UNITED STATES
NUCLEAR REGULATORY COMMISSION
WASHINGTON, D.C. 20555-0001

July 28, 2023

ALL AGREEMENT STATES
CONNECTICUT, INDIANA, WEST VIRGINIA

LICENSING GUIDANCE MEMO FOR SUPERFICIAL
MANUAL BRACHYTHERAPY CIVADERM™ DEVICE (STC-23-056)

Purpose: To provide guidance to the Agreement States for licensing the superficial manual brachytherapy Civaderm™ device.

Background: On September 20, 2019, CivaTech Oncology Inc. received 510(k) clearance for CivaDerm™ from the U.S. Food and Drug Administration. CivaDerm™ is used as a superficial temporary brachytherapy source. CivaDerm™ consists of several components including a bio-absorbable polymer substrate, a gold foil, a sealant, and the radioisotope palladium-103 (Pd-103) provided in individual radiation components called CivaDots™. CivaDerm™ is assembled by placing an appropriate therapeutic number of the CivaDots™ in an array within the bio-absorbable polymer substrate. CivaDots™ have a shielded and unshielded side, which provides directional treatment. The shielded side includes the gold foil, which provides shielding away from the patient. The unshielded side is blue in color and intended to be applied directly to the skin. Holes in the substrate between the CivaDots™, called fenestration holes, assist with device attachment to the patient's body. Due to the proposed superficial application of a brachytherapy source, the U.S. Nuclear Regulatory Commission (NRC) staff received questions and carefully reviewed the safety aspects of the medical use of the CivaDerm™ to determine if it should be licensed under Title 10 of the *Code of Federal Regulations* (10 CFR) Part 35, Subpart F, "Manual Brachytherapy" or 10 CFR Part 35, Subpart K, "Other Medical uses of Byproduct Material or Radiation From Byproduct Material."

Following its evaluation, the NRC staff recommended to the joint NRC/Agreement State Standing Committee for the Review of Emerging Medical Technologies (Standing Committee) that CivaDerm™ be licensed under 10 CFR Part 35, Subpart F. The staff made this recommendation as it found the use of CivaDerm™ is addressed in regulations contained in 10 CFR Part 35, Subpart F and has radiation safety concerns similar to other temporary brachytherapy devices used in manual brachytherapy as shown in the attached table. The Standing Committee agreed with the staff's recommendation and determined CivaDerm™ should be licensed under 10 CFR 35.400, "Use of sources for manual brachytherapy." If the NRC becomes aware of future developments related to the production, distribution, or medical use of the CivaDerm™ that may impact radiation safety, the NRC and the Standing Committee will revisit this licensing decision.

Because CivaDerm™ will be licensed under 10 CFR Part 35, Subpart F, NUREG-1556, Volume 9, "Consolidated Guidance About Materials Licenses: Program-Specific Guidance About Medical Use Licenses," provides the guidance for licensing. In addition, please refer to the Sealed Source and Device Registry, NC-1311-S-102-S, for additional considerations regarding safe use of CivaDerm™. However, the Standing Committee recommended that NRC staff provide additional guidance for patient release considerations as CivaDerm™ is superficially

affixed. Because application of CivaDerm™ is superficial, there is a higher potential for the source to become dislodged from a patient. The NRC staff identified several focus areas with regards to the licensing and oversight of CivaDerm™ sources and this memorandum provides additional guidance to address potential concerns. This memorandum is not intended for use of the CivaSheet®, which is used intraoperatively and not affixed superficially.

