Enclosure 6

Summary of Specific Agreement State and Organization of Agreement States[1] Comments on the Draft Final Rule and Staff Responses

Section 35.2 – "Definitions." - Treatment Site

Comment 1

Summary: An Agreement State commented that the current definition for treatment site is not compatible with the proposed activity-based written directive and medical event criteria for permanent brachytherapy proposed in revisions to §§ 35.40 and 35.3045. As currently defined, "Treatment site" means the anatomical description of the tissue intended to receive a radiation dose, as described in a written directive; but the proposed revisions specify source strength and number of sources (activity). The commenter stated that the definition for "treatment site" must be modified for consistent application and enforceability.

Response: No changes were made in response to this comment. The proposed rule language in § 35.40(6)(i) was revised based on public comments. Section 35.40(6)(i) was revised to remove the requirement to include the intended absorbed dose to the treatment site and, if appropriate, the expected absorbed doses to normal tissues located within the treatment site in the written directive before implantation. For permanent brachytherapy implants, the "treatment site" is the area of tissue that the authorized user (AU) intends to expose to radiation to treat the tissue for a specific purpose. The AU will accomplish this by creating a treatment plan to determine the total source strength necessary to reach the desired radiation dose to the treatment site.

Section 35.40 – "Written Directives"

Comment 2

Summary: An Agreement State stated that § 35.40(b)(6)(ii) and (b)(7) specifically require certain AUs to sign written directives for § 35.400 uses and high dose remote afterloaders. The State also stated that the regulation does not specify which AU must sign the written directive for teletherapy or § 35.300 uses. The State stated that the NRC should use a consistent format for the written directive requirement formats.

[1] Note that nine Agreement States submitted comment letters supporting the comments submitted by the Organization of Agreement States.

Response: The rule text was revised based on this comment. The additional specificity that was added to § 35.40(b)(6)(ii) and (b)(7) has been removed. Section 35.40(a) already requires that a written directive must be dated and signed by an AU. It is understood and a long-standing practice that an AU is only authorized for, and thus should only sign written directives for, the uses that are specified on a license or permit.

Section 35.41 – "Procedures for Administrations Requiring a Written Directive"

Comment 3

Summary: The Organization of Agreement States (OAS) stated that a requirement to verify brachytherapy treatments that use permanent brachytherapy seeds in lung mesh is unnecessary. Because the lung mesh is visually placed and sewn into the location identified in the written directive, the commenters believe that verification of the total source strength administered outside of the treatment site compared to the total source strength documented in the post-implantation portion of the written directive 60 calendar days after treatment is not necessary. The commenter recommended that the lung mesh treatments be exempted from the 60-day verification requirement.

Response: No changes were made in response to this comment. Although meshes may be used in conjunction with surgery for the treatment of lung cancer, there is no specific mesh referred to as a "lung mesh." Also, NRC is aware that there are other anatomical areas where such mesh materials are used in conjunction with permanent brachytherapy sources. All meshes that have permanent brachytherapy sources incorporated into them are considered permanent brachytherapy under the regulations. Based on previous comments regarding the proposed requirements in § 35.41(b)(6), NRC modified the regulations to eliminate the requirement for licensees to determine the absorbed dose to normal tissues located both outside and within the treatment site. However, the NRC retained the requirement to determine, within 60 calendar days from the date the implant was performed, the total source strength administered outside of the treatment site compared to the total source strength documented in the post-implantation written directive. The NRC retained § 35.41(b)(6)(i) because it is important to determine the total source strength administered outside of the treatment site compared to the total source strength documented in the post-implantation written directive for all permanent brachytherapy. This requirement is important to ensure that the use of the radionuclide is in accordance with the AU's directions. Because the NRC cannot anticipate all of the possible uses for meshes that would incorporate permanent brachytherapy sources, all of the regulatory requirements pertaining to the verification of the total source strength implanted into the treatment site must apply to use of meshes.

Comment 4

Summary: An Agreement State stated that § 35.41(b)(6) as proposed would effectively require a physician to order/direct an x-ray imaging procedure for his/her patient for the regulatory purpose of determining if an NRC-defined medical event had occurred. The State noted that the NRC recognizes that imaging is the only method for such an assessment. The State noted that the NRC stated that: "Although there is no requirement to determine dose to normal tissue, imaging is the best (and maybe the only) method to determine source strength outside of the treatment site and is routinely practiced in most clinical facilities." The State stated that it is inappropriate for the NRC to effectively direct a physician to perform a medical procedure, including an imaging

procedure, and that requiring such appears to be in conflict with the NRC's medical policy statement. The determination for the need to perform a medical procedure, including an imaging study, is a practice of medicine issue that involves the physician and his/her patient.

