SPECTRUM™
PHARMACEUTICALS
Redefining Cancer Care

March 15, 2016

Chairman Stephen G. Burns
U.S. Nuclear Regulatory Commission
Mail Stop O-16G4
Washington, DC 20555-0001

Re: Training and Experience Requirements For Alpha and Beta Emitters Patient Ready Doses

Dear Chairman Burns:

I am writing to follow up on the NRC's January meeting with Spectrum Pharmaceuticals and the Council on Radionuclides and Radiopharmaceuticals (CORAR) to discuss the training and experience requirements for Authorized Users (AUs) of patient-ready doses of alpha and beta emitters. I greatly appreciate your time and consideration of this issue and the attention given to the issue by the Advisory Committee on the Medical Use of Isotopes (ACMUI). However, I am disappointed that at the recent March 10th meeting as well as in their Subcommittee Report, ACMUI failed to justify why 700 hours of training and experience is appropriate for patient-ready doses of alpha- and beta-emitting therapies such as Zevalin. While ACMUI acknowledged that the educational paradigm has shifted and that the requirements need to be updated, they voted to approve the Subcommittee Report on Training and Experience for Authorized Users of Alpha and Beta Emitters under 10 CFR 35.390, which maintains the current requirements. We urge the NRC to adopt a more appropriate training and experience requirement in the current rulemaking since this issue was raised with the NRC as far back as December 2011, before the current rulemaking was issued. If that does not have the votes, we request that the NRC initiate a separate rulemaking proceeding to address the issue and, as an interim measure, establish an exemption process for qualified clinicians to become authorized to administer these unique and life-saving therapies.

Despite the clear charge from the NRC to establish a recommendation for the appropriate training and experience for AUs of alpha and beta emitters that balances safety with reasonable patient access, the ACMUI continues to be focused instead on practice of medicine issues. It is undisputed that Zevalin is an FDA-approved therapeutic anti-cancer agent that provides a significant benefit to a subgroup of patients with non-Hodgkin's lymphoma. Additionally, it is clear that in certain communities in regions of the Nation there is a lack of AUs available to administer products like Zevalin outside of academic medical centers. Laura Weil, ACMUI Patients' Rights Advocate, correctly and clearly noted in her dissent to the Subcommittee Report that the 700-hour requirement negatively impacts patient access in the community setting and impacts patients unable to travel to metropolitan areas, such as the elderly and frail.

11500 South Eastern Ave. • Suite 240 • Henderson, NV 89052 • Tel: 702.835.6300 • Fax: 702.260.7405
www.sppirx.com • NASDAQ: SPPI

Additionally, the Subcommittee acknowledged that alpha and beta emitters have an "exceptional" safety record. However, this does not mean that the current 700-hour requirement should not be modified for patient-ready doses of alpha and beta emitters that are prepared by licensed radiopharmacies and delivered to the physician as a pre-filled syringe on the day the treatment is administered. Compared to the use of other radiolabeled products covered under this Subpart, the physician is not involved in mixing or handling the radioactive isotopes for these alpha and beta emitters. Moreover, the evidence on the record is clear that oncologists who became an AU under the 80-hour alternate pathway continue to administer alpha and beta emitters today without any safety events. This means that physicians who became AUs under the 80-hour requirements have since been administering beta emitters wholly without any safety issue or incident. Contrary to the statement in the Subcommittee Report, "[w]hether or not the safety records would be comparable in the hands of AU's with considerably less T&E [than 700 hours]" is *not* "a matter of conjecture."

The Subcommittee correctly concluded that the educational paradigm has shifted toward competency-based certifications and that the current requirements, which were established nearly 15 years ago, need to updated. However, we are concerned with the Subcommittee's suggestion that this cannot be completed in the near future. The NRC, ACMUI, and interested stakeholders have devoted a considerable amount of time and attention to this issue over the past 18 months, and the NRC and ACMUI have been presented with significant evidence that an 80-hour didactic course would allow a clinician to demonstrate competency with the safety profiles of alpha and beta emitters. We urge the NRC to address the training and experience requirement in the Final Rule. Based on the expert stakeholder commentary provided by Dr. Joseph Mace and Kristina Wittstrom, Kara Weatherman, and Nicki Hilliard, which is attached, we have prepared proposed regulatory text for a new training and experience paradigm for patient-ready doses of alpha and beta emitters, a copy of which is also attached.

