

NATIONAL MATERIALS PROGRAM PILOT PROJECT FOUR

AGREEMENT STATE ASSUMPTION OF RESPONSIBILITY FOR DEVELOPMENT OF GUIDANCE FOR NEW USE OR MODALITY NOT PREVIOUSLY REVIEWED AND APPROVED

EXECUTIVE SUMMARY

This report is to be used by the staff to provide the Commission understanding on the feasibility and viability of the Alliance Option as described in the National Materials Program Working Group Report.

The National Materials Program Pilot Project Four is one of five pilot projects undertaken by the Nuclear Regulatory Commission (NRC), Conference of Radiation Control Program Directors (CRCPD), Inc., and the Organization of Agreement States (OAS). The project is designed to have an Agreement State, groups of Agreement States, or individual experts within the Agreement States develop licensing and inspection guidance for a new use of material, or new modality, not previously reviewed and approved by the NRC.

The objectives of this project are to develop inspection and licensing guidance for the new use of material and work with the OAS and NRC to determine the process for accepting the guidance and incorporating it into the existing licensing and inspection system.

Membership in this project includes four Agreement State representatives and one NRC representative. The primary resources were labor and travel expense. The total labor hours were approximately 315 hours as of September 9, 2004.

The final work products consist of two documents specifying licensing and inspection guidance for a new use of material, radioactive seed localization (RSL) for non-palpable lesions.

Responses to the eight Success Measures described in SECY-02-0074 are in the report.

BACKGROUND

The National Materials Program Pilot Project Four is one of five pilot projects undertaken by the NRC, CRCPD, and the OAS. The pilot project is designed to have an Agreement State, group of Agreement States, or individual experts within the Agreement States develop licensing and inspection guidance for a new use of material or a new modality not previously reviewed and approved.

A centralized, or national program, approach for accomplishing the development of licensing and inspection guidance for a new use of material would use senior license reviewers and inspectors as its "center of expertise." This group is comprised of individuals from Agreement States and federal government. The members are knowledgeable of the issues pertaining to the licensing and inspection of emerging technologies because they regularly participate in the

decision-making activities that surround it.

The use of centers of expertise optimizes the resources of federal, state and professional organizations and reduces duplicate efforts. The NRC and the individual Agreement States would not have to develop independent guidance information for this new use of material in order to license its use. Centralized development of guidance information would help to ensure that state and federal programs remain comparable nationwide.

The objectives of this pilot project were to develop the licensing and inspection guidance for a new use of material and work with the OAS and NRC to determine the process for accepting the guidance and incorporating it into the existing licensing and inspection system.

DISCUSSION

The project involved two tasks. First, the working group surveyed the Agreement States, NRC Headquarters, and the NRC Regions to ascertain if there is a new use of material or a new modality that would qualify under this pilot project. The working group reviewed a number of emerging issues before selecting Iodine-125 and Palladium-103 low dose rate brachytherapy seeds used for localization of non-palpable lesions for development of guidance. This medical procedure was chosen because it met two important criteria: it involves the use of Atomic Energy Act (AEA) material and therefore is regulated by the Agreement States and the NRC, and it does not fit cleanly into the existing regulatory framework.

Iodine-125 and palladium-103 seeds are brachytherapy sources designed for the treatment of cancerous tumors. The radioactive seeds are currently regulated under 10 CFR 35.400: "Use of sources for manual brachytherapy" and equivalent Agreement State regulations. In this application, the radioactive seeds are implanted for localization and are not intended to deliver a therapeutic dose to tissue. This application does not fall under 10 CFR 35.500: "Use of sealed sources for diagnosis," because these sources are currently not approved for diagnostic use in the sealed source and device registry. Therefore, use of these seeds for radioactive seed localization procedures will be regulated under 10 CFR 35.1000: "Other medical uses" and equivalent Agreement State regulations.

Task two involved development of the licensing and inspection guidance for radioactive seed localization. To accomplish this, the working group reviewed the requirements under 10 CFR 35.200 and 10 CFR 35.400 and incorporated the relevant requirements into the guidance.

