

Alpha Tau Alpha DaRT™ Manual Brachytherapy Licensing Guidance

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1 10 CFR 35.1000 Use

Alpha DaRT™ (Diffusing Alpha-emitters Radiation Therapy) are manual brachytherapy sources, with many unique properties that merit radiation safety considerations other than those required by Title 10 of the *Code of Federal Regulations* (CFR) Part 35, Subpart F, “Manual Brachytherapy.” These unique properties include the release of radon-220 (Rn-220), an alpha emitting noble gas from the radium-224 (Ra-224) parent source, in tissue. As a result, Alpha DaRT™ is regulated under [10 CFR 35.1000](#), “Other medical uses of byproduct material or radiation from byproduct material.”¹

2 Device Description

The Alpha DaRT™ device contains a source and applicator and is designed for manual brachytherapy. The Alpha DaRT™ contains Ra-224 seeds², which are implanted into the tumor using an Alpha DaRT™ applicator according to a pre-determined plan. Inside the tumor, the Ra-224 decays by alpha emission and the seeds release Rn-220 by recoil. Rn-220 is a noble gas and will diffuse in the extra- and intra-cellular space near the seed, occasionally entering and leaving the porous network of tumor blood vessels. Irradiation of tissue continues through beta and alpha emissions throughout the remainder of the short-lived decay chain.

The applicator comprises two major components:

- A needle or catheter, in the form of a Kapton tube, with the Alpha DaRT™ seeds placed in it. The Alpha DaRT™ seeds are strung on a biocompatible suture and loaded inside a rigid needle or flexible catheter and encapsulated inside with glycerin; and
- A stylet (plunger) inserted into the needle cannula (or catheter), reaching the back end of the Alpha DaRT™ seeds. During administration, the strung seeds are pushed through the glycerin into the tumor volume via the plunger.

In addition, there are two auxiliary components of the applicator:

- A protective cap is attached to the needle or catheter to prevent inadvertent damage during transportation; and
- A safety screw, which secures the needle and the stylet firmly together.

The applicator and auxiliary components will arrive in a sterile sealed bag. More information about the device can be found in its Sealed Source and Device Registry, MA-1426-D-101-S. The Alpha DaRT™ series device was conditionally approved by the U.S. Food and Drug Administration in Investigational Device Exemption number G180076, dated May 10, 2018, for temporary implant therapy.

¹ 10 CFR 35.1000 is designated as Compatibility Category D. Agreement States are not required to adopt these regulations for purposes of compatibility but are not prohibited from adopting Compatibility Category D regulations if they so choose. If Agreement States choose to adopt this licensing guidance, references to 10 CFR should be changed to the equivalent Agreement State regulations.

² “Seeds” are the small metal sources containing Ra-224 that are implanted into a tumor during treatment. The seeds are made of either stainless steel or titanium and have a layer of Ra-224 affixed to their surface.

3 Licensing Guidance

The license conditions listed in this document provide applicants with the acceptable means in satisfying the requirements for a license for the use of Alpha DaRT™. This information is not intended to be the only means of satisfying the requirements. The applicant should submit the information required to meet [10 CFR 30.33](#), “General requirements for issuance of specific licenses,” and [35.12](#), “Application for license, amendment, and renewal”, as described below. The applicant should either submit the additional information and commitments requested below or, unless the information is specifically required by regulation, submit alternative information and commitments for review by the U.S. Nuclear Regulatory Commission (NRC) staff to make a licensing determination. The commitments incorporated into the license by license condition will be reviewed during routine inspections. If an applicant commits to the guidance provided below, the applicant must follow commitments described with the use of the word “should.” This guidance may be revised as additional experience is gained regarding the medical use of Alpha DaRT™.

Applicants should also refer to [NUREG-1556, Volume 9, Revision 3](#), “Consolidated Guidance About Material Licenses: Program-Specific Guidance about Medical Use Licenses,” as it provides overall licensing guidance for all medical uses of byproduct material, including applicable model procedures for audits, occupational dose monitoring program and surveys. Guidance specific for the use of Alpha DaRT™ under [10 CFR 35.1000](#), “Other medical uses of byproduct material or radiation from byproduct material” are contained herein.

4 Requirements not Specific to 10 CFR 35.1000 Use

Applicants should commit to meet the general requirements in 10 CFR Part 35, Subpart A, “General Information;” Subpart B, “General Administrative Requirements;” Subpart C, “General Technical Requirements;” Subpart L, “Records;” and Subpart M, “Reports,” and Subpart N, “Enforcement,” except as specified in this guidance. Additionally, applicants should meet applicable requirements of 10 CFR Part 19, “Notices, Instructions and Reports to Workers: Inspection and Investigations;” Part 20, “Standards for Protection Against Radiation;” and Part 30, “Rules of General Applicability to Domestic Licensing of byproduct material.” The enclosed consolidated technical analysis table provides guidance on applicable requirements.