During the teleconference, some ACMUI members expressed concern that updating the training and experience requirements for alpha and beta emitters in the current rulemaking would delay the rule's finalization by up to two years. While we disagree that such a delay would be necessary, should the NRC decide not to reduce the training and experience requirements in the current proceeding, we request that the Final Rule direct the NRC and ACMUI to initiate a standalone rulemaking on training and experience requirements for alpha and beta emitters on an expedited basis.

In the interim, the NRC should create an exemption pathway under 10 CFR 35.19 for practicing hematologists and oncologists such as Dr. Jennifer Cultrera of Florida Cancer Specialists, who stated at the teleconference that she would welcome the opportunity to demonstrate her competency through an 80-hour alternative to the 700-hour requirement, which she is unable to satisfy because of the demands of her practice. Such an exemption would address the concerns of Michael O'Hara, ACMUI FDA Representative, who asked during the teleconference what the NRC could do in the interim to address shortages of AUs.

In conclusion, we continue to believe that no justification has been offered for why 700 hours of training and experience is required to administer patient-ready doses of alpha and beta emitters. We respectfully request that the NRC act swiftly to address these outdated requirements to ensure that patients have access to a safe and life-saving cancer treatment option. We continue to be available to speak with you and the NRC staff and provide any additional information as needed.

Sincerely,

Rajesh C. Shrotriya, MD

Cc: NRC Commissioner Jeff Baran
NRC Commissioner William C. Ostendorff
NRC Commissioner Kristine L. Svinicki

11500 South Eastern Ave. • Suite 240 • Henderson, NV 89052 • Tel: 702.835.6300 • Fax: 702.260.7405
www.sppirx.com • NASDAQ: SPPI

Training for the Administration of Alpha- and Beta-Emitting Radiopharmaceuticals Prepared as Patient-Ready Doses by Licensed Nuclear Pharmacists at Licensed Radiopharmacies

Except as provided in 35.57, the licensee shall require an authorized user for the administration of pre-prepared patient-ready doses of alpha- and beta-emitting radiopharmaceuticals requiring a written directive to be a physician who--

(a) Is certified by a medical specialty board whose certification process has been recognized by the Commission or an Agreement State and who meets the requirements in paragraphs (c)(1) and (c)(2) of this section. (Specialty boards whose certification processes have been recognized by the Commission or an Agreement State will be posted on the NRC's Web page.); or

(b) Is an authorized user under § 35.390 for uses listed in § 35.390(b)(1)(ii)(G)(2) or equivalent Agreement State requirements; or

(c)(1) Has successfully completed 80 hours of classroom and laboratory training, applicable to the medical use of alpha- and beta-emitting radiopharmaceuticals administered as pre-prepared patient-ready doses for procedures requiring a written directive. The training must include—

(i) Nuclear physics and instrumentation;

(ii) Radiation biology;

(iii) Regulations and radiation protection; and

(iv) Mathematics pertaining to the use and measurement of radioactivity; and

(2) Has completed experiential training exercises, under the supervision of an authorized user who meets the requirements in §§ 35.57, 35.390, [this regulation], or equivalent Agreement State requirements. A supervising authorized user, who meets the requirements in § 35.390(b), must also have experience in administering dosages as specified in § 35.390(b)(1)(ii)(G)(2). The experiential training exercises must involve—

(i) Completion of not less than 10 hours of experiential training in radiation safety techniques, protocols, and procedures;

(ii) Participation in or observation of the administration of the specific radiopharmaceutical to not less than 3 patients; and

(3) Has obtained written attestation that the individual has satisfactorily completed the requirements in paragraphs (c)(1) and (c)(2) of this section, and has achieved a level of competency sufficient to function independently as an authorized user for medical uses authorized under § 35.300. The written attestation must be signed by a preceptor authorized user who meets the requirements in §§ 35.57, 35.390, [this regulation], or equivalent Agreement State

requirements. A preceptor authorized user, who meets the requirements in § 35.390(b), must also have experience in administering dosages as specified in § 35.390(b)(1)(ii)(G)(2).

