Date: January 25, 2016

To: Chairman Stephen G. Burns
Commissioner William C. Ostendorff

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Regarding: The NRC's Authority to Establish Appropriate Training and Experience Requirements for Alpha and Beta Emitters in Current Rulemaking Process

I. Introduction and Background

On July 21, 2014, the Nuclear Regulatory Commission (NRC) issued a Notice of Proposed Rulemaking (NPRM) on the Medical Use of Byproduct Material: Medical Event Definitions, Training and Experience.[1] Following publication of the proposed rulemaking, the NRC and the Advisory Committee on the Medical Use of Isotopes (ACMUI) heard public testimony from stakeholders that the 700-hour training and experience requirements contained in 10 C.F.R. § 35.390 are excessive for beta-emitting therapeutic radiopharmaceuticals, and, as a result, have limited patient access to this safe and effective cancer treatment option. However, the NRC did not substantively address this issue in its Draft Final Rule, noting that "[n]o change was made to the rule text."[2] The NRC has subsequently stated that it cannot address changes to the training and experience requirements without a lengthy "two-year" comment period, which could result in delaying resolution of this issue until the next rulemaking cycle in 2021.

Even if the NRC determines that it cannot make a reasoned judgment on the change in hours under the terms of the NPRM, we believe that the NRC can accomplish a change to the training and experience requirements by either (1) issuing the Final Rule with a post-publication comment period to consider the recommendations presented at the March 17th-

[1] 79 Fed. Red. 42410 (July 21, 2014).
[2] Preliminary Draft for ACMUI Review, RIN 3150-AI63, at 82 (2015).

18th ACMUI meeting on the appropriate level of training requirements, or (2) using its exemption authority to license specific hematologists or oncologists who want to become Authorized Users.

II. The NRC Solicited & Received Substantial Public Comment on the Appropriateness of the Training and Experience Requirements

A. Public Stakeholders Submitted Extensive Comment on the Training and Experience Requirements

In its Proposed Rule, which expressly includes "training and experience" in the title, the NRC broadly addresses changes to the training and experience requirements for the medical use of byproduct material, including alpha and beta emitters. In particular, the NRC specifically requested public comment on whether its regulations "**discourage licensees from using certain therapy options or otherwise adversely impact clinical practice, and if so, how**."[3] Moreover, the NRC extensively discussed its proposed changes to 10 C.F.R. § 35.390, Training for use of unsealed byproduct material for which a written directive is required.[4] Further evidence of the anticipated breadth of this rulemaking can be found in the Proposed Rule's Executive Summary, where the NRC noted that its regulations relating to the medical use of byproduct material were last amended "in their entirety" in 2002.[5]

In the proposed changes to Section 35.390, the NRC addressed an ambiguity that exists under the current regulations as to how the training and experience requirements for certain new technologies should be determined.[6] The proposed language creates a new division among radionuclides to include one category for radionuclides used primarily for electron emission, beta radiation, or photon energy less than 150keV, and a second category for radionuclides used primarily for alpha radiation.[7] In addition to clarifying the categories of radionuclides, the NRC proposed changes to the training and experience requirements for the various radionuclides, providing that the options for a physician to become an Authorized User for this type of administration were to be modified as follows: (a) become an Authorized User under § 35.390, (b) become an Authorized User under § 35.490 or § 35.690, (c) become board certified under § 35.490 or § 35.690, **OR** (d)(1) have "successfully completed 80 hours of classroom and laboratory training, applicable to parenteral administrations listed in § 35.390(b)(1)(ii)(G)" (along with the relevant supervised work experience listed in (d)(2)).[8] The parenteral administrations referenced include the "[p]arenteral administration of any radionuclide that is primarily used for its … beta radiation characteristics … for which a written directive is required."

During the public comment period on the Proposed Rule, the NRC received significant stakeholder input on the training and experience requirements for alpha and beta

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[3] 79 Fed. Reg. 42410, 42418 (July 21, 2014).
[4] *See id.* at 42424-25.
[5] *Id.* at 42410 (emphasis added).
[6] *Id.* at 42424.
[7] *Id.*
[8] *Id.* at 42443.

emitters.[9] Following the close of the comment period, the NRC held a public meeting on February 12, 2015 to hear from patients and clinicians on how the training and experience requirements limited treatment options and adversely impacted clinical practice. Next, ACMUI hosted a June 16, 2015 public webinar to discuss, among other matters, the requirements' impact on access to cancer treatments. And then, on October 8, 2015, ACMUI held an in-person meeting during which it heard additional testimony on the disproportionate nature of the 700-hour requirement training and experience requirements as compared to the safety profile of beta emitters. ACMUI is holding a third meeting on March 17th and 18th to discuss the appropriate level of training requirements. Thus, not only did the agency solicit public comment on this issue, but it also received significant, substantive public feedback from affected stakeholders requesting that the training and experience requirements be lowered to 80 hours for alpha and beta emitters, which were required before the 2002 rule change and are currently required for sodium iodide I-131,[10] a product with a higher risk profile than beta emitters such as Zevalin. An 80-hour requirement would sufficiently prepare Authorized Users to safely administer beta emitters, just as it did prior to 2002.