5 Specific Licensing Guidance for Alpha DaRT™

5.1 Radionuclides, Form, Possession Limits, and Purpose of Use

Pursuant to [10 CFR 35.12\(c\)](#), the applicant should identify the radionuclide, chemical/physical form, requested maximum possession limit, and purpose of use. The information in the table below provides the suggested format for completing Item 5 (Radioactive Material) and Item 6 (Purpose of Use) on the [NRC Form 313](#), “Application for Materials License.”

Radionuclides (NRC Form 313 Item 5a)	Radium-224 permitted by 10 CFR 35.1000
Chemical/Physical Form (NRC Form 313 Item 5b)	Sealed sources (Manufacturer Alpha Tau Medical, Inc., Model No. _____)
Maximum Possession Limit (NRC Form 313 Item 5c)	____ mCi
Purpose of Use (NRC Form 313 Item 6)	Diffusing alpha emitting brachytherapy procedure permitted by 10 CFR 35.1000.

5.2 Training and Experience

Licensees must have at least one Authorized User (AU) and Radiation Safety Officer (RSO) for Alpha DaRT™ before the source can be added to the license. NRC staff has determined the following training and experience (T&E) criteria is appropriate to authorize AUs and RSOs for Alpha DaRT™. Applicants should submit documentation showing this criterion is met, but the applicant may submit alternative T&E commitments to be reviewed on a case-by-case basis by NRC staff. The alternative T&E commitments should include an explanation of why the applicant believes the alternative T&E commitments demonstrate that the individuals are qualified to be an AU.

5.2.1 Authorized Users (AU)

NRC has determined that individuals meeting the AU T&E criteria A and B, provided below, can be authorized for the use of Alpha DaRT™.

A.

1. Is identified as an AU for medical use in [10 CFR 35.1000](#) for Alpha DaRT™ or [10 CFR 35.400](#), “Use of sources for manual brachytherapy;” or
2. Meets the T&E requirements of [10 CFR 35.490](#), “Training for use of manual brachytherapy sources,” including a written attestation when necessary.

And

B.

Has successfully completed training in delivery, safety procedures, and clinical use for Alpha DaRT™. This training may be provided by either the vendor for new users or by receiving training supervised by an AU authorized for Alpha DaRT™. Safety procedures and clinical use training should include preparing, implanting, and removing the seeds; using administrative controls to prevent a medical event; and using procedures to minimize the risk of and monitor for contamination and to ensure proper decontamination. The individual has a written attestation that the AU has satisfactorily completed these requirements and is able to independently fulfill the radiation safety-related duties as an AU for use of Alpha DaRT™ brachytherapy.

5.2.2 Radiation Safety Officer (RSO)

The RSO should have training as specified in [10 CFR 35.50](#), “Training for Radiation Safety Officer and Associate Radiation Safety Officer,” including training in radiation safety, regulatory issues, and emergency procedures for Alpha DaRT™. This training requirement may be satisfied by completing training that is supervised by an RSO, an Associate RSO, or AU authorized for Alpha DaRT™, as appropriate. In addition, RSO’s should be aware of all license conditions and procedures specific to the individual license.

6. License Conditions

The applicant should commit to follow all applicable requirements in 10 CFR Part 35 for brachytherapy sources and manual brachytherapy use and should commit to the following licensing commitments. The table contained in the appendix provides more details on applicable 10 CFR Part 35 requirements.

6.1 Procedures for Administration

The licensee must have procedures for administration requiring a written directive as specified in [10 CFR 35.41](#), “Procedures for administrations requiring a written directive,” specifically to ensure high confidence that the patient’s or human research subject’s identity is verified before each administration and each administration is in accordance with the written directive. In addition to requirements in [10 CFR 35.41](#), licensees should commit to include verification that seeds are fully contained within the patient’s body during treatment to avoid significant daughter products leakage and contamination. Additionally, licensees should commit to evaluating the location of the seeds prior to removal to determine if the seeds moved during treatment to determine if a medical event occurred. Similar to [10 CFR 35.2041](#), “Records for procedures for administrations requiring a written directive,” licensees should retain a copy of these procedures for the duration of the license. See NUREG-1556, Volume 9, Revision 3, Section 8.10.13, “Procedures for Administration when a Written Directive is Required,” and NUREG-1556, Volume 9, Revision 3, Appendix S for more information.