11500 South Eastern Ave. • Suite 240 • Henderson, NV 89052 • Tel: 702.835.6300 • Fax: 702.260.7405
www.sppirx.com • NASDAQ: SPPI

STATEMENT OF JOSEPH R. MACE, M.D.
Medical Oncologist and Licensed Authorized User
Florida Cancer Specialists
to the
Advisory Committee on the Medical Use of Isotopes Subcommittee on Training and Experience for Beta-emitters

I. Introduction

1. My name is Joseph Mace, and I am writing to provide the ACMUI Subcommittee with my opinion and recommendations as it reviews the appropriate level of training and experience requirements for hematologists and medical oncologists to safely administer beta-emitters under 10 CFR 35.390. As set out in my statement, I have been an Authorized User for over a decade and have safely administered beta emitters, including Zevalin (ibritumomab tiuxetan), to over 40 patients.

2. I have detailed my training and clinical experience for the Subcommittee. I believe that the information provided in my statement supports a modification to the training and experience requirements to provide a limited authorization for beta emitters prepared by a licensed radiopharmacy and delivered to the hematologist/ medical oncologist in a pre-filled syringe.

3. I strongly urge that the ACMUI Subcommittee consider a modified alternate pathway of requiring 80 hours of training and experience for hematologists/ medical oncologists seeking to administer beta-emitting therapeutic radiopharmaceuticals such as Zevalin.

II. Academic and Clinical Qualifications

4. I received a Bachelor of Arts with highest honors, from the State University of New York at Binghamton in 1989 and a Doctor of Medicine, *summa cum laude*, from the State University of New York Health Science Center at Syracuse in 1993.

5. I served as a Diagnostic Radiology Resident at the Hospital of the University of Pennsylvania between 1994 and 1996, an Internal Medicine Resident at the State University of New York Health Science Center at Syracuse between 1996 and 1998, and was a Hematology and Medical Oncology Fellow at the University of Michigan Medical Center from 1999 to 2002.

6. Starting in the summer of 2002, I practiced as an Attending Physician at Gulfcoast Oncology Associates in St. Petersburg, FL. I founded both the Gulfcoast Oncology Associates' Clinical Research, and Radioimmunotherapy Programs, and served as director until our merger with Florida Cancer Specialists in February of 2011. I continue to serve as an Authorized User (AU) of radioimmunotherapy agents, treating patients at our St. Petersburg office location. In addition, I travel to several additional Florida Cancer Specialists office locations to administer radioimunitherapy agents, in an effort to expand patient access to these important and effective therapies. I also serve as a Thought Leader for Lymphoma, Leukemia, bone marrow disorders, as well as benign hematology within Florida Cancer Specialists' Clinical Research Program .

III. Authorized User Training and Experience

7. I obtained my AU license from the Nuclear Regulatory Commission in 2006, after completing an on-site, eight-day, 100-hour radiation safety and handling course offered through the University of Chicago.[1]

8. This course consisted of didactic lectures and two daily written examinations. Course topics included radiation physics, instrumentation, protection, and biology, as well as mathematics pertaining to radioactivity; and radiopharmaceutical chemistry. Specific characteristics and aspects of use surrounding those radioisotopes that are commonly in use for both medical diagnostic and therapeutic indications, across all medical subspecialities, were reviewed in detail. In part owing to this, and as I explain in greater detail below, the 100-hour course I attended did cover a notable volume of material that was/ is superfluous for those physicians seeking to use/ administer solely beta emitters.

9. I have been safely administering Zevalin at multiple office locations in Florida since I received an AU license in 2006, as discussed above.

IV. Medical Experience with Beta Emitters

11. During my fellowship training at the University of Michigan Medical Center, I had the unique opportunity to work closely with Dr. Mark Kaminski in the Lymphoma clinic from 1999 through 2002. During this three year period, the use of radioimmunotherapy was commonplace, and as a result I obtained significant experience with their pharmacology, safe handling, and administration. Upon completing my

[1] Until the regulations were changed in 2002 to require 700 hours of training, one could become an AU with 80 hours of training and experience. Because Florida did not implement the rule until 2006, the 80-horu requirements were grandfathered.

Hematology and Medical Oncology fellowship, and joining Gulfcoast Oncology Associates in St. Petersburg, I was uniquely positioned to enhance the services our practice provided. I felt then, as I do now, that Zevalin offers many advantages for our Non-Hodgkin Lymphoma (NHL) patient population.

