UNITED STATES
NUCLEAR REGULATORY COMMISSION
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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

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10 CFR 35 Placement Evaluation for CivaDerm™

Section	Description	Applicable Rule	Notes
Subpart A – General Information			
35.1	Purpose and scope	☒Yes ☐No ☐N/A	
35.2	Definitions	☒Yes ☐No ☐N/A	
35.5	Maintenance of records	☒Yes ☐No ☐N/A	
35.6	Provisions for the protection of human research subjects	☒Yes ☐No ☐N/A	
35.7	FDA, other Federal, and State requirements	☒Yes ☐No ☐N/A	
35.8	Information collection requirements: OMB approval	☒Yes ☐No ☐N/A	
35.10	Implementation	☒Yes ☐No ☐N/A	
35.11	License required	☒Yes ☐No ☐N/A	
35.12	Application for license, amendment, or renewal	☒Yes ☐No ☐N/A	
35.13	License amendments	☒Yes ☐No ☐N/A	
35.14	Notifications	☒Yes ☐No ☐N/A	
35.15	Exemptions regarding Type A specific licenses of broad scope	☒Yes ☐No ☐N/A	
35.18	License issuance	☒Yes ☐No ☐N/A	
35.19	Specific exemptions	☒Yes ☐No ☐N/A	
Subpart B – General Administrative Requirements			
35.24	Authority and responsibilities for the radiation protection program	☒Yes ☐No ☐N/A	
35.26	Radiation protection program changes	☒Yes ☐No ☐N/A	
35.27	Supervision	☒Yes ☐No ☐N/A	
35.40	Written directives (WDs)	☒Yes ☐No ☐N/A	Requirements in 10 CFR 35.40(b)(7) can be used for CivaDerm. As implant is defined as to insert or fix, the term implantation in this regulation is the process of fixing the sources to the skin.
35.41	Procedures for administrations requiring a WD	☒Yes ☐No ☐N/A	
35.49	Suppliers for sealed sources or devices for medical use	☒Yes ☐No ☐N/A	

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Section	Description	Applicable Rule	Notes
35.50	Training for Radiation Safety Officer (RSO) and Associate RSO	☒Yes ☐No ☐N/A	
35.51	Training for an authorized medical physicist (AMP)	☒Yes ☐No ☐N/A	
35.55	Training for an authorized nuclear pharmacist (ANP)	☒Yes ☐No ☐N/A	
35.57	Training for experienced RSO, teletherapy or medical physicist, AMP, authorized user (AU), nuclear pharmacist, and ANP	☒Yes ☐No ☐N/A	
35.59	Recentness of training	☒Yes ☐No ☐N/A	
Subpart C – General Technical Requirements			
35.60	Possession, use, and calibration of instruments used to measure the activity of unsealed byproduct material	☒Yes ☐No ☐N/A	
35.61	Calibration of survey instruments	☒Yes ☐No ☐N/A	
35.63	Determination of dosages of unsealed byproduct material for medical use	☒Yes ☐No ☐N/A	
35.65	Authorization for calibration, transmission, and reference sources	☒Yes ☐No ☐N/A	
35.67	Requirements for possession of sealed sources and brachytherapy sources	☒Yes ☐No ☐N/A	
35.69	Labeling of vials and syringes	☒Yes ☐No ☐N/A	
35.70	Surveys of ambient radiation exposure rate	☒Yes ☐No ☐N/A	
35.75	Release of individuals containing unsealed byproduct material or implants containing byproduct material	☒Yes ☐No ☐N/A	Implant is defined as inserted or affixed. As CivaDerm is medically affixed, it meets the definition of an implant. However, additional guidance is needed in situations which source is dislodged.
35.80	Provision of mobile medical service	☐Yes ☐No ☒N/A	
35.92	Decay-in-storage	☒Yes ☐No ☐N/A	
Subpart D – Unsealed Byproduct Material – Written Directive Not Required			
35.100	Use of unsealed byproduct material for uptake, dilution, and excretion studies for which a WD is not required	☐Yes ☐No ☒N/A	
35.190	Training for uptake dilution, and excretion studies	☐Yes ☐No ☒N/A	