B. A Change in the Final Rule Would Be a Logical Outgrowth

The NRC has raised the question of whether altering the training and experience requirements in its Final Rule would satisfy the "logical outgrowth" test. As discussed above, the NRPM and the subsequent comment period addressed these issues, and we believe that a court would find that changes in the Final Rule would constitute a logical outgrowth of the Commission's initial proposal. In the past, courts have upheld NRC rulemakings despite challenges to changes made in the Final Rule.[11]

A key factor in determining if a final rule will be deemed to be the logical outgrowth of a proposed rule is whether "a new round of notice and comment would . . . provide commentators with their first occasion to offer new and different criticisms . . . ."[12] As noted, there have been numerous opportunities for public comment on this particular topic both during the comment period and subsequent to the comment period. Moreover, ACMUI is scheduled to hold a public meeting on March 17th and 18th on this topic. Any public input received at this meeting could be used to inform and finalize the current rulemaking process.

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[9] The NRC received numerous comments from public stakeholders that specifically addressed 10 C.F.R. § 390. *See, e.g.*, Nov. 18, 2014 comment from Keith Brown, PhD, CHP; July 29, 2014 comment from James A. Ponto, MS, RPh, BCNP; Nov. 18, 2014 comment from Andrew Zimnoch; Nov. 6, 2014 comment from the State of Washington's Office of Radiation Protection; Nov. 17, 2014 comment from Bayer Healthcare LLC.; Nov. 18, 2014 comment from the Board of the Organization of Agreement States; Nov. 18, 2014 comment from the Community Oncology Alliance; Nov. 18, 2014 comment from the American Society for Radiation Oncology; undated comment from the Council on Radionuclides and Radiopharmaceuticals; Nov. 18, 2014 comment from Spectrum Pharmaceuticals.

[10] 10 C.F.R. §§ 35.932, 35.934.

[11] *See Connecticut Light & Power Co. v. NRC*, 673 F.2d 525 (D.C. Cir. 1982) (upholding a Final Rule that contained protective measures different from those proposed, since "[t]he agency need not renotice changes that follow logically from or that reasonably develop the rules it proposed originally. Otherwise, the comment period would be a perpetual exercise rather than a genuine interchange resulting in improved rules"), *cert. denied*, 459 U.S. 835 (1982); *Massachusetts v. United States*, 856 F.2d 378 (1st Cir.1988) (finding that information accompanying the NPRM provided sufficient notice of regulations adopted in the Final Rule).

[12] *Int'l Union v. MSHA*, 626 F.3d 84, 95 (D.C. Cir. 2010) (internal quotations and citations omitted).

Similarly, courts have held that when an agency broadly identifies a problem and solicits comments on potential solutions, affected parties should have anticipated that the agency might adopt a solution in the final rulemaking, even if such a solution was not specifically proposed in the NPRM.[13] Given that the NRC's Proposed Rule broadly discussed changes to the training and experience requirements contained in Part 35 and specifically discussed changes to Section 35.390, the NRC has met this requirement. Moreover, as discussed above, the NPRM proposed revising 10 C.F.R. § 35.396 such that physicians who complete 80 hours of training and have the relevant work experience would be eligible for Authorized User status to administer parenteral radiopharmaceuticals.[14] Stakeholders voiced their support for this change, but the NRC dismissed this proposed revision as "administrative error" in its Draft Final Rule.[15]

The current rulemaking does not present facts similar to those held invalid by courts for making no reference to a topic addressed in a Final Rule. In those cases, agencies neither solicited public comment on an issue nor provided any notice that would have led interested parties to anticipate the enacted change.[16] In fact, a change in the Final Rule to 80 hours would be similar in terms of notice to what occurred in 1998, when the NRC last overhauled 10 C.F.R. Part 35.[17] In its NPRM for that proceeding, the NRC had similarly proposed broad changes to its training and experience requirements.[18] The NRC heard from a variety of commenters on this change, some of whom were in favor of a lower amount, some of whom were in support of a higher amount, and others who opposed any strict hour requirement on the ground that it is arbitrary.[19] In the Final Rule in 2002, the NRC significantly increased the level to 700 hours.[20] The 700 hours were neither proposed nor discussed in the 1998 NPRM.