12. As compared to conventional chemotherapy regimens, beta emitters such as Zevalin provide an invaluable treatment option for patients NHL. For one, treatment with beta emitters is far less intrusive and cumbersome for patients; It can be completed in approximately one week and involves the administration of one dose of radiolabeled antibodies. In addition, antibody-bound beta emitters target NHL cells highly selectively, which translates into mild and generally well tolerated side effects. Patients do not need to be admitted to a hospital for treatment, and beta emitters such as Zevalin typically do not result in significant adverse impact on patients' quality of life, functional capacity, or their other medical problems. Taken in total, it is the clinical features of Zevalin that make it so appealing to those of us who treat Lymphoma patients on a regular basis, particularly where a large proportion of patents are elderly, and unable to tolerate conventional cytotoxic therapy.

13. Beta emitters are employed at many stages of a NHL patient's clinical course. Their tolerability and efficacy are well established in the setting of indolent NHL, which comprises a large percentage of new NHL diagnoses and, unfortunately, is a non-curable disease. This being said, indolent NHL typically runs a very long clinical course thats can be measured in years to decades, with intermittent treatments required over time. This fact highlights the importance of having as many effective agents in our arsenal as possible. In essence, it is crucial that proven agents, such as the antibody-

bound Beta emitters be readily available to patients with indolent NHL, as optimal improvements in life span and survival will be achieved by employing many different treatments over the course of their disease. The antibody-bound Beta emitters have well established efficacy particularly in those patients who have received many prior conventional chemotherapy agents, where responses to subsequent conventional chemotherapeutic agents is less frequent and of shorter duration.

14. Recognizing this, after I received my AU license I worked to establish a "hot lab" as well as an administration area at our practice location. It soon became clear that the ability to provide Zevalin locally, thereby precluding the need for outside referrals to either radiation oncology or a regional academic center, was of tremendous benefit to our patients. While it might be unusual for a hematologist/ medical oncologist to obtain an AU license for RIT administration, there are clear advantages to doing so. We have a unique understanding of chemotherapy, including its administration, potential short- and long-term side effects, as well as the requisite monitoring both during and after treatment. In addition, a hematologist/ medical oncologist is ideally suited to manage patients who receive Zevalin, and the ability to actually administer this agent (as opposed to referring a patient elsewhere to do so) improves convenience, access, and provides for optimal continuity of patient care.

15. As a result, I received consultations for Zevalin therapy, not only from within Gulfcoast Oncology, but also from physicians outside our practice across the state of Florida. Patients clearly appreciated seeing the same physician for their consultation to review and discuss Zevalin therapy, for the administration of the agent, and for the requisite monitoring over the subsequent two to three months thereafter.

16. I have been administering Zevalin for approximately ten years now and have not had a single safety event. I strongly believe that completing an intensive 100-hour course provided me with more than sufficient training to administer this safe and straight forward therapy.

V. Shortage of AUs

17. Since the introduction of the 700-hour training and experience requirements, I have observed an immediate and dramatic impact on access to beta emitters. In my own practice at Florida Cancer Specialists, there are many oncologists who would like to administer beta emitters, however it is not logistically feasible or realistic for them to pursue the 700-hour training requirement. It is difficult to fathom a practicing hematologist/ medical oncologist being able to take an aggregate 700 hours away from patient care, in order to attend a radiation safety and handling course, be it at a brick and mortar facility, or online. In fact, to my knowledge, no oncologist has been able to receive AU status under the alternate pathway of 700 hours, since the regulations went into effect.

18. Accordingly, there is in my opinion, a marked shortage of physician "champions" in any given community who are willing to undertake what is now an extensive number of hours to obtain an AU license. In turn, this decreases patient access to this important and effective therapy.

19. The lack of access to beta emitters is an especially acute problem for the elderly, for whom Zevalin is an especially advantageous treatment option. St. Petersburg has a particularly large population of elderly cancer patients, and owing to this, the incidence of low-grade lymphoma occurs with greater frequency than the national average. Not unexpectedly, a majority of elderly patients are not only less able tolerate

conventional chemotherapy, but are also less mobile, and thus typically cannot manage the rigorous clinic visit schedules associated with these chemotherapies.

20. The problem is severe enough that in order to provide patients with access to beta emitters, I initiated a "traveling AU" program, wherein I see patients in consultation, and for administration of Zevalin at multiple office locations throughout Florida. While the program has been effective in modestly increasing access to beta emitters, increasing the number of oncologist AUs in a given community would be far more impactful. This could be accomplished by lowering the training and experience requirements to a more appropriate level.

