

Alpha Tau Alpha Dart™ Manual Brachytherapy Licensing Guidance

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NRC Contact

Katie Tapp (301) 415-0236

MedicalQuestions.Resource@nrc.gov

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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) in tissue, an alpha emitting noble gas from the radium-224 (Ra-224) source. As a result, Alpha DaRT™ is regulated under 10 CFR 35.1000, “Other Medical Uses of Byproduct Material or Radiation from Byproduct Material.”

2 Device description

The Alpha DaRT™ device is a source and applicator designed for manual brachytherapy. The Alpha DaRT™ source are Ra-224 seeds which are implanted into the tumor using an Alpha DaRT™ applicator. 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 decay chain. The seeds are made of a stainless steel with layer of Ra-224 affixed to the surface of the tube.

In the Alpha DaRT treatment, a number of Alpha DaRT seeds are inserted into the tumor via the Alpha DaRT applicator according to a pre-determined plan.

The applicator comprises two major components:

1. A needle or catheter 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 sealed inside with glycerin.
2. 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:

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

More information about the device can be found in its sealed source and device registry, MA-1426-D-101-S.

Alpha Tau Medical, Inc. Model Alpha DaRT™ series device was conditionally approved by the U.S. Food and Drug Administration (FDA) in Investigational Device Exemption number G180076, dated May 10, 2018, for temporary implant therapy. No change in this guidance is expected should the FDA permit the device for permanent implant therapy.

3 Licensing Guidance

The applicant must 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. Applicants should 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. Guidance and license conditions 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. The guidance and 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 for a license. The applicant should submit additional information and commitments requested below or may, unless the information is specifically required by regulation, submit alternative information and commitments for review by the 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 is committing to follow commitments described with the use of the word "should."

4 Requirements not Specific to 10 CFR 35.1000 Use

Applicants must 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," except as specified in this guidance. Additionally, applicants must meet applicable requirements of 10 CFR Parts 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."

5 Specific Licensing Guidance for Alpha DaRT™

5.1 Radionuclides, Form, Possession Limits, 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

Licenses 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 have determined the following training and experience (T&E) criteria is appropriate to authorize AUs and RSOs for Alpha Dart. Applicants may submit documentation showing this criteria is met or 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

NRC has determined that individuals meeting the Authorized User (AU) training and experience (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 training and experience 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 requirement may be satisfied by completing a training program provided by the vendor for new users or by receiving training supervised by an AU who is 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 control contamination and proper decontamination. The applicant should have 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

The Radiation Safety Officer (RSO) must 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, authorized medical physicist, authorized nuclear pharmacist, or authorized user, as appropriate, who is authorized for Alpha DaRT. In addition, RSO's should be aware of conditions and procedures specific to the individual license.

6. License Conditions

The applicant shall commit to follow all applicable requirements in 10 CFR Part 35 for brachytherapy sources and manual brachytherapy use, except as specified in 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 shall commit to include verification that seeds are fully contained without leakage outside the patient's body after administration. In addition, licensees shall commit to evaluating the location of the seeds prior to removal for temporary use 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 shall 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" with the exceptions listed below.

- Licensees will not be required to report a medical event caused by a leaking source in accordance with 10 CFR 35.3045(a)(1)(ii)(e) or 10 CFR 35.3045(2)(iii)(D) as AlphaDart seeds are not a sealed source.
- Licensee shall commit to report any event in which the seed is planted 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 radium-224 activity.
- Licensees shall commit to 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 Therapy-related computer systems

The licensee must complete acceptance testing on the treatment planning system of therapy-related computer systems in accordance with 10 CFR 35.457, "Therapy-related computer systems." The licensee shall commit to having an authorized medical physicist perform additional acceptance testing on any modifications to a treatment planning system specifically made for Alpha DaRT therapy to ensure accuracy of dose; graphic displays, as needed for treatment planning; and software used to determine sealed source positions from radiographic images.

6.4 Labeling

Labeling requirements in 10 CFR 35.69, "Labeling of vials and syringes," are not required for Alpha DaRT seeds. The seeds are not a radioactive drug. Licensees shall commit to keep the applicator in its labeled container (i.e. sterilized bag) provided by the manufacturer until its needed for use or conditions in 10 CFR 35.92, "Decay-in-storage," are met.

6.5 Surveys

In addition to area surveys required by 10 CFR Part 20 and 10 CFR 35.70, "Release of individuals containing unsealed byproduct material or implants containing byproduct material", a licensee shall commit to survey with a radiation detection survey instrument after each administration of Alpha DaRT seeds where prepared for use or administered. Similar to 10 CFR 35.2070, "Records of surveys for ambient radiation exposure rate", licensees shall retain a record of the surveys after each administration for 3 years. The record must 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" and Appendix R, "Model Procedures for Area Surveys" for more information regarding surveys.

In addition to surveys required by 10 CFR 35.404, "Surveys after source implant and removal", licensees shall commit to perform a removable contamination survey of the patient to ensure no contamination or leakage prior to patient release. Similar to 10 CFR 35.2404, "Records of surveys after source implant and removal," shall maintain a record of these surveys for 3 years. Each record must include the date and results of the survey, the survey instrument used, and the name of the individual who made the survey. Licensees shall commit to file a report within 5 days if this survey reveals the presence of 185 Bq (0.005 μ Ci) or more of removable contamination similar to reports required per 10 CFR 35.2067, "Records of leaks tests and inventory of sealed sources and brachytherapy sources." The report must be filed with the appropriate NRC Regional Office listed in 10 CFR 30.6 of this chapter, by an appropriate method listed in 10 CFR 30.6(a) of this chapter, with a copy to the Director, Office of Nuclear Material Safety and Safeguards. The written report must include the type of applicator and lot number, if assigned; the radionuclide and its estimated activity; the results of the test; the date of the test; and the action taken.

6.7 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 shall 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 instead of making their own measurements. However, there is a potential that radon-220 could leak from the applicator, which would mean equilibrium with decay products would not be present during administration as anticipate. Therefore, licensees shall commit to ensure the integrity of the applicator seal prior to administering seeds to a patient to verify that leakage has not occurred. This could be completed by performing a survey of the sterilization bag after the applicator has been removed, but prior to administration, to ensure no leakage. Similar to 10 CFR 35.3432, licensees shall retain a record of their validation of the integrity of the applicator seal for 3 years after its use.

6.8 Radiation Protection Program Changes

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 change process similar to [10 CFR 35.26](#). Such a change process can allow some future changes to radiation safety programs without a license

amendment provided that the change process requires the following conditions to be met for revisions to the radiation safety program:

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 (SSD) certificate, the limited specific medical use licensee shall request an amendment for the new conditions, and a broad scope licensee shall 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 radium-224 activity needs to be included. The licensee shall 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 his or her release in accordance with [10 CFR 35.75](#), "Release of individuals containing unsealed byproduct material or implants containing byproduct material." Licensees should note temporary use affixed by sutures which protrude outside of the body have a potential to become dislodged or allow for gaseous release. Patients should not be released from the licensed facility if it is possible under normal conditions for a seed or seal has a potential to become dislodged 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 must 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 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 Brachytherapy Source Accountability

Licensees shall 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 shall maintain records of brachytherapy sources accountability in accordance with 10 CFR 35.2406, "Records of brachytherapy source accountability." Licensees should document the location which the patient plans to reside and spend a significant period of time (i.e. such as work) as locations of use when used as a temporary implant on an outpatient basis. 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](#), 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 collection 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.