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[13] For example, in *Int'l Union v. MSHA*, the court held that because the agency "identified the problem of low height mines" and solicited public feedback on it in its NPRM, it was foreseeable that the agency might adopt a solution not set forth in the proposed rule. 626 F.3d 84, 95-96 (D.C. Cir. 2010). And in *City of Portland, Or. v. EPA*, the court concluded that it was foreseeable that the agency's final rule might require treating effluent, since the agency solicited comments on the issue in its NPRM.[13] 507 F.3d 706, 715 (D.C. Cir. 2007).

[14] 79 Fed. Reg. 42410, 42443 (July 21, 2014).

[15] Preliminary Draft for ACMUI Review, RIN 3150-AI63, at 81-82 (2015).

[16] *See, e.g.*, *Shays v. FCC*, 337 F. Supp. 2d 28, 101 (D.C. Cir. 2004) ("A review of the [FCC's] NPRM reveals no such solicitation of comments on this provision. Nor does the NPRM provide any notice so that interested parties reasonably could have anticipated the final rulemaking from the draft rule." (internal citations and quotations omitted)).

[17] 63 Fed. Reg. 43516 (Aug. 13, 1998).

[18] *Id.* at 43520, 43564, 43572.

[19] *See* 67 Fed. Reg. 20250, 20263-64 (Apr. 24, 2002) ("Numerous comments both supported and opposed the duration of the proposed training and experience requirements for individuals who would like to become an AU for unsealed byproduct material. Some commenters strongly supported the proposed reduction of the training and experience requirements for use of unsealed byproduct material in diagnostic nuclear cardiology because of the minimal risk to patients and public safety. Some commenters believed that NRC should not establish an 'arbitrary' number of training and experience hours. They indicated that it may take some individuals more time to master needed information. They believe that classroom training should focus on radiation safety and that there should be a requirement to show evidence of mastery in comprehensive nuclear and radiation science through an exam. In addition, they believe that the rule should clearly identify what knowledge and skills an individual should have.").

[20] *Id.* at 20381.

C. The NRC's Regulations Expressly Provide for a Post-Publication Comment Period

Even if the NRC believes that there was insufficient opportunity for public comment on changes to the training and experience requirements associated with beta emitters, 10 C.F.R. § 2.804(d)(2) allows for the adoption of regulations outside of the notice-and-comment process where strict adherence to these procedures would be impracticable, unnecessary, or when such changes are in the public interest. The NRC could therefore issue new requirements for training and experience in the Final Rule and, pursuant to 10 C.F.R. § 2.804(e), allow for a thirty-day post-publication comment period. The NRC could also use this procedure and wait to adjust the requisite hours of training and experience until it has had the opportunity to consider the recommendations that ACMUI will present at its March 17th and 18th meeting.

Contrary to the statements at the January ACMUI teleconference, it would not be necessary for the NRC to engage in an additional round of notice and comment, which would reportedly extend the rulemaking process by another two years. This is because the NRC and ACMUI have already solicited and received feedback on these issues from multiple parties on multiple occasions. Courts have repeatedly held that notice and comment is unnecessary where there has already been an actual opportunity to participate in the rulemaking process.[21]

Moreover, the "good cause" exemption to the notice-and-comment procedures is especially appropriate where the regulatory change is narrow in scope.[22] Changing the training and experience requirements for Authorized Users seeking to administer a very limited class of beta emitters is a particularly narrow request. In fact, prior to the NRC's 2002 rulemaking, only 80 hours of training and experience were required for such Authorized Users, and the NRC has not been able to articulate why this was changed.

Providing an additional round of notice and comment is unnecessary and would not further the public interest. As the NRC is well aware, such a process would take a considerable amount of time. Until a new rule is finalized, patient access to a unique and potentially life-saving treatment option would remain severely restricted. This is a particularly acute problem for the frail elderly and those living outside of major metropolitan areas. Bypassing an additional round of comment would serve the public interest and better protect human health and welfare, especially since treatments such as Zevalin are safely administered as patient-ready doses prepared at licensed radiopharmacies.

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[21] *See, e.g., Duquesne Light Co. v. EPA*, 481 F.2d 1, 8-9 (3d Cir. 1973) (finding that the agency was not bound by rulemaking procedures under the "good cause" exception where hearings had already been held at the state level and federal hearings would elicit duplicitous testimony); *Appalachian Power Co. v. EPA*, 477 F.2d 495, 503 (4th Cir. 1973) (same); *Mobil Oil Corp. v. EPA*, 35 F.3d 579, 584 (D.C. Cir. 1994) (acknowledging that an agency might be able to invoke the "good cause" exception where it has already obtained commentary that is still "fresh").

[22] *See Council of Southern Mountains, Inc. v. Donovan*, 653 F.2d 573, 582 (D.C. Cir. 1981) ("[T]he limited scope of the . . . order influences our finding that the [agency] had good cause to dispense with prior notice and comment.").