VII. 80 Hours of Training is Sufficient

21. Based on my own experience with the course, 80 hours of training and experience would sufficiently prepare AUs to administer beta emitters such as Zevalin, which is delivered to the AU as a treatment-ready dose prepared by a licensed radiopharmacy. Its administration is not complex, requiring only an acrylic shield and adherence to standard radiation precautions. It does not even require patient isolation or exposure measurements

22. Zevalin has an excellent safety profile, particularly when compared to cytotoxic chemotherapeutic agents. Rates of nausea, vomiting, alopecia, hepatorenal injury and dysfunction, cardiopulmonary toxicity, neuropathy, and constitutional decline, are all less frequent with Zevalin. Like many cytotoxic chemotherapeutic agents, Zevalin does produce myelosuppression, and once again, it is the medical oncologist/ hematologist who is best prepared to manage this common and expected side effect of NHL therapy.

23. By contrast, the administration of sodium iodide I-131 based therapies is a much more involved process requiring a greater degree of precautionary measures. The patient must be isolated, and anyone handling the patient's fluids must wear protective clothing, including eye protection and a mask. In addition, the patient is not permitted to share toothbrushes, towels, or even a bed with another person. Yet currently, this therapy only requires 80 hours of training to administer.

24. The currently required 700 hours of training is vastly disproportionate to Zevalin's safety profile. Indeed, the requirements contained in 10 CFR 35.390 appear to be aimed at physicians seeking to become board certified in nuclear medicine. Board-certified nuclear medicine practitioners handle an array of radioactive substances in diagnosing and treating a variety of diseases. The course that I completed in 2005 covered topics ranging from diagnostic medical imaging, non-medical radiation uses, historical radiation events, to therapeutic thyroid I-131 administration—all superfluous from the standpoint of radionuclide management and safe handling of Beta emitters. That course was 100 hours, and while I am a strong proponent of general knowledge and academic pursuit, this highlights that 700 hours of training is unnecessarily prohibitive for hematologists/ medical oncologists seeking specifically to administer a limited class of beta-emitting products.

25. By reducing the requirements, practicing hematologists/ medical oncologists who either specialize in, or have an interest in NHL, can feasibly complete the required coursework and have an immediate impact on access within their community. In addition, with less onerous requirements in place, improvement in the

degree of familiarity and comfort with using Zevalin would undoubtedly follow, which in turn would translate into even greater access to these important therapies.

26. I believe the current training and experience requirements should be modified with respect to beta emitters. The course content can be appropriately focused on issues related to the administration and handling of beta emitters in order to lessen the time burden, while still resulting in proficiency on the part of the individual physician.

27. Based on my experience, the relevant components of the 700 hours of training for beta emitters can be successfully encompassed by focused study within an 80 hour course/ pathway. Topics essential to this should include training on:

(a) Radiation physicsand biology

(b) Radiation instrumentation, with particular attention to those used and setting appropriate for beta emitter therapy

(c) Radiation protection

(d) Mathematics pertaining to the use and measurement of radioactivity

(e) Pharmacology and chemistry of radioactive materials in the context of medical use.

(f) Safe handling practices for radioactive material and instrumentation

(g) Performance of standard quality-control procedures on instrumentation (those used to determine the activity of dosage, survey meters, etc.), and on received dose packaging, as well as reviews of personnel badges/ rings, and periodic radiation exposure reports.

(h) Calculation, measurement, and safe preparation of patient or human research subject doses (despite the fact this is performed by a licensed radiopharmacy).

(i) Review of the standard administration practices for specific Beta emitters.

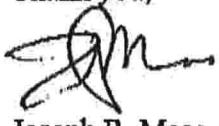
28. In such an 80-hour program, prospective AUs would gain ample experience with the logistics, medical and scientific, as well as administrative aspects and requirements of therapy. This would successfully serve to prevent and/or address adverse events associated with drug misadministration, personnel exposures and decontamination procedures, as well as with procedures for containing spilled radioactive material.

29. The above recommendations can be encompassed and successfully covered with a dedicated 80-hour training and experience requirement. A 700-hour requirement is unnecessary and deprives NHL patients of a valuable treatment option that is needed in many communities.

30. Stakeholders have proposed requiring 80 hours of training and experience to obtain an AU license as part of the current NRC rulemaking on radiolabeled materials, and I fully support this proposal.

