. Radiation physics
        i. Structure and properties of atoms
        ii. Radiation and radioactivity
            - Characteristics of radioactivity
            - Radioactive decay (simple and complex), half-lives, energies
            - Calculation of radioactive decay and activity remaining
            - Primary radionuclides and contaminants
        iii. Interaction of radiation with matter (direct and indirect)
            - Radiological properties of low energy photons, beta emissions, alpha emissions, and mixed emissions
        iv. Radionuclide production
        v. Units of radiation and radioactivity

    b. Instrumentation
        i. Operation and use of instrumentation (e.g., gas-filled detectors [ion chambers, survey meters, and dose calibrators], sodium iodide detectors [well counters]) and advantages and disadvantages for measuring and detecting different radionuclides and mixed radionuclides.
        ii. Dosage and dose measurements
        iii. Instrumentation to monitor and measure unit dosage without modification or adjustment, unit dosage with adjustment, unit dosage with modification, multi-dosage, kit preparation, and generator elution
        iv. Frequency of calibration
        v. Operation and use of personnel monitoring devices
        vi. Routine quality assurance parameters (including calculations) for detection and measurement of radioactivity

    c. Radiation protection for protection of workers, family members, public, and patient as it relates to the regulations in 10 CFR Parts 19, 20, and 35
        i. Radiation protection associated with dose measurements and handling (unit dosage with modification, multi-dosage, kit preparation, and generator elution)
        ii. Performing calculations necessary to comply with regulations (e.g., patient release, medical events)
        iii. Maintaining doses as low as reasonably achievable (ALARA), including external and internal exposures
        iv. Basic shielding (e.g., syringe shields, aprons)
        v. Protective clothing/devices to include the lens of the eye

Commented [WX1]: Currently lead aprons and protective clothing are not used in the Nuclear Medicine setting. Can NRC provide justifications for the utilization of the lead aprons and protective clothing at Nuclear Medicine?

vi. Surveys and monitoring
vii. Dosimeters
viii. Minimizing and clean-up of contamination and spills (e.g., when handling unit dosage without modification or adjustment, unit dosage with adjustment, unit dosage with modification, multi-dosage, kit preparation, and generator elution)
ix. Ordering, receiving, and unpacking radiopharmaceutical
x. General understanding of radiation safety officer (RSO) responsibilities including their authority to stop work
xi. Understanding public and occupational dose limits
xii. Waste control and radioactive storage
xiii. Radiation protection for patient to prevent unwanted exposure
    - Patient identity verification
    - Appropriate use of a written directive
    - Written directives verification
    - Properly performing radiopharmaceutical therapy delivery equipment
    - Minimizing and clean-up of contamination and spills
xiv. Signage
xv. Appropriate occupational dose guidance for the pregnant worker
xvi. Application of guidance for the nursing mother receiving radiopharmaceuticals

d. Mathematics pertaining to the use and measurement of radioactivity
    i. Decay equations (simple and complex)
    ii. Half value layers
    iii. Exposure calculations (internal and external)
    iv. Calculations associated with instrumentation
    v. Radiation dose (including external and internal dosimetry)
    vi. Converting activity to dose
    vii. Organ/tissue uptake to dose
    viii. Calculations necessary to comply with regulations (e.g., patient release, medical events, etc.)
    ix. Unit dosage with adjustment, unit dosage with modification, multi-dosage, kit preparation, and generator elution

e. General patient release determination
    i. Transportation and release location
    ii. Patient specific parameters, such as living and working conditions
    iii. Exposure to sensitive populations – pregnant women and children
    iv. Radiation effects due to low energy photons, beta emissions, alpha emissions
    v. Combined radiation effects from mixed emissions and mixed half-lives and decay chains
    vi. Pharmacological effects of specific drugs and resulting radiation doses, route of administration, and route of elimination

vii. Pharmacological effects on normal adults, pregnant women, fetuses, nursing infants, nursing women, and compromised patients and resulting radiation doses, differing routes of administration, and routes of elimination