III. The NRC May Grant a Specific Exemption to the Training and Experience Requirements

In the event that the NRC elects not to address the training and experience requirements through formal rulemaking, we believe there is an intermediate approach that the NRC can undertake prior to the next rulemaking, which begins in 2019. Section 35.19 of the NRC's regulations grants the agency the power to, "upon application of any interested person or upon its own initiative, grant exemptions from the regulations in [governing training and experience] that it determines are authorized by law and will not endanger life or property or common defense and security and are otherwise in the public interest."[23] Such exemptions are granted on a case-by-case, license-by-license basis.[24] Thus, Section 35.19 would allow the NRC to relax the training and experience requirements outside of the regulatory space, via license issuance or amendment.

"Requests for relaxation of, or exemptions from, the training and experience requirements of 10 C.F.R. Part 35" are coordinated with ACMUI.[25] The NRC has specified that proponents of such an exemption must provide descriptions of the following:

- Exemption and justification of why it is needed.
- Proposed compensatory safety measures intended to provide a level of health and safety equivalent to the regulation for which the exemption is being requested.
- Alternative methods for complying with the regulation and compliance with the existing regulations is not feasible.[26]

We believe that sufficient information has been presented to the NRC and ACMUI to satisfy the above requirements. However, Spectrum Pharmaceuticals would be happy to work closely with the NRC, ACMUI, and interested licensees towards obtaining limited-scope exemptions pursuant to Section 35.19. The NRC has shown itself amenable to this option in the past. By way of one example, the NRC previously granted companies an exemption under 35.19 where a particular therapy was not listed as an authorized use and no safety issues were present.[27] Here, treating cancer with beta emitters *is* listed as an authorized use; it is just that the level of training and experience required to administer this limited class of unique therapies is widely regarded as excessive.

In addition, at its October 8, 2015 meeting, ACMUI discussed whether Geranium-68/Gallium-68 (Ge-68/Ga-68) generators should be exempted from Decommissioning Funding Plan (DFP) requirements.[28] NRC staff was present and pointed out that Ge-68/Ga-

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[23] *Id.* § 35.19.
[24] *See* 67 Fed. Reg. 20250, 20282 (Apr. 24, 2002) ("Section 35.19 recognizes that an applicant for a license or licensee filing an amendment request may seek to be exempted from a specific requirement [in Part 35]".).
[25] Consolidated Guidance About Materials Licenses, 9 NUREG-1556, at 4-24 (2008).
[26] *Id.* at 10-1.
[27] *See* Revised Guidance for Licensing Intravascular Brachytherapy Procedures, NRC (June 6, 2011).
[28] Official Transcript of Proceedings: ACMUI Open Session, NRC (Oct. 8, 2015), *available at* http://pbadupws.nrc.gov/docs/ML1529/ML15294A421.pdf.

68 generators are safe and that the cost of a DFP limits access to the devices and the radiopharmaceutical they produce.[29] The NRC staff acknowledged that the ultimate goal was to obtain a permanent solution in the regulations, but viewed 35.19 as providing a valuable interim alternative.[30] The NRC staff recommended that NRC regional offices be authorized to grant the exemption.[31]

Similar to Ge-68/Ga-68 generators, Zevalin is a safe and effective product whose availability has been restricted by incommensurate regulatory burdens. The NRC's own regulatory impact analysis makes this clear. When it increased the training and experience requirements from 80 hours to 700 in 2002, the NRC estimated that four physicians per year would seek to become Authorized Users under the training and experience pathway set forth in 10 C.F.R § 35.390(b)."[32] However, not a single physician has obtained Authorized User status under that section since the requirements were increased. For these reasons, if the NRC will not adjust the training and requirements in its current rulemaking, it should use 10 C.F.R. § 35.19 to exempt physicians seeking to administer radiopharmaceuticals such as Zevalin.

IV. Conclusion

The NRC initiated a rulemaking on the Medical Use of Byproduct Material: Medical Event Definitions, Training and Experience, and Clarifying Amendments and specifically solicited commentary on the impact of the training and experience requirements on patient access to alpha and beta emitters. Both the NRC and ACMUI have received significant testimony from interested parties on this issue. Therefore, the NRC has satisfied applicable rulemaking requirements and can adopt a more appropriate training and experience requirement in the Final Rule. Moreover, the NRC has the authority to provide an additional comment period following publication of the Final Rule. In the event that the NRC is unwilling to change its regulations and chooses to not address this issue in the Final Rule, the NRC should grant an exemption for those seeking to administer beta emitters. For the NRC to not take this opportunity to address this issue will mean that patients suffering from non-Hodgkin's lymphoma may find their access to a valuable treatment option severely restricted for years to come.

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[29] *Id.* at 187-88.
[30] *Id.*
[31] *Id.*
[32] Final Regulatory Analysis: Comprehensive Revision of 10 C.F.R. Part 35, at 5-60, NRC (May 18, 2000).