31. I appreciate that the ACMUI is taking the opportunity to consider the appropriate training and experience requirements for beta emitters. I urge the ACMUI to consider my experience and recommendations as you prepare your Subcommittee report. I would welcome the opportunity to provide the ACMUI Subcommittee with any additional information that might prove helpful. Please feel free to contact me with any questions.

Thank you,



Joseph R. Mace, M.D.
Florida Cancer Specialists
1201 5th Avenue North, Suite 505
St. Petersburg, FL 33705
(727) 821-0017
jmace@flcancer.com

UAMS
COLLEGE OF PHARMACY
UNIVERSITY OF ARKANSAS FOR MEDICAL SCIENCES

OFFICE OF THE DEAN

Education Building II/6-104
4301 West Markham, #522
Little Rock, AR 72205-7199

501-686-5557
501-686-8315 (fax)

www.uams.edu/cop

Pharmaceutical Sciences Department
Biomedical Research Center
501-686-5937
501-686-6057 (fax)
Education Building II
501-686-6280
501-526-6510 (fax)

Pharmacy Practice Department
501-686-6390
501-296-1168 (fax)

Doctor of Pharmacy Degree Non Traditional Program
501-686-7124
800-245-3256 (toll free)
501-526-6872 (fax)

Arkansas Poison Control
501-686-5540
800-3POISON (toll free)
501-296-1451 (fax)

Drug Information
501-686-5072
888-228-1233 (toll free)

Continuing Education Program
501-686-5396

February 9, 2016

Ms. Sophie Holiday
Health Physicist / ACMUI Coordinator
U.S. Nuclear Regulatory Commission (NRC)
Washington, DC 20555-0001

Re: NRC Training and Experience Requirements for Alpha and Beta Emitters

Dear Members of the Advisory Committee on the Medical Use of Isotopes,

As experienced nuclear pharmacists and experts in the field of radiation safety education and training, we appreciate the opportunity to submit our comments on the training and experience requirements for authorized users of alpha and beta emitters.

It is discouraging to see radiopharmaceuticals with documented clinical impact not used because they are not readily available in physician treatment regimens. For example, Zevalin (Ibritumomab tiuxetan) has been approved for first line therapy against Non-Hodgkin's lymphoma, the seventh most common type of cancer. Xofigo (Radium-223 dichloride) was fast-tracked by the FDA after demonstrating an increased patient life span and pain control in prostate cancer patients. However, the regulatory restrictions on access drive oncologists to use less effective chemotherapy regimens associated with significant side effects and diminished patient outcomes.

These current alpha and beta emitting radiopharmaceuticals, and others under development, are delivered to licensed healthcare sites as patient-ready doses with no additional manipulations needed before patient administration. The needed training and experience for safe handling of these specific drugs does not appear to warrant the full 200 hours of didactic training and 500 hours handling experience.

We recommend that NRC, as part of the current rulemaking, modify the training & experience requirements for authorized users for patient ready alpha and beta emitters to a didactic program which consists of 80 hours of educational material. This will provide a strong foundation for practitioners who wish to become involved in the administration of alpha and beta emitting radiopharmaceuticals. A program such as this would also include enhancements to the distance based didactic education, including specific

requirements for experiential radiation safety hands-on exercises as well as supplemental handling experience for each specific radiopharmaceutical. A representative outline of our consensus for a training program is included as an addendum to this letter.

An addition to the user training requirements, each facility is mandated to have a radioactive materials license and radiation safety officer. With adequate training, radiation safety procedures and guidance documents in place, the risks should be minimal while providing the maximum benefit in patient care.

Sincerely,

Nicki L. Hilliard, Pharm.D, MHSA, BCNP, FAPhA
Professor of Nuclear Pharmacy
University of Arkansas for Medical Sciences
NLHilliard@uams.edu

Kara D. Weatherman, PharmD, BCNP, FAPhA
Clinical Assistant Professor of Pharmacy Practice
Director – Nuclear Pharmacy Programs
Purdue University
kdwman@purdue.edu

Kristina Wittstrom, PhD, RPh, BCNP, FAPhA
Director of Professional Curriculum
Director of Continuing Pharmacy Education
University of New Mexico
KWittstrom@salud.unm.edu