Licensing Guidance: *Procedures for Administration*

CivaDerm™ is expected to be applied as an outpatient procedure, with the patient returning to have the apparatus removed. In accordance with 10 CFR 35.41, "Procedures for administration requiring a written directive", licensees must develop, implement, and maintain written procedures to provide high confidence that each administration is in accordance with the written directive. This written procedure must contain necessary affixation processes to ensure the CivaDerm™ will not become loose or dislodged from the patient under normal conditions to provide high confidence that the procedure will be in accordance with the written directive required in 10 CFR 35.40. Consistent with the manufacturer's instruction for use, CivaDerm™ should be attached using robust techniques and minimize patient access to the device to reduce the risk it could become loose or dislodged. See the manufacturer instruction for use for guidance on robust attachment techniques. This procedure must include a step to verify sources were affixed in the appropriate direction to ensure the unshielded side, known as the hot side, is facing the treatment location and the cold side faces away from the body. In addition, in accordance with 10 CFR 35.41, licensees must have written procedures to determine if a medical event has occurred. If a patient is released in accordance with 10 CFR 35.75, "Release of individuals containing unsealed byproduct material or implants containing byproduct material," while treatment is ongoing, written procedures need to include how a licensee will determine if the source moved or became dislodged to report if a medical event occurred.

Patient Release Considerations

Under regulations in 10 CFR 35.75, licensees may release any individual from its control who has been administered byproduct material if the total effective dose equivalent (TEDE) to any other individual from exposure to the released individual is not likely to exceed 5 millisieverts (mSv) (0.5 rem). Regulatory Guide 8.39, "Release of Patients Administered Radioactive Material," provides guidance for releasing patients.

As described in 10 CFR 20.1002, "Scope," public dose limits[1] in 10 CFR Part 20, "Standards For Protection Against Radiation," do not apply to exposure to individuals released under 10 CFR 35.75. However, public dose limits in 10 CFR Part 20 do apply if the source becomes separated from the patient. Patients may not be released from the licensed facility if it appears that the CivaDerm™ sources are not affixed properly and could become dislodged under normal conditions.

Additionally, licensees must have preventative measures in place to ensure public dose limits are not exceeded in the event the source becomes dislodged after the patient's release. Preventative measures include providing patients with a shielded container to place the CivaDot(s) in if the source becomes dislodged. In addition, licensees should provide patients emergency contact information with 24-hour a day coverage and instructions to immediately contact the licensee if a source(s) becomes loose or, after placing a source in the shielding

[1] Public dose limits in Part 20 are provided in 10 CFR 20.1301, "Dose limits for individual members of the public" and are 0.1 rem in a year and 0.002 mrem in any one hour.

container, becomes dislodged, If a licensee discovers a member of the public exceeds the public dose limits in 10 CFR 20.1301, “Dose limits for individual members of the public,” due to exposure from a source no longer affixed to a released patient, licensees must report the event in accordance with 10 CFR 20.2203, “Reports of exposures, radiation levels, and concentrations of radioactive material exceeding the constraints or limits.”

Source Accountability

Licensees must maintain accountability at all times for CivaDerm™ brachytherapy sources in storage or use in accordance with 10 CFR 35.406, “Brachytherapy sources accountability”. In addition, licensees must also maintain records of CivaDerm™ source accountability, in accordance with 10 CFR 35.2406, “Records of brachytherapy source accountability.” Specifically, the records of source accountability for temporary implants must include the location of use. For CivaDerm™ sources used on an outpatient basis, locations of use must include where the patient will spend a significant amount of time, which may include the patient's residence(s) after treatment and workplace.

If a licensee is unable to retrieve the source from the patient following treatment, 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 that have not been found. In addition, as stated in 10 CFR 35.400(a), manual brachytherapy sources must be used in accordance with the radiation safety conditions and limitations described in the Sealed Source and Device Registry. One such condition listed in the sealed source and device registry is that the physician must attach the label provided by the manufacturer to the cold side of the device after application. This would ensure the source is labeled should it go lost or missing.

Contacts: If you have any questions regarding this correspondence, please contact me at 301-415-3340 or the individual named below:

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Signed by Giantelli, Adelaide
on 07/28/23

Adelaide Giantelli, Chief
State Agreement Liaison Programs Branch
Division of Materials Safety, Security, State,
and Tribal Programs
Office of Nuclear Material Safety
and Safeguards

Enclosures:
1. 10 CFR 35 Placement Evaluation
For Civaderm™

STC-23-056- Licensing Guidance Memo for Superficial Manual Brachytherpy CivadermTM device 10 CFR 35 Placement Evaluation for Civaderm DATE July 28, 2023

DISTRIBUTION:

ADAMS Accession No.: ML23164A105

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