The project has afforded the working group the opportunity to successfully develop sensible guidance for the licensing and inspection of a new use of radioactive material that focus on the key elements necessary for authorizing its use.

• Success Measures

1. *Provide insights into whether an informal coalition of State programs and NRC, as envisioned under the Alliance Option, is viable and can produce products meeting the needs of both NRC and the Agreement States.*

This project is another in a series of collaborative efforts between NRC, the OAS and CRCPD to develop common use products, regulations and guidance. Many of the emerging technologies in use today had their origin in an Agreement State, and this trend is likely to continue due to the ever increasing number of Agreement States. Pilot 4, implemented by the OAS with majority membership of Agreement State personnel, illustrates the successful collaboration between federal and state programs to develop regulatory products (licensing and inspection guidance) to meet the needs of both the NRC and the Agreement States. The Working Group developed licensing and inspection guidance for a new medical use of material involving brachytherapy seeds used as markers for the localization of non-palpable lesions. The pilot project exemplifies the high quality collaboration that can occur between the NRC, states, organizations and industry as envisioned under the Alliance Option.

2. *Provide insights that the Alliance Option has the potential to be a sustainable program structure for the NMP which will result in fewer NRC resources being needed for the development of products needed by NRC and the Agreement States.*

The working group's opinion is that the Alliance Option is a sustainable program structure for the NMP. The Working Group involved with the development of the guidance for the new medical use of material was comprised of senior licensing and inspection staff from states which have medical centers leading the field in the development of emerging medical technology. Use of such centers of expertise is an integral component of the Alliance Option and should continue as a collaborative between the Agreement States and the NRC. The development of guidance which will be used by both the NRC and Agreement States will result in resource savings for all participants by eliminating duplication of efforts and will provide consistent regulatory oversight across the nation.

3. *Provide demonstration that States can assume and carry out greater responsibility for the development and maintenance of products under a NMP.*

The successful completion of this pilot project demonstrates that States can assume and carry out greater responsibility for the development of regulatory products under a NMP. The working group was implemented by the OAS and consisted of four Agreement State members and one NRC member. At this time the working group is uncertain of its role in the maintenance of the guidance information.

4. *Provide greater assurance that individual State programs are willing and able to commit resources, and to produce products on a schedule that can be utilized by NRC and the Agreement States.*

Individual State programs have long been willing and able to commit resources and staff in support of the development of products to be utilized by both the NRC and the Agreement States. Many Agreement State staff have served as members of working groups and writing teams for NUREGs and other technical documents. The experience of the Pilot 4 Working Group serves to illustrate the commitment of each of our State programs, and those other state programs we collaborated with during the development

of our work products, to provide staff resources in support of a National Materials Program.

5. *Provide insights into whether the NRC will be able in the future to realize resource savings and efficiency gains through shifting of work to States under an Alliance structure.*

The Alliance structure allows for the development of regulatory products for use by both the NRC and Agreement States utilizing centers of expertise. The use of the licensing and inspection guidance developed for the RSL procedure by Agreement States and the NRC will result in resource savings for all parties by eliminating the need for each Agreement State or the NRC to develop separate guidance and will provide consistent regulatory oversight across the nation.

6. *Provide demonstration that NRC can operate in a NMP framework and will be able to use products which may have been developed by a single State or group of States without the need for major changes.*

The guidance document was developed following the model of a TAR to NRC Headquarters to facilitate its acceptance without the need for major changes. At this time no other direct demonstration is available to address this success measure.

7. *Provide demonstration that NRC is willing to share with the States the establishment of priorities for the NMP including rule and guidance work needed to support the materials and waste arenas.*

The NRC has for many years invited States participation when developing rules and guidance in support of its regulatory program. This pilot project utilized the regulatory priorities established by the NMP Pilot 1 Working Group in its selection of a new use of materials to focus on development of guidance.