Response: No changes were made in response to this comment. Although the Agreement State believes that the requirement in § 35.41(6) effectively orders a physician to perform a specific medical procedure, the regulation requires a licensee to compare the total source strength administered outside of the treatment site to the total source strength documented in the post-implantation portion of the written directive to determine the final outcome of the administration. The NRC does not require the physician to perform a specific medical procedure to determine the final outcome of the permanent brachytherapy implant administration but allows the physician or licensee to determine the best method by which to meet this requirement.

Comment 5

Summary: An Agreement State commented that it may retain the dose-based criteria as well as adopt the NRC's proposed activity-based medical event (ME) criteria for permanent brachytherapy. The Agreement State stated that it would share the events that meet the activity-based ME criteria with the NRC as consistent with a national standard, and use dose-based criteria for its internal use only. The State noted that its program is involved in the practice of medicine as well as physician discipline, areas clearly outside of the NRC's authority. The State also indicated that it uses dose-based criteria for equipment-based prostate cancer treatments, and therefore needs to maintain a consistent standard to avoid unintentionally influencing a physician's choice of treatment modality. The State asserted that adoption of the proposed activity-based medical event criteria in conjunction with retention of dose-based criteria would not have any transboundary implications, would not cause confusion, and it would not cause any gaps, conflicts, or duplication.

Response: The NRC has determined that activity-based criteria is the appropriate criteria for medical event reporting and that medical event reports should only include activity-based criteria. Dose-based criteria instead of, or in addition to, activity-based criteria for reporting permanent implant brachytherapy medical events in § 35.3045(a)(2) would result in reporting of non-significant events. Reporting of non-significant events could create inconsistencies in the national reporting program and hinder the NRC and Agreement States' ability to use the national reporting program to evaluate trends. Specifically, the NRC staff concluded that the continued use of a dose-based criteria could: 1) preclude a practice in the national interest to have a consistent reporting and notification standard; 2) impair effective communication about medical events between the NRC and Agreement States; and 3) preclude an effective review or evaluation by the Commission and Agreement State programs with respect to protection of public health and safety.

In its report dated February 7, 2012 (ADAMS Accession No. ML12038A279), the ACMUI's Permanent Implant Brachytherapy Subcommittee indicated that that a dose-based criteria for the treatment site, especially in prostate permanent implant brachytherapy, suffers from several limitations. Specifically, the ACMUI cited the following:

1. True anatomic prostate volume or shape changes can occur during and after the implant procedure, particularly due to edema,
2. Differences in estimated prostate volumes can occur due to inherent limitations of identifying organ or target boundaries using CT and ultrasound (or any other modality), and
3. Volume estimate uncertainties due to artifacts caused by the seeds and the resultant indistinct prostate boundaries seen on post-implant CT images.

The NRC has also determined that the use of different reporting criteria between various regulators, could cause confusion. This is of particular concern when AUs are performing permanent implant brachytherapy procedures in more than one regulatory jurisdiction.

Use of only an activity-based medical event reporting criteria for permanent implant brachytherapy by an Agreement State would not preclude the use of a dose-based reporting criteria for other radiation sources not regulated by the NRC, such as x-ray machines.

§ 35.50 – "Training for Radiation Safety Officer and Associate Radiation Safety Officer"

Comment 6

Summary: An Agreement State commented that 10 CFR 35.50(c)(3) should not refer to a "new" Agreement State license because the requirements in 10 CFR Part 35 are written for NRC licensees as the target audience. The applicant applying for a new license under this requirement would only be requesting a license from the NRC. The Agreement State believes that when an Agreement State adopts this requirement, the wording would be modified to refer to a license issued by that Agreement State.

Response: The rule text was revised based on this comment. After reviewing § 35.50(c)(3), the NRC has determined that the commenter is correct and the reference to a new Agreement State license is not necessary. Therefore, the reference to a new Agreement State license has been deleted.

§ 35.204 – "Permissible Molybdenum-99, Strontium-82, and Strontium-85 Concentrations."

Comment 7

Summary: An Agreement State commented that the phrase, "at the time of generator elution," is misplaced and seems to modify the word "report;" therefore, the commenter believes that the reporting is to occur at the time of generator elution, but the reporting time frame in § 35.3204 is 7 days. Therefore, the commenter proposes to change the provision to read, "The licensee shall report, in accordance with § 35.3204, any measurement taken at the time of generator elution that exceeds the limits in paragraph (a) of this section."