6.2 Medical Event Reporting

Licensees are required to report medical events in accordance with [10 CFR 35.3045](#), “Medical event reporting.” Because Alpha DaRT seeds are not sealed sources, licensees would not be required to report a medical event caused by a leaking source as is required by [10 CFR 35.3045\(a\)\(1\)\(ii\)\(E\)](#) or [10 CFR 35.3045\(2\)\(iii\)\(D\)](#). Therefore, the licensee should commit to:

- Report any event in which the seed is implanted directly into a location discontinuous from the treatment site, as documented in the post-implantation portion of the written directive. As stated above, total source strength only needs to include Ra-224 activity.
- Report any discovered event where the dose to the skin or an organ or tissue other than the treatment site that exceeds by 0.5 Sv (50 rem) or more the expected dose to that site from the procedure if the administration had been given in accordance with the written directive prepared or revised before administration; and 50 percent or more the expected dose to that site from the

procedure if the administration had been given in accordance with the written directive prepared or revised before administration.

6.3 Labeling

Alpha DaRT seeds are not a radioactive drug and therefore the labeling requirements in [10 CFR 35.69](#), “Labeling of vials and syringes,” are not required for Alpha DaRT™ seeds. Therefore, licensees should commit to keep the applicator in the labeled container (i.e., sterilized bag) provided by the manufacturer until the applicator is needed for use or conditions in [10 CFR 35.92](#), “Decay-in-storage” are met, if the applicator is not used and remains at the licensee facility.

6.4 Surveys

In addition to area surveys required by [10 CFR 20.1501](#) and [10 CFR 35.70](#), “Surveys of ambient radiation exposure rate,” a licensee should commit to survey with a radiation detection survey instrument the area where Alpha DaRT™ seeds were prepared for use or administered after each administration. Both ambient radiation and contamination surveys should be performed in all areas where the material is handled. Additionally, personnel surveys should include surveys of the hands for AU and the hands of supporting staff. Contamination surveys should also include the packaging (sterile bag) of the Alpha DaRT™ applicator. Glycerin is used to encapsulate the Alpha DaRT™ seeds in the applicator needle during the Alpha DaRT™ radiation therapy procedure and there is potential for Rn-220 to escape into the sterile bag prior to use. The applicator packaging (sterile bag) should not be disposed of as regular trash until it is verified to be indistinguishable from background consistent with [10 CFR 20.1501](#).

Similar to [10 CFR 35.2070](#), “Records of surveys for ambient radiation exposure rate,” licensees must retain a record of the surveys after each administration for 3 years. The record should include the date of the survey, the results of the survey, the instrument used to make the survey, and the name of the individual who performed the survey. See NUREG-1556, Volume 9, Revision 3, Section 8.10.12, “Area Surveys,” Appendix K, “General Radiation Monitoring Instrument Specifications and Survey Instrument Calibration Program,” and Appendix R, “Model Procedures for Area Surveys” for more information regarding ambient radiation and contamination surveys.

6.5 Calibration

As Alpha DaRT™ is a brachytherapy device, licensees do not need to determine unsealed byproduct activity in accordance with [10 CFR 35.63](#), “Determination of dosages of unsealed byproduct material for medical use.” Licensees should commit to following [10 CFR 35.432](#), “Calibration measurements of brachytherapy sources,” and [10 CFR 35.2432](#), “Records of calibration measurements of brachytherapy sources,” for calibration and recordkeeping. In accordance with [10 CFR 35.432](#), licensees may use measurements provided by the source manufacturer.

6.6 Contamination Control

In addition to safety precautions required in [10 CFR 35.415](#), the licensee should commit to placing all unsealed seeds that are not in use and contaminated waste in a sealable container. To reduce the spread of contamination during an emergency, licensees should have a sealable

container readily available in case a device is damaged or in case there are unused seeds. These containers should be at all locations of preparation or use. The container(s) should be rigid, large enough in size to contain the entire source packaging and contents, sealable in a way that reduces spread of contamination, and sealable in a way that contains Rn-220 gas. Licensees can dispose of waste in accordance with [10 CFR 35.92](#), “Decay-in-storage,” or other appropriate methods allowed in 10 CFR Part 20.