8. *Provide insights to help understand the degree to which Agreement States are aligned with NRC Policy direction to use a risk informed and performance based regulatory approach.*

The product developed under this Pilot does not provide insight into the alignment of the Agreement States with NRC's risk informed, performance based regulatory approach. The guidance incorporated the prescriptive requirements and performance base criteria as defined in 10 CFR Part 35 and equivalent Agreement State regulations.

RECOMMENDATION

In the future, the NRC should coordinate with the OAS and the CRCPD in the development of similar licensing and inspection guidance for emerging technologies. Routine meetings of these entities should include discussions of emerging technologies and where the best center of expertise for guidance development exists. The OAS and CRCPD should continue to

encourage states to provide resources in support of the development of such regulatory products.

RESOURCES

Approximately 346.5 hours were specifically involved in the NMP Pilot 4 project, as follows:

Working Group Team Leader	145.0 hours
Working Group Members	201.5 hours

Iodine-125 Seed Localization for Non-Palpable Lesions

Purpose

Radioactive seed localization (RSL) uses currently available radioactive seeds previously approved for the treatment of cancerous tumors. For instance, iodine-125 titanium seeds¹, typically between 200 – 300 µCi/seed, are implanted into a breast lesion using a standard 18-gauge needle. These seeds are normally implanted within mammography, ultrasound or MR suites and removed within surgical suites between 2 and 5 days post implantation. Use of more seeds or different implant locations may arise in the future. RSL differs from current localization procedures where a wire is implanted into the lesion site and excised along with the affected tissue. The radioactive seed(s) can be easily located with a hand-held gamma probe (using a technique with which surgeons are familiar because of its similarity to sentinel lymph node biopsy and radioguided parathyroidectomy) and surgically removed with minimal injury to non-affected tissue. The seed(s) may be removed from the tissue specimen in surgery, or the tissue specimen with the seed(s) can be sent to pathology for removal of the seed and analysis of the tissue. The seed or seeds are then disposed of in accordance with 10 CFR 35.92 or equivalent Agreement State regulations.

Inspection Guidance

Iodine-125 seeds are brachytherapy sources designed as permanent implants for the treatment of benign and malignant abnormalities. The iodine-125 seeds are currently regulated under 10 CFR 35.400: “Use of sources for manual brachytherapy” and equivalent Agreement State regulations. In this application, the iodine seeds are implanted for localization and not to deliver a dose to tissue. This application does not fall under 10 CFR 35.500: “Use of sealed sources for diagnosis,” because these sources are not approved for diagnostic use in the sealed source and device registry. Therefore, use of these sources for radioactive seed localization procedures will be regulated under 10 CFR 35.1000: “Other medical uses” and equivalent Agreement State regulations.

NRC inspectors should use Inspection Procedure 87132: Brachytherapy Programs, found in the NRC Inspection Manual (IMC 2800), to conduct inspections of facilities performing radioactive seed localization procedures. Agreement State inspectors should use their own inspection procedure for brachytherapy programs in which no written directive is required.

Through discussion with cognizant licensee representatives, direct observations of licensed activities, and if necessary a review of selected records, NRC inspectors should ensure that each of the focus elements described in IP87130 are met. For example, for focus element 5, Radiation Instrumentation and Surveys, the inspector should independently verify that the licensee has implemented the procedures to monitor the implantation/explantation area to ensure all seeds remained intact following each RSL procedure and removal from excised tissue, including the use of appropriate instrumentation.

¹ Multiple seeds may be used to define the margins of irregularly shaped lesions.

Iodine-125 and Palladium-103 Low Dose Rate Brachytherapy Seeds Used for Localization of Non-Palpable Lesions

Purpose

Radioactive seed localization (RSL) uses currently available radioactive seeds previously approved for the treatment of cancerous tumors. For instance, iodine-125 titanium seeds¹, typically between 200 – 300 µCi/seed, are implanted into a breast lesion using a standard 18-gauge needle. These seeds are normally implanted within mammography, ultrasound or MR suites and removed within surgical suites between 2 and 5 days post implantation. Use of more seeds or different implant locations may arise in the future. RSL differs from current localization procedures where a wire is implanted into the lesion site and excised along with the affected tissue. The radioactive seed(s) can be easily located with a hand-held gamma probe (using a technique with which surgeons are familiar because of its similarity to sentinel lymph node biopsy and radioguided parathyroidectomy) and surgically removed with minimal injury to non-affected tissue. The seed(s) may be removed from the tissue specimen in surgery, or the tissue specimen with the seed(s) can be sent to pathology for removal of the seed and analysis of the tissue. The seed or seeds are then disposed of in accordance with 10 CFR 35.92 or equivalent Agreement State regulations.

