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Irene Wu, P.E.
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and
Maryann Ayoade
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Re: Questionnaire on the Evaluation of Tailored Training and Experience Requirements for Different Categories of Radiopharmaceuticals

Dear Ms. Wu and Ayoade:

The Radiation Safety Officer (RSO) at UCLA, Bryan Ruiz, received this questionnaire from you on 04-13-18, requesting a response in two weeks. On 04-26-18, Mr. Ruiz asked Christiaan Schiepers, M.D., Ph.D. and me for help with this document. Dr. Schiepers has very recently retired as Professor and Director of the Nuclear Medicine Residency Program at UCLA, and I am also a Professor in that department, mainly retired but working part-time.

My first observation is that this questionnaire went to an RSO, a health physicist who knows very little about this subject. One needs to be board-certified in Nuclear Medicine to understand the subject. The questionnaire should have gone to the three professional organizations representing Nuclear Medicine, the Society of Nuclear Medicine and Molecular Imaging (SNMMI), formerly the Society of Nuclear Medicine (SNM), the American College of Nuclear Medicine (ACNM), which joined with the American College of Nuclear Physicians (ACNP), which no longer exists as a separate entity, and the American Board of Nuclear Medicine (ABNM).

My second observation is that you gave my RSO only two weeks to answer your questionnaire, basically guaranteeing that you won't get much of an answer. Mr. Ruiz is a very busy man, and extraneous questionnaires like this are a waste of his time.

My third observation is that you have made his response voluntary, which pretty much assures that he and other non-nuclear medicine physician RSOs may not even respond.

By sending this voluntary questionnaire to the wrong people, with a short response time, you will then get back nothing much and then tell the Commission that you received no substantive comments against your suggestions. **This is fraud**, and the NRC has done

this before, such as with the National Academy of Sciences-Institute of Medicine (NAS-IOM) Report "Radiation in Medicine. A Need for Regulatory Reform", National Academy Press, Washington, D.C., 1996, when NRC sent it to the Governors of each state for comment, instead of to the SNM, ACNP, and the ABNM. Figuring that no Governor would read a 298-page report, the NRC "summarized" it for them. The NRC's spin defied credibility. While the NRC paid for the NAS-IOM study, the NRC ignored its findings. The NAS-IOM recommended that Congress remove NRC's statutory authority in medicine and medical research. That's how bad they thought the NRC's "medical" program had become. And, it hasn't improved in the intervening years.

Competence of the Regulators

It is painfully evident that the authors of this questionnaire know nothing about Nuclear Medicine or Nuclear Medicine therapy, and have nothing positive to contribute. For example, I found four places where the authors talk about the need to train residents in kit preparation and generator elution for therapy radiopharmaceuticals, ***even though there are no kits or generators for therapy radiopharmaceuticals that practicing physicians can acquire, and never have been any.*** There is one radiopharmaceutical (Y-90 Zevalin) that uses a kit, but by agreement between the manufacturer and the FDA, only a nuclear pharmacy can receive the kits. There may be an industrial Sr-90/Y-90 generator for Y-90 separation (that is one way to make it) but it has never been commercially available to nuclear medicine practitioners. In addition, the authors go on about the need to train residents in the pharmacologic effects of therapy radiopharmaceuticals, when few have ever had any pharmacologic effects because they are tracers. Large masses of I-131 MIBG and antibodies can have pharmacologic effects, but the great majority of therapy radiopharmaceuticals exert their effects only because of radiation.

We do not need naïve dilletantes at the NRC deciding what Nuclear Medicine physicians need to learn. This is the rightful place of the American Board of Nuclear Medicine and the Residency Review Committees, as well as the SNMMI and ACNM, and they are perfectly capable of doing a credible job, as similar groups do for every other medical specialty. The job of the NRC should be limited to radiation protection, not the details of medical practice, and the NRC doesn't even understand radiation protection, clinging with bloody fingernails to the Linear Non-Threshold (LNT) myth, when it has been thoroughly obliterated by valid science for decades.

The NRC's Program is Dangerous to Patients

The NRC, rather than enhancing the safety of Nuclear Medicine over that which would occur without the NRC, has made it of lower and lower quality because of NRC's insatiable greed for licensing money in order to support a feather-bedded non-medical "medical" staff. Radiation is not a danger in Nuclear Medicine so long as the radioactive material is handled and managed by competent professionals. The danger in Nuclear Medicine is poorly competent or incompetent Authorized Users (AUs) who do not design their procedures, do not vary their procedures for individual patients as appropriate, do not make sure that the right medications have been stopped or restarted as appropriate, do

not supervise their technologists (because they don't know how), do not talk to patients (because they cannot answer their patients' questions), and often have their technologists do "preliminary readings" of the studies and just basically copy them and then bill for their services. No technologist is capable of practicing Nuclear Medicine. This leads to confused and unhappy patients, wrong diagnoses, and non-optimal therapies. The United States is the only first world country that chops up Nuclear Medicine into pieces and then tries to decide what training and experience is necessary for the little pieces that result. While this leads to the licensing of many, many more AUs, with much more income to the NRC from licensing fees, **it is the patients that suffer**. In all other first world countries (and many other countries) only physicians board-certified in Nuclear Medicine may practice in any area of Nuclear Medicine. This ensures that the physicians have comprehensive education, training, and experience necessary for competence. The NRC is basically obliterating the specialty of Nuclear Medicine in the United States by selling all its business away to other physicians. At present, there are only 69 Nuclear Medicine residents in the United States, 70% of whom are foreign medical graduates. **The patients of the United States would be much better off, and much safer, if their Nuclear Medicine physicians were board-certified in Nuclear Medicine.** And, the NRC's job would be much simpler. All of Part 35 could be obliterated and replaced by the requirement for board certification in Nuclear Medicine in order to practice any or all of it. And virtually all of its non-medical "medical" staff could be unbudgeted. Licensing fees could be miniscule and AUs could concentrate on their patients instead of on the enormous paperwork burden imposed upon them by a regulator looking for more things to regulate. Inventing busywork for a useless and often dangerous staff who continue to fool the Commissioners into accepting the self-serving, bureaucratically maximized plans that the staff concocts shows that the Commissioners have no understanding of what is going on and are incapable of meaningful leadership in the medical area.