Authorized User Training for Alpha & Beta Patient Ready Radiopharmaceuticals

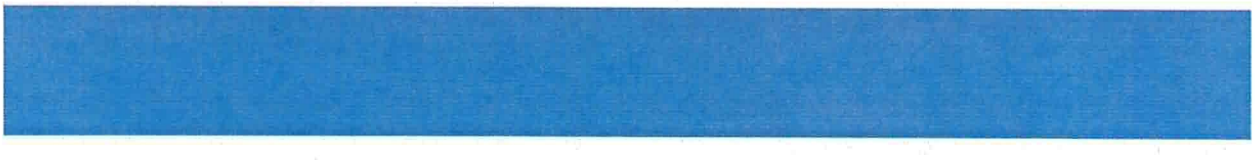
Recommendation for ACMUI Subcommittee Report

Developed by:

Kristina Wittstrom, PhD, RPh, BCNP, FAPhA
University of New Mexico

Kara Weatherman, PharmD, BCNP, FAPhA
Purdue University

Nicki Hilliard, PharmD, MHSA, BCNP, FAPhA
University of Arkansas for Medical Sciences



Summary of Needs

In that patient access to clinically meaningful therapeutics for treatment of oncologic conditions can be enhanced through better access, it is proposed that individual medical oncologists or urologists be licensed by the NRC or Agreement States for the isotope-specific radiopharmaceutical products. The licensure would consist of

1. Completion of an 80-hour didactic program in basics of radioactive materials handling suitable to alpha/beta emitting products to which access will be granted;

2. Completion of not less than 10 hours of experiential training in radiation safety techniques, protocols, and procedures;

3. Observe/participate in the administration of the specific radiopharmaceutical to not less than 3 patients.

4. Completion of not less than 4 hours of product–specific handling and patient administration techniques including record-keeping and patient counseling as provided by the radiopharmaceutical manufacturer; and

5. Addition to an existent or pending radioactive materials license with restriction in access and use to isotope, form and maximum activity.

Instructional Notes

a. *Suggest restriction to specific radiopharmaceuticals rather than a classification to maximize considerations of patient safety. For example, safe use of Ra-223 is different from safe use of Y-90.*
b. *There is no need for instruction on radiochemistry if use is restricted to patient-ready doses and there is no need for radiolabeling, reconstitution, or preparation of radiopharmaceuticals. Product quality control testing is also not needed.*
c. *Increased didactic and experiential training in radiation safety is recommended to maximize safety of patient and the general public.*
d. *As therapeutic uses do not involve imaging, training on imaging equipment is not needed. Testing and quality assurance of imaging equipment is not needed.*
e. *The requirement of dose calibrators will be variable dependent upon state requirements. Training is included. Instrumentation for contamination wipes and area surveys is included – function, testing, calculations, etc.*
f. *This training does NOT address issues specific to the use and handling of radioiodine products.*

Authorized User Didactic Training to Administer
Patient- Ready Alpha / Beta Emitting Radiopharmaceuticals

Block I: Nuclear Physics & Instrumentation: 25 hours

I. Structure and Properties of Atoms
II. Radiation and Radioactive Decay
III. Production of Radionuclides
IV. Interaction of Radiation with Matter
V. Gas-Filled Detectors
VI. Scintillation Counters
VII. Personnel Monitoring Devices

Block II: Radiation Biology: 20 hours

I. Physical Effects of Radiation
II. Chemical effects of Radiation
III. Cellular Effects of Radiation
IV. Biological Effects of High Dose Radiation
V. Biological Effects of Low Dose Radiation
VI. Therapeutic Application of Particulate Radiation

Block III: Regulations and Radiation Protection: 25 hours

I. Characteristics of Ionizing Radiation
II. Definitions of Radiation Measurement
III. Principles of Radiation Protection
IV. Personnel Monitoring & Safety Precautions
V. Regulatory Agencies
VI. Documentation and Regulatory Reporting
VII. Sealed Reference Sources
VIII. Area Monitoring
IX. Waste Management & Disposal
X. Packages containing Radioactivity

Block IV: Mathematics Pertaining to Use & Measurement of Radioactivity: 10 hours

Includes fundamental calculations: decay equation, half-value layers, exposure calculations, instrumentation needs.

Note: The traditional Radiochemistry material is not included here as the intended Authorized User will not be mixing, radiolabeling, or preparing patient doses. All radiopharmaceuticals will be received in patient-specific, ready-to-inject unit dose form.