Licensing Guidance

Use of these iodine-125 seeds are currently regulated under 10 CFR 35.400: “Use of sources for manual brachytherapy” and equivalent Agreement State regulations. In this application, the iodine seeds are implanted for localization by an authorized user and are not intended to deliver a therapeutic dose to tissue. This application does not fall under 10 CFR 35.500: “Use of sealed sources for diagnosis,” because these sources are currently not approved for diagnostic use in the sealed source and device registry. Therefore, use of these seeds for radioactive seed localization procedures will be regulated under 10 CFR 35.1000: “Other medical uses” and equivalent Agreement State regulations.

This guidance is intended to address cases where the locations of implant, excision, and recovery of the seed(s) are all governed by the same radioactive materials license. In the case of a facility intending to use an external pathology laboratory not currently listed on any materials license, the license reviewer should request the external laboratory submit an application for a new license.

This guidance represents one means acceptable to the NRC and Agreement State staff of complying with regulations and is not intended to be the only means of satisfying requirements for a license. Therefore, to meet the requirements of 10 CFR 35.12 or equivalent Agreement State regulations, unless specifically required by regulation, the applicant must provide the information requested below or submit alternative commitments that will be reviewed by the NRC or Agreement State to determine whether they meet regulatory requirements. In addition,

the commitments contained therein will be reviewed during routine inspections.

Applicants are reminded that licenses issued pursuant to 10 CFR 35.1000 must still meet the General requirements in 10 CFR Part 35, or equivalent Agreement State regulations (e.g., applicable section of Subparts A, B, C, L, and M.). For instance, 10 CFR 35.67 contains requirements for leak testing sealed sources, 10 CFR 35. contains provisions for release of patients containing implants, and 10 CFR 35.3045 contains requirements for reporting events when the effective dose equivalent of 50 rem to an organ or tissue is exceeded.

General

Items 5-6: Identify the radionuclides, chemical/physical form, maximum quantity per treatment and total, and purpose of use. For example, the following provides the format for an acceptable response:

Item 5: Iodine-125 or Palladium-103;

Sealed sources [manufacturer' and model number to be supplied by licensee 0.30 millicuries per source; 1.5 millicuries maximum per treatment and 15 millicuries total;

Item 6 For use as temporary implants to localize non-palpable lesions.

Facility Diagram: Submit a description of the location where the radioactive sources will be used, administered and stored. The description should include the rooms where the seeds will be: (1) stored when not in use; (2) implanted into the patient; (3) explanted from the patient; (4) removed from the tissue sample; and (5) stored for decay. If the tissues sent to pathology will still contain the seed(s), or more than 1 microcurie of I-125 or 100 microcuries of Pd-103 contamination from a leaking source, the licensee needs to clarify whether the tissues will be processed in its own pathology laboratory or sent to an external pathology laboratory. Provide a diagram of these locations, in addition to an overall floor plan that shows the proximity of these locations of use to other occupied areas of the building or floor. [30.33(a)(2), 35.12(b)(1)].

Authorized Users: Identify all authorized users and document his/her training and experience to use the iodine-125 or palladium-103 seeds for the RSL procedure. The authorized user will be considered qualified for implantation, localization, and removal of the seeds if the individual meets either the criteria in:

10 CFR 35.490 (or before October 24, 2005, the requirements in 10 CFR 35.940); or

10 CFR 35.290 (or before October 24, 2005, the requirements in 10 CFR 920) and preceptorship training by a 10 CFR 35.490 authorized user to include: work experience that