Section	Description	Applicable Rule	Notes
35.200	Use of unsealed byproduct material for imaging and localization studies for which a WD is not required	☐Yes ☐No ☒N/A	
35.204	Permissible Mo-99, Sr-82, Sr-85 concentrations	☐Yes ☐No ☒N/A	
35.290	Training for imaging and localization studies	☐Yes ☐No ☒N/A	
Subpart E – Unsealed Byproduct Material – WD Required			
35.300	Use of unsealed byproduct material for which a WD is required	☐Yes ☐No ☒N/A	
35.310	Safety instruction	☐Yes ☐No ☒N/A	
35.315	Safety precautions	☐Yes ☐No ☒N/A	
35.390	Training for use of unsealed byproduct material for which a WD is required	☐Yes ☐No ☒N/A	
35.392	Training for the oral administration of NaI I-131 requiring a WD in quantities <= 1.22 GBq (33 mCi)	☐Yes ☐No ☒N/A	
35.394	Training for the oral administration of NaI I-131 requiring a WD in quantities > 1.22 GBq (33 mCi)	☐Yes ☐No ☒N/A	
35.396	Training for the parenteral administration of unsealed byproduct material requiring a WD	☐Yes ☐No ☒N/A	
Subpart F – Manual Brachytherapy			
35.400	Use of sources for manual brachytherapy	☒Yes ☐No ☐N/A	
35.404	Surveys after source implant and removal	☒Yes ☐No ☐N/A	As licensees can still make this survey after the final source is removed, this regulation can be met and there is no need for additional conditions.
35.406	Brachytherapy sources accountability	☒Yes ☐No ☐N/A	Like other outpatient temporary brachytherapy uses, such as eye plaques, licensees can maintain brachytherapy source accountability. However, additional guidance for outpatient use is needed.
35.410	Safety instruction	☒Yes ☐No ☐N/A	
35.415	Safety precautions	☒Yes ☐No ☐N/A	
35.432	Calibration measurements of brachytherapy sources	☒Yes ☐No ☐N/A	
35.433	Sr-90 sources for ophthalmic treatments	☐Yes ☐No ☒N/A	

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Section	Description	Applicable Rule	Notes
35.457	Therapy-related computer systems	☐Yes ☐No ☒N/A	
35.490	Training for use of manual brachytherapy sources	☒Yes ☐No ☐N/A	
35.491	Training for ophthalmic use of Sr-90	☐Yes ☐No ☒N/A	
Subpart G – Sealed Sources for Diagnosis			
35.500	Use of sealed sources and medical devices for diagnosis	☐Yes ☐No ☒N/A	
35.590	Training for use of sealed sources and medical devices for diagnosis	☐Yes ☐No ☒N/A	
Subpart H – Photon Emitting Remote Afterloader Units, Teletherapy Units, and Gamma Stereotactic Radiosurgery (GSR) Units			
35.600	Use of a sealed source in a remote afterloader unit, teletherapy unit, or GSR unit	☐Yes ☐No ☒N/A	
35.604	Surveys of patients and human research subjects treated with a remote afterloader unit	☐Yes ☐No ☒N/A	
35.605	Installation, maintenance, adjustment, and repair	☐Yes ☐No ☒N/A	
35.610	Safety procedures and instructions for remote afterloader units, teletherapy units, and GSR units	☐Yes ☐No ☒N/A	
35.615	Safety precautions for remote afterloader units, teletherapy units, and GSR units	☐Yes ☐No ☒N/A	
35.630	Dosimetry equipment	☐Yes ☐No ☒N/A	
35.632	Full calibration measurements on teletherapy units	☐Yes ☐No ☒N/A	
35.633	Full calibration measurements on remote afterloader units	☐Yes ☐No ☒N/A	
35.635	Full calibration measurements on GSR units	☐Yes ☐No ☒N/A	
35.642	Periodic spot-checks for teletherapy units	☐Yes ☐No ☒N/A	
35.643	Periodic spot-checks for remote afterloader units	☐Yes ☐No ☒N/A	
35.645	Periodic spot-checks for GSR units	☐Yes ☐No ☒N/A	
35.647	Additional technical requirements for mobile remote afterloader units	☐Yes ☐No ☒N/A	
35.652	Radiation surveys	☐Yes ☐No ☒N/A	
35.655	Full-inspection servicing for teletherapy and GSR units	☐Yes ☐No ☒N/A	
35.657	Therapy-related computer systems	☐Yes ☐No ☒N/A	