Name of Trainee (Please print)

Assignments	**Operator**	**Supervisor**
1. Use basic operational functions of GM meters.		
2. Use basic operational functions of dose calibrator.		
3. Perform area wipe test for contamination.		
4. Perform regulatory performance checks of SCA / MCA		
5. Perform area-monitoring (surveys) for contamination.		
6. Perform decontamination procedure in a contaminated area.		
7. Dispose of radioactive waste and radioactive labels.		
8. Radioactive materials package check-in procedure.		
9. Determine appropriate patient-specific dose/ dose volume for ordering and administering radiopharmaceutical doses.		
10. Know regulatory requirements for, and how to arrange for, calibration of survey meters.		
11. Perform regulatory requirements for dose calibrator performance. (If applicable)		
12. Take appropriate steps to ensure that the right patient receives the right drug, in the right dosage, at the right time, via the right route of administration		
13. Interpret radioactive material license, applications, amendments.		
14. Locate applicable state/federal regulations for handling radioactive materials		
15. Demonstrate the proper selection, placement and handling of radiation dosimetry devices.		
16. Compile and maintain appropriate documentation to meet regulatory requirements		

Name of Supervisor *Signature* *Date*

Licensed Facility Name

Mailing Address

City, State Zip

Date(s) of Training

Biographical Information

Nicki L. Hilliard, PharmD, MHSA, BCNP, FAPhA

Dr. Hilliard was the manager and radiation safety officer in a nuclear pharmacy for 7 years before coming to UAMS to start a nuclear pharmacy education program. In the past 30 years she has taught thousands of authorized users both at the University and through the Nuclear Education Online program. Among her numerous awards she has received the William H. Briner Distinguished Achievement in Nuclear Pharmacy Practice and the American College of Nuclear Medicine Personal Mentor of the Year.

Kara D. Weatherman, PharmD, BCNP, FAPhA

Dr. Weatherman is a Board Certified Nuclear Pharmacist, with experience in both operational and clinical aspects of nuclear pharmacy practice prior to moving to academia as a member of the nuclear pharmacy program at Purdue University College of Pharmacy in 1998. Through her faculty appointment and as Director of Nuclear Pharmacy Programs at the College, she has focused on the development and implementation of various authorized user training programs, both via live and distance based education. In addition, she coordinates Purdue's continuing education program in nuclear pharmacy and maintains a research program in areas relating to nuclear pharmacy practice.

Kristina Wittstrom PhD, RPh, BCNP, FAPhA

As a Board Certified Nuclear Pharmacist since 1983, Dr. Wittstrom has extensive experience in operating a nuclear pharmacy both as manager and RSO. Her nuclear experience combined with a doctorate in adult education supports nuclear science education at the University of New Mexico in the classroom, the dispensing pharmacy and in the online environment.

McCloskey, Bridin

From: Vietti-Cook, Annette
Sent: Thursday, March 17, 2016 5:08 PM
To: Zorn, Jason; Baggett, Steven; Moore, Johari; Castleman, Patrick; Frazier, Alan; Bloomer, Tamara; Powell, Amy; Shane, Raeann
Cc: McCloskey, Bridin; Speiser, Herald
Subject: FW: Spectrum Letter to NRC
Attachments: Letter to the NRC 2016-03-16.pdf

From: Clarine Nardi Riddle [mailto:CNRiddle@kasowitz.com]
Sent: Thursday, March 17, 2016 10:03 AM
To: Vietti-Cook, Annette <Annette.Vietti-Cook@nrc.gov>
Subject: [External_Sender] Spectrum Letter to NRC

Annette,

There was a formatting issue with the letter that I sent you last night. Could you please distribute this version to the Chairman and the Commissioners. So sorry for any inconvenience.

Thank you so much,
Clarine

Please be advised that the Washington DC office of Kasowitz, Benson, Torres & Friedman LLP will be moving. Effective March 28, 2016, the new address will be:

1399 New York Avenue
Suite 201
Washington, DC, 20005

All phone numbers and e-mail addresses will remain the same.

Clarine Nardi Riddle
Kasowitz, Benson, Torres & Friedman LLP
2200 Pennsylvania Avenue, N.W.
Suite 680W
Washington, DC 20037
Tel. (202) 760-3402
Fax. (202) 379-9785
CNRiddle@kasowitz.com