The NRC Doesn't Enforce Its Own Regulations for T&E

On March 1, 2018 NRC's Advisory Committee on Medical Uses of Isotopes (ACMUI) held a meeting concerning radiopharmaceutical therapy training and experience. It appears that that staff wanted to decrease the requirements for radiopharmaceutical therapy so that patients in small towns would not be inconvenienced by having to travel to larger population centers for such therapy. This would, of course, create more AUs and more licensing fees to support the non-medical "medical" staff. The ACMUI shot that down totally, supporting the current 700 hours (200 hours of formal training and 500 hours of experience). **However, the NRC has refused for 21 years to enforce this requirement.** After obtaining memoranda of understanding from the relevant medical boards, the NRC has never inspected residency training programs to make certain that the requirement is actually being met. NRC enforcement is nonexistent. As I stated at the ACMUI meeting, I did not believe that there was a Diagnostic Radiology residency program in the country that provided that level of training and experience and that documented that the residents actually came to the training that was offered. (You can offer lectures, but if the residents have no interest and don't show up, it doesn't count toward the required hours.) Failure to fulfill the regulatory training and experience requirement is certainly one reason why some Diagnostic Radiology residents go out into

practice and do a poor job. **But NRC doesn't want to inspect and enforce its own requirement, because it might lead to a decrease in the number of AUs and a decrease in licensing income. This is a tremendous regulatory conflict of interest.** It seems to me that instead of wasting time writing a proposal like the one which you are circulating, that you instead adopt a policy of inspection and enforcement. Otherwise, it doesn't matter what requirements you make. **If they are not enforced, they mean absolutely nothing**.

The Concept of a Competency Examination

In the event that the NRC persists in trying to sell licenses to as many physicians as possible, which would be a grave mistake, you introduce the idea of a competency examination. **It is important for you to understand that this is not a new idea.** Near the end of my second term on the ACMUI, around 1994, the ACMUI, disgusted with the fact that many AUs were not sufficiently competent to practice Nuclear Medicine, voted unanimously to impose a basic nuclear and radiation science competency examination. The thought was that if a physician cared enough to study the necessary basic science material and pass the exam he would likely learn the clinical material as well. When the regulations for Part 35 were redone shortly thereafter, such a competency examination was part of the Proposed Rule. However, when the Final Rule came out in 1997, the requirement for the basic nuclear and radiation science competency examination mysteriously disappeared, without any public comment period or announcement in the Federal Register. The excuse was that there were so many types of AU that it would be too difficult to write different exams for each group. This, of course, was a lie. Only one examination was envisioned, as there is only one body of basic nuclear and radiation science knowledge. It was obvious that the staff realized that many potential AUs couldn't pass such an examination, and the licensing fees would decrease, and with decreased fees some of the staff in the "medical" program would have to be laid off, and that was unacceptable to them. They were able to hoodwink the Commission, unfortunately, and so the requirement was removed. And, unless there is effective leadership from the Commission, that will likely happen again. **Follow the money. Nothing that decreases licensing fees has much of a chance of getting through the NRC.**

If such an examination were, by some miracle, to be approved, the entity that writes the single examination is of paramount importance. The examination can easily be dumbed down as needed to preserve licensing fees, and would therefore be of no value whatsoever. The only entity competent to write this examination would, in my mind, be the ABNM. And, I don't believe that the NRC would ever let this happen.

Conclusion

This draft document is a naïve scientific and medical mess that needs to be obliterated. Appropriate Nuclear Medicine entities decide what should be taught to residents, not non-medical bureaucrats at the NRC. The existing NRC training and education requirements should be enforced by the NRC, in order to remove potential AUs who are

not competent to provide high quality Nuclear Medicine therapy to patients. The NRC's "medical" program at present is a detriment to patients in the United States.

Thank you for the opportunity to comment on this proposal.

Sincerely,

Carol S. Marcus, Ph.D., M.D.

Prof. of Molecular and Medical Pharmacology (Nuclear Medicine), of Radiation Oncology, and of Radiological Sciences (ret.), David Geffen School of Medicine at UCLA, and

Past Vice President, SNM
Past President, ACNP-California
Past member of the ACMUI

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, 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, 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
        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, 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, 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
    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

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. Use of dose blockers, if necessary

    d. Route of administration
        i. Ability to determine administration under special patient conditions such as gastrostomy, tracheostomy, renal failure, dialysis, liver failure, incontinence, unable 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

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

    g. 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)

    h. 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

    i. Post verification (to determine dosage and if medical event occurred)
        i. Appropriate modality (e.g. imaging)
        ii. Understanding artifacts

    j. 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. Radiation Protection specific to radiopharmaceutical
    i. Unique or additional handling concerns
    ii. Unique ordering, receiving, and unpacking concerns
    iii. Calculation, measurement, and preparation 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?
    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?