Response: No changes were made based on this comment. The regulation requires a licensee to report any measurement that exceeds the limits at the time of generator elution. The phrase "in paragraph (a) of this section" is directing the licensee to the limits. This requirement does not require the licensee to make a report at the time the

generator is eluted. As noted in the regulation, the licensee must report any measurement that exceeds the limits in accordance with § 35.3204, which requires reporting within seven calendar days. The NRC believes that this provision is sufficiently clear.

§ 35.396 – "Training for the Parenteral Administration of Unsealed Byproduct Material Requiring a Written Directive."

Comment 8

Summary: An Agreement State commented that § 35.396 contained in the Draft Final Rule shows a stricken "or" after paragraph (c). The Agreement State proposed to add clarity to the section by adding an "or" after paragraphs (a) and (b) of the draft final rule. As the regulation would currently read, the prospective AU would have to meet (a), (b), and (c) and meet the requirements of paragraph (d).

Response: The structure of the rule text was changed based in part on this comment. This section has been restructured so that it clarifies the specific requirements. Specifically, § 35.396(a), (b), and (c), which specify the authorization pathways, are low located in § 35.396(a)(1), (a)(2), and (a)(3), respectively. Section 35.396(d), which specifies training and experience requirements that apply to the pathways in (a)(2) and (a)(3), is now located in § 35.396(b).

Comment 9

Summary: The OAS commented that NRC should change the references to § 35.390(b)(1)(ii)(G) found in § 35.396(d)(2) to 35.390(b)(1)(ii)(G)(*3*) and (*4*). A number of Agreement States concurred with this request.

Response: The rule text in § 35.396(d)(2) was changed in part based on this comment. In reviewing this section, the NRC determined that references to § 35.390(b)(1)(ii)(G)(*1*) and (*2*) specify the oral administration of isotopes. Therefore, these references are not necessary when referring to procedures involving only parenteral administrations and could possibly lead to confusion. Based on a recommendation from the Advisory Committee on the Medical Uses of Isotopes (ACMUI), § 35.390(b)(1)(ii)(G)(*4*) was combined within § 35.390(b)(1)(ii)(G)(*3*). The rule text was changed to specifically reference § 35.390(b)(1)(ii)(G)(*3*). Also, in response to another comment, § 35.396(d) has been re-designated as § 35.396(b) to clarify the requirements within § 35.396.

§ 35.433 – "Strontium-90 Sources for Ophthalmic Treatments."

Comment 10

Summary: An Agreement State indicated that Medical Physics is a licensed profession in their State and it is unclear if an "Ophthalmic Physicist" will meet the State's licensure requirements. Additionally, the State expressed a concern that the draft final rule states that, "Further, in § 35.13, License Amendments, only specific use licensees and not broad scope licensees can name an ophthalmic physicist on their licenses as broad scope licensees have ready access to authorized medical physicists."

Response: The rule text was revised based on this comment. After reviewing this comment, the NRC has revised the definition of "ophthalmic physicist" in § 35.2 to also include broad scope medical use licensees and master material license broad scope medical use permittees. Additionally, the NRC has made corresponding revisions to § 35.433(a)(2). The NRC has also revised the Statement of Considerations to delete discussions that stated that broad scope licensees cannot use an ophthalmic physicist.

Regarding the State's concern that the ophthalmic physicist may not meet the State's licensure requirements, the NRC has no jurisdiction over Agreement State licensing requirements for professional occupations.

§ 35.3045 – "Report and Notification of a Medical Event."

Comment 11

Summary: As a general comment, the OAS is supportive of the NRC's position to assign a Compatibility Category "C" designation for the reporting requirements found in § 35.3045

Response: The NRC notes the support for the change in compatibility category designation and no further response is necessary.

Comment 12

Summary: The OAS stated that the requirements of § 35.3045(a)(1)(iii)(C) contradict the requirements in § 35.3045(a)(1)(ii). The OAS indicated that the requirement of § 35.3045(a)(1)(iii)(C) states that if one [permanent brachytherapy implant] seed is implanted outside of the treatment site, that it would be required to be reported as a medical event even if the erroneously implanted seed falls within the 20% activity. The OAS does not understand the requirement and recommends that the requirement be deleted from the Medical Event definition.

Response: No changes were made based on this comment. The NRC believes that OAS is actually referring to: (1) § 35.3045(a)(2)(iii)(C), which addresses sealed source(s) implanted directly into a location discontiguous from the treatment site, as defined in the written directive, and (2) § 35.3045(a)(2)(ii), which addresses the total source strength administered outside of the treatment site exceeding 20 percent of the total source strength documented in the post-implantation portion of the written directive. It should also be noted that § 35.3045(a)(2)(iii)(C) was modified in response to a

recommendation from the ACMUI to read, “Sealed source(s) implanted directly into a location discontiguous from the treatment site, as defined in the written directive.”

