U.S. Nuclear Regulatory Commission (NRC)
Advisory Committee on the Medical Uses of Isotopes (ACMUI)

Licensing Guidance for Superficial Manual Brachytherapy CivaDerm Device

Final Report
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Charge

In October 2021, the ACMUI Chairman, Dr. Darlene Metter, charged the Regulatory Guide 8.39 Subcommittee to review the draft CivaDerm™ licensing guidance with regard to patient release.

Background

The CivaTech Oncology CivaDerm™ manual brachytherapy device (CivaDerm) contains sealed palladium-103 seeds and is FDA-approved for use as an interoperative or superficial temporary brachytherapy source to treat skin cancer or other lesions. The primary intended use is superficial application.

Following evaluation, NRC staff determined the use of CivaDerm will be licensed under 10 CFR 35.400, "Manual Brachytherapy" because radiation protection concerns for this device are adequately covered under existing regulations in 10 CFR 35, Subpart F. However, NRC Staff determined additional guidance is needed regarding patient release as sources have the potential to become dislodged. NRC staff have added a relevant section in draft Regulatory Guide 8.39 (Section 6, "Material Separated from the Patient"); however, as the Regulatory Guide will take time to finalize and CivaDerm is already approved by the FDA for use, NRC decided to prepare separate guidance for CivaDerm at this time.

General Comments:

1. The Subcommittee agrees that CivaDerm should be licensed under 10 CFR 35.400 as it does not present any unique radiation safety issues not already covered by Part 35.

2. The subcommittee strongly disagreed with newly proposed Regulatory Guide 8.39, Section 6 "Material Separated from the Patient", that stated the dose limits in 10 CFR Part 20 apply to exposure from radioactive material separated from a released patient, with the exception of temporary implants. While the CivaDerm device may have a higher potential for the

source(s) to become dislodged from a patient due to its superficial application than with previous manual brachytherapy devices, the potential is not high enough to warrant specific consideration for patient release in Regulatory Guide 8.39. Other temporary implants such as eye plaques also have the potential for becoming dislodged or lost. Regulations and licensing guidance already exist that require licensees to develop, implement, and maintain written procedures to provide high confidence that each administration is in accordance with the written directive.

3. Since NRC determined that CivaDerm may be licensed under 10 CFR 35, Subpart F, the Subcommittee recommends developing shorter guidance, more consistent with past examples[1]. The guidance should focus on the specific radiation safety challenge, rather than providing comprehensive considerations for use.
4. The Subcommittee notes that it would be highly unlikely for a member of the public to exceed the public dose limits in 10 CFR 20.1301 due to exposure from a palladium-103 source no longer affixed to a released patient. Although Table 1, Column 2 in draft Regulatory Guide 8.39 indicates that an implant containing 2.1 mCi of Pd-103 can lead to a 100 mrem total effective dose equivalent to a bystander, this assumes an occupancy factor of 1 at a distance of 1 meter until the source physically decays away. With a 17-day half-life, a bystander would need to be continuously near the Pd-103 source for over 3 months. This is unrealistic. Also, the low energy photons from Pd-103 do not result in a whole body effective dose equivalent, based on the exposure rate constant as do higher energy photon emitters, due to tissue shielding of the exposed individual[2].

Specific Comments:

1. Background section, 1st paragraph: the guidance should also acknowledge that CivaDerm may be used intraoperatively.

2. Background section, 2nd paragraph: Remove sentence, "In accordance with 10 CFR 35.400, the Pd-103 sources must be listed on a Sealed Source and Device Registry (SSDR) for manual brachytherapy and used in accordance with the radiation safety conditions and limitations described in that SSDR or in research under an active Investigational Device Exemption as described in 10 CFR 35.400(b)."

3. Background section, 3rd paragraph: Remove sentence, "The manufacturer states the Civaderm sources can be affixed to a patient's skin by a variety of means, such as staples, glue, tape, sutures, or cast."

4. Procedures for Administration section:
    a. Remove sentence, "If a Civaderm source becomes loose or dislodged, it is likely the administration would not go in accordance with the written directive and result in a medical event as defined in 10 CFR 35.3045, "Reports and notification of a medical event." This is a negative, what if, worst case scenario that is not appropriate for an introductory sentence.

[1] Licensing of Lutetium-177, June 1, 2018. ML18136A824.
[2] Boyce DE and Sheetz, MA, "Patient Release Criteria for Low Dose Rate Brachytherapy Implants", Health Physics (104(4):413-418), 2013

b. Remove phrase, "to ensure high confidence the procedure will be in accordance with the written directive. In addition, licensees must have procedures to determine if a medical event has occurred in accordance with 10 CFR 35.41." It is not necessary to describe the regulations.
c. Remove sentence, "If the NRC becomes aware of future developments related to the production, distribution, or medical use of the Civaderm that may negatively impact radiation safety, the NRC staff will revisit this licensing decision for any additional actions."

5. Patient Release Considerations section:
    a. First paragraph, remove "unsealed byproduct material or." This phrase is not relevant for CivaDerm use.
    b. Remove sentence, "As members of the public could be exposed to the hot side of the source, it is possible that public dose limits could be exceeded if the source becomes loose. Therefore, licensees must ensure that the Civaderm sources are affixed to the patient so that they are highly unlikely to become loose or dislodged."
    c. Remove sentences, "As described in 10 CFR 20.1003, public dose limits in 10 CFR Part 20 do not apply to exposure to individuals released under 10 CFR 35.75. However, public dose limits would apply if the source became dislodged or separated from the patient, as Part 20 does not exclude exposure from sources which are no longer affixed to a patient."

6. Source accountability section:
    a. First paragraph, remove last sentence. The Subcommittee believes that licensees should only be held accountable for locations of use prior to patient release.
    b. Change the second paragraph to read, in its entirety: "If a licensee is unable to retrieve the source from the patient following treatment for whatever reason such as the source fell off or the patient does not return, the source would be considered lost or missing and would need to be reported in accordance with 10 CFR 20.2201 "Reports of theft of loss of licensed material." It is highly unlikely that a Pd-103 brachytherapy implant would exceed the activity threshold (100 mCi) requiring immediate reporting; however, 30-day notification is required for aggregated activities exceeding 1 mCi which have not been found."

Respectfully submitted,

Subcommittee on Regulatory Guide 8.39 Release of Patients Administered Radioactive Materials,
Advisory Committee on the Medical Uses of Isotopes,
U.S. Nuclear Regulatory Commission

The ACMUI unanimously approved this report as presented during its public teleconference meeting on December 15, 2021.