f. Chemistry of byproduct material for medical use
   i. Original and final chemical form
   ii. Generators
   iii. Kit preparation
   iv. Interaction with environment, spills, release to environment

g. Radiation biology
   i. Chemical and physical effects of ionizing radiation of alpha emissions, beta emissions, and low energy photos on biological systems (molecular and cellular damage)
   ii. Chemical and physical effects of ionizing radiation from mixed emissions and mixed half-lives and decay chains on biological systems
   iii. Comparison of relative risks of low level radiation with other health risks
   iv. Biological effects of high dose radiation (acute, late, fetal)
   v. Biological effects of low dose radiation (acute, late)
   vi. Therapeutic use of radionuclides including mechanisms of action of particulate radiation
   vii. Pharmacological effects of specific drugs and resulting radiation doses, route of administration and route of elimination
   viii. Pharmacological effects on normal adults, pregnant women, fetuses, nursing infants, nursing women, and compromised patients and resulting radiation doses, differing routes of administration, and routes of elimination
   ix. 4Rs – repair, redistribution, repopulation, and reoxygenation

h. Medical events
   i. Definition of a medical event (including patient intervention)
   ii. Determination of a medical event occurrence
   iii. Evaluation of the medical consequences of a medical event
   iv. Root cause analysis and determination of appropriate corrective actions
   v. Controls and programs to prevent medical events

i. NRC requirements
   i. General understanding of 10 CFR Parts 19, 20, and 35
   ii. Dose limits in 10 CFR Parts 20 and 35
   iii. Reporting requirements who, when, and where to report – in 10 CFR Parts 20 and 35
   iv. Training requirements
   v. Recordkeeping requirements
   vi. Licensee procedures including (written directive procedures and safety procedures for each use)
   vii. Need for amendments
   viii. Need for notifications
   ix. Need for change or transfer of control

Commented [WX2]: What is the definition of high dose radiation?

Commented [WX3]: What is the definition low dose radiation?

x. Need for license termination and decommissioning
xi. Guidance for appropriate 10 CFR 35.1000 uses
xii. Appropriate waste and transportation requirements
xiii. Security and control of license material, and access control
~~xiii.~~

2. What additional knowledge is necessary for a physician to administer specific types of radiopharmaceuticals under 10 CFR 35.390? Below is a draft list that NRC staff has developed. Please add/delete topics from this list.

a. Indication of use and normal/abnormal response to the treatment

b. Knowledge of clinical dose and risks of prescribing a different dose

c. Ordering, calculating, and measurement of the dose

~~c.~~d. Use of dose blockers, if necessary (e.g., amino acid infusion prior and during peptide receptor radionuclide therapy)

~~d.~~e. Route of administration
i. Ability to determine administration under special patient conditions such as gastrostomy, tracheostomy, renal failure, dialysis, liver failure, incontinence, ~~unable~~ inability to swallow, ostomies, body tubes/catheters, etc.
ii. How to perform administration
iii. Patient risks associated with route of administration
iv. Radiation protection for workers associated with route of administration

f. Known side effects from the radiopharmaceutical.

~~e.~~g. Specific risks associated with toxicity of the radiopharmaceutical (i.e., minor differences between prescribed and administered activity can result in different consequences for patient)

~~f.~~h. Specific risks associated with the type of radiation emitted (alpha, beta, gamma, low energy photon)

~~g.~~i. Specific risks associated with the delivery method of the drug to the target (if the radionuclide needs to be tagged to a chemical component, what happens if it isn't tagged or tagged incorrectly or possible altered biodistribution (extrahepatic) with the use of hepatic microspheres therapy)

~~h.~~j. Medical event specific to a radiopharmaceutical
i. Prevention (QA/QC on any necessary equipment used to ensure appropriate dose/dosage is delivered)
ii. Evaluation
iii. Reporting
iv. Medical intervention or response if a medical event occurs

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Commented [HD4]: This covers common side effects from typical doses rather than toxicity, radiation type, and delivery method covered in the next three sections.

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Commented [WX5]: Microspheres therapy is categorized under 10 CFR 1000 currently. So I am not sure whether microspheres therapy should be mentioned in this section or not.