The NRC agrees that typical permanent implant procedures may result in some sources being implanted outside the treatment site as described in the written directive. However, while it may appear that § 35.3045(a)(2)(iii)(C) is in conflict with the provisions of § 35.3045(a)(2)(ii), the two provisions are independent of each other. Under § 35.3045(a)(2)(ii), a medical event occurs when the total source strength administered outside of the treatment site exceeds 20 percent of the total source strength documented in the post-implantation portion of the written directive. Therefore, this section of the regulations captures instances where more than twenty percent of the total source strength administered is outside the treatment site but is contiguous to the treatment site.

The provisions of § 35.3045(a)(2)(iii)(C) addresses situations where a sealed source is, or sealed sources are, implanted directly into a location discontiguous from the treatment site, as defined in the written directive. This section of the regulation captures instances where a sealed source is, or sealed sources are, implanted in a location that is not physically adjacent to the treatment site, as defined in the written directive.

Comment 13

Summary: An Agreement State commented that the proposed requirement in § 35.3045(a)(2)(iii)[C] which states, "Sealed source(s) directly delivered to the wrong treatment site implanted directly into a location where the radiation from the source(s) will not contribute dose to the treatment site, as defined in the written directive” is not enforceable and is subject to interpretation. The Agreement State indicated that the inclusion of a specified distance from the treatment site boundary would be clear and enforceable.

Response: In response to a recommendation from the ACMUI, the NRC has modified the wording of the requirement in § 35.3045(a)(2)(iii)(C) to read “Sealed source(s) implanted directly into a location discontiguous from the treatment site, as defined in the written directive.” Although the modification does not give a specified distance from the treatment site, the change does make it clear that the permanent brachytherapy seed is implanted into a location that is not physically adjacent to the treatment site.

Comment 14

Summary: An Agreement State commented that, as written, § 35.3045(b)(iii)(C) allows the licensee to choose either the pre- or post-treatment site defined in the two-part written directive.

Response**:** The rule text was revised based on this comment. The NRC believes that the Agreement State is actually referring to § 35.3045(a)(2)(iii)(C). This provision is based on the post-implantation portion of the written directive. The NRC has revised this section to make it clear that it is based on the post-implantation portion of the written directive. This requirement is consistent with other provisions contained within § 35.3045(a)(2).

§ 35.3204 – "Written Report of an Eluate Exceeding Permissible Molybdenum-99, Strontium-82, and Strontium-85 Concentrations."

Comment 15

Summary: The OAS recommended that the NRC modify the wording in § 35.3204(a) to read "... when the manufacturer/distributor was notified ..." since the licensee is required to notify both the NRC and the manufacturer/distributor when an eluate concentration exceeds the limit.

Response: The rule text was changed based on this comment. Because the requirement specifically states that the NRC and the manufacturer/distributor must be notified by the licensee when an eluate exceeds the concentration limit, it appears redundant and unnecessary to have the licensee notify the NRC whether or not the licensee notified the manufacturer/distributor. It would be more beneficial to report when the manufacturer/distributor was notified. Therefore, the rule text was revised to require the licensee to report when the manufacturer/distributor was notified.

"Categorization of Ra-223 Dichloride"

Comment 16

Summary: An Agreement State asked for clarification on the categorization of Ra-223 dichloride. The discussion of this draft final regulation states that Ra-223 dichloride is a § 35.390(b)(1)(ii)(G)(*4*) drug because it "is used primarily for its alpha emission." This contradicts the information provided by NRC in its medical webinar to Agreement States on November 5, 2015.

Response: Ra-223 dichloride is *a* beta-emitting radiopharmaceutical, but it is *used primarily for* its alpha radiation characteristics. Thus, thus under the draft final rule it would have been placed in the category of drugs described at § 35.390(b)(1)(ii)(G)(*4*). However, in response to a recommendation from the ACMUI, § 35.390(b)(1)(ii)(G)(*3*) and (*4*) have been merged into one paragraph. Section 35.390(b)(1)(ii)(G)(*3*) of the final rule encompasses parenteral administration of radioactive drugs that contain a radionuclide that is used for its electron emission, beta radiation characteristics, alpha radiation characteristics, or for its photon energy of less than 150 keV, for which a written directive is required. Therefore, in the final rule, Ra-223 dichloride will be regulated under § 35.390(b)(1)(ii)(G)(*3*).