Section	Description	Applicable Rule	Notes
35.690	Training for use of remote afterloader units, teletherapy units, and GSR units	☐Yes ☐No ☒N/A	
Subpart L – Records			
35.2024	Records of authority and responsibilities for radiation protection programs	☒Yes ☐No ☐N/A	
35.2026	Records of radiation protection program changes	☒Yes ☐No ☐N/A	
35.2040	Records of WDs	☒Yes ☐No ☐N/A	
35.2041	Records for procedure for administrations requiring a WD	☒Yes ☐No ☐N/A	
35.2060	Records of calibrations of instruments used to measure the activity of unsealed byproduct materials	☐Yes ☐No ☒N/A	
35.2061	Records of radiation survey instrument calibrations	☒Yes ☐No ☐N/A	
35.2063	Records of dosages of unsealed byproduct material for medical use	☐Yes ☐No ☒N/A	
35.2067	Records of leaks tests and inventory of sealed sources and brachytherapy sources	☒Yes ☐No ☐N/A	
35.2070	Records of surveys for ambient radiation exposure rate	☒Yes ☐No ☐N/A	
35.2075	Records of the release of individuals containing unsealed byproduct material or implants containing byproduct material	☒Yes ☐No ☐N/A	
35.2080	Records of mobile medical services	☐Yes ☐No ☒N/A	
35.2092	Records of decay-in-storage	☒Yes ☐No ☐N/A	
35.2204	Records of Mo-99, Sr-82, and Sr-85 concentrations	☐Yes ☐No ☒N/A	
35.2310	Records of safety instruction	☐Yes ☐No ☒N/A	
35.2404	Records of surveys after source implant and removal	☒Yes ☐No ☐N/A	
35.2406	Records of brachytherapy source accountability	☒Yes ☐No ☐N/A	
35.2432	Records of calibration measurements of brachytherapy sources	☒Yes ☐No ☐N/A	
35.2433	Records of decay of Sr-90 sources for ophthalmic treatments	☐Yes ☐No ☒N/A	
35.2605	Records of installation, maintenance, adjustment, and repair of remote afterloader units, teletherapy units, and GSR units	☐Yes ☐No ☒N/A	

Section	Description	Applicable Rule	Notes
35.2610	Records of safety procedures	☐Yes ☐No ☒N/A	
35.2630	Records of dosimetry equipment used with remote afterloader units, teletherapy units, and GSR units	☐Yes ☐No ☒N/A	
35.2632	Records of teletherapy, remote afterloader, and GSR full calibrations	☐Yes ☐No ☒N/A	
35.2642	Records of periodic spot-checks for teletherapy units	☐Yes ☐No ☒N/A	
35.2643	Records of periodic spot-checks for remote afterloader units	☐Yes ☐No ☒N/A	
35.2645	Records of periodic spot-checks for GSR units	☐Yes ☐No ☒N/A	
35.2647	Records of additional technical requirements for mobile remote afterloader units	☐Yes ☐No ☒N/A	
35.2652	Records of surveys of therapeutic treatment units	☐Yes ☐No ☒N/A	
35.2655	Records of full-inspection servicing for teletherapy and GSR units	☐Yes ☐No ☒N/A	
Subpart M – Reports			
35.3045	Report and notification of a medical event	☒Yes ☐No ☐N/A	
35.3047	Report and notification of a dose to an embryo/fetus or a nursing child	☒Yes ☐No ☐N/A	
35.3067	Report of a leaking source	☒Yes ☐No ☐N/A	
35.3204	Report and notification for an eluate exceeding permissible Mo-99, Sr-82, and Sr-85 concentrations	☐Yes ☐No ☒N/A	
Subpart N – Enforcement			
35.4001	Violations	☒Yes ☐No ☐N/A	
35.4002	Criminal penalties	☒Yes ☐No ☐N/A	
Additional Considerations			