6.7 Radiation Protection Program Changes

As this guidance may be revised as additional experience is gained regarding the medical use of Alpha DaRT™, an applicant initially applying for authorization for the medical use of Alpha DaRT™ may request to incorporate into its license a radiation protection program revisions process similar to [10 CFR 35.26](#). Such a change process can allow future changes to radiation safety programs without a license amendment, provided that the change process requires the following conditions to be met:

1. the revision is in compliance with the regulations; and
2. the revision is based upon NRC’s current 10 CFR 35.1000 use guidance for Alpha DaRT™ posted on the [NRC’s Medical Uses Licensee Toolkit Web site](#); and
3. the revision has been reviewed and approved by the licensee’s RSO and licensee’s management; and
4. the affected individuals are instructed on the revised program before the change is implemented; and
5. the licensee will retain a record of each change for five years; and
6. the record will include a copy of the appropriate website guidance, the old procedure, the new procedure, the effective date of the change, and the signature of the licensee management that reviewed and approved the change.

7. Notes to Licensees

7.1 Change in Physical Conditions of Use

If the physical conditions of use differ from those reported in the sealed source and device registry, a limited specific medical use licensee should request an amendment for the new conditions and a broad scope licensee should perform its own engineering and radiation safety evaluation addressing those differences.

7.2 Written Directives

The licensee must complete a written directive in accordance with [10 CFR 35.40](#), “Written directives.” When total source strength is required to be recorded on the written directive, only Ra-224 activity needs to be included. The licensee must retain a copy of the written directive in accordance with [10 CFR 35.2040](#), “Records of written directives.”

7.3 Patient Release

The licensee should develop procedures that describe measures taken to ensure that radiation emissions from each patient or human research subject permits their release in accordance with [10 CFR 35.75](#), “Release of individuals containing unsealed byproduct material or implants containing byproduct material.”. Patients should not be released from the licensed facility if it is

likely that the seed or seal will become dislodged under normal conditions and potentially cause public dose limits to be exceeded. If there is a potential for a seed or seal to become dislodged under unique situations, licensees should have preventative measures in place to ensure public dose limits are not exceeded. Licensees must report lost sources in accordance with [10 CFR 20.2201](#), “Reports of theft or loss of licensed material” if a seed becomes dislodged lost and is not recovered or if temporary implants issued to a patient are not returned to the licensee. Additional guidance for release of patients or human research subjects following administration of radioactive materials may be found in [Regulatory Guide 8.39](#), “Release of Patients Administered Radioactive Materials.”

7.4 Sealed Source and Device Registry

In accordance with 10 CFR 35.400, licensees may use Alpha DaRT™ sources for manual brachytherapy uses that are not explicitly listed in the sealed source and device registry. However, the sources must be used in accordance with the radiation safety conditions and limitations described in the sealed source and device registry. As the applicators for the Alpha DaRT™ are specific for radiation safety as they are designed to minimize contamination, licensees should only use the applicators as described in the sealed source and device registry for administration.

7.5 Brachytherapy Source Accountability

Licensees must maintain accountability at all times for all brachytherapy sources in storage or use in accordance with [10 CFR 35.406](#), “Brachytherapy sources accountability.” In addition, licensees must maintain records of brachytherapy sources accountability in accordance with [10 CFR 35.2406](#), “Records of brachytherapy source accountability.” Licensees should document the location the patient plans to reside. Licensees should also have patient contact information and provide the patient with instructions on actions to take if source is dislodged during treatment.

8. Notes to Regulators

8.1 Inspection Frequency

Licenses authorizing Alpha DaRT™ should be inspected every two years. Per Enclosure 1 to [Inspection Manual Chapter 2800, “Materials Inspection Program”](#) licenses authorizing emerging technology under 10 CFR 35.1000 are assigned a Priority 2 inspection code.

8.2 Program Code

The NRC regions should use program code 02240.

9. Paperwork Reduction Act Statement

This licensing guidance provides voluntary guidance for implementing the mandatory information collections in 10 CFR Parts 30 and 35 that are subject to the Paperwork Reduction Act of 1995 (44 U.S.C. 3501 et. seq.). These information collections were approved by the Office of Management and Budget (OMB), approval numbers 3150-0017 and 3150-0010. Send comments regarding this information collection to the Information Services Branch (T6-A10M), U.S. Nuclear Regulatory Commission, Washington, DC 20555-0001, or by e-mail to Infocollects.Resource@nrc.gov, and to the OMB reviewer at: OMB Office of Information and

Regulatory Affairs (3150-0017, 3150-0010), Attn: Desk Officer for the Nuclear Regulatory Commission, 725 17th Street, NW Washington, DC 20503;
e-mail: oir_submission@omb.eop.gov.

10. Public Protection Notification

The NRC may not conduct or sponsor, and a person is not required to respond to, a collection of information unless the document requesting or requiring the collection displays a currently valid OMB control number.