~~j.~~k. Post verification (to determine dosage and if medical event occurred)
   i. Pre and post administration measurements and calculations (e.g., for microspheres hepatic therapy)
   ~~i.~~ii. Appropriate modality (e.g. imaging) to determine radiopharmaceutical biodistribution
   ~~ii.~~iii. Understanding artifacts

~~j.~~l. Patient release instructions specific to a radiopharmaceutical
   i. When to provide discussion and instructions
   ii. Transportation~~,~~ and release location
   iii. Patient specific parameters, such as living and working conditions
   iv. Exposure to sensitive populations – pregnant women, nursing mother and child, and children
   v. Radiation effects due to low energy photons, beta emissions, alpha emissions
   vi. Combined radiation effects from mixed emissions and mixed half-lives and decay chains
   vii. Pharmacological effects of specific drugs and resulting radiation doses, route of administration, and route of elimination
   viii. Pharmacological effects on normal adults, pregnant women, fetuses, nursing infants, nursing women, and compromised patients and resulting radiation doses, differing routes of administration, and routes of elimination

~~k.~~m. Radiation Protection specific to radiopharmaceutical
   i. Unique or additional handling concerns
   ii. Unique ~~ordering,~~ receiving~~,~~ and unpacking concerns
   iii. ~~Calculation, measurement, and~~P ~~p~~reparation of radiopharmaceutical dose
   iv. Disposal of radiopharmaceutical
   v. Shielding specific to a radiopharmaceutical
   vi. Use of procedures to contain spilled radioactive material and use of proper decontamination procedures
   vii. Dosimetry
   viii. Volatility
   ix. Circumstances which require a call to the RSO and/or the regulator
   x. What to do in the event of medical emergency or if the patient dies or cremation is planned
   xi. Unique protective clothing or shielding
   xii. Remote handling devices, if any

3. How should the physician acquire the knowledge topics listed above? Classroom/laboratory training and supervised work experience (including clinical experience)? Please provide an estimate for the number of hours or clinical experience needed for the knowledge topics listed above.

4. How should a physician's knowledge in the topics listed above and ability to function independently be evaluated?
   a. Exam?

Commented [HD6]: Imaging does not determine the dose for microspheres

Commented [HD7]: These items have been moved to section 2.c

b. Both a written exam and practical exam?
c. Attestation by a qualified authorized user?
d. How would you structure a competency model to demonstrate knowledge of the fundamental knowledge areas?
e. Who should administer the written exam and/or practical exam or oversee the competency model – the regulator, medical specialty board, or professional societies?

For sections 3 & 4: It is important to note that the education will occur both in residency/fellowship for trainees and clinical training for physicians already in practice. There will be many new therapies that will be made available in the coming years that even newly graduated residents/fellows might have no experience with.

A combination of classroom/didactic and supervised clinical experience with attestation from a qualified AU is reasonable to attain the necessary education. The current requirement of a total 700 hours in nuclear medicine training including at least 200 hours of classroom/labs in nuclear medicine remains reasonable. The requirement of supervised clinical experience with at least 3 administrations of each type of therapy also remains reasonable.

I would leave it up to the medical specialty board to create a competency model and administer the exam since they have experience with both. However, I do not believe that there needs to be a separate board exam for therapies. The content is already tested on the initial board certification exam and re-tested with updates on the re-certification exam. The medical specialty boards will have to integrate any new requirements from the NRC into the competency model and ultimately, into the exam itself.

Sections 1 and 2 are very detail oriented. The American Board of Nuclear Medicine has training requirements for the ABNM certifying examination, which include one year of preparatory clinical training in an accredited program and the completion of Nuclear Medicine training in an ACGME approved program. It might be worthwhile for NRC to review the ACGME accreditation requirements to see what's covered and what's not, before putting too many details into the regulations. Also how many pages will the NRC Form 313A have to be in order to include the whole list of items?

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Dr. Dam added some examples of microspheres therapy in section 2. If microspheres therapies are still categorized under 35.1000, then the examples don't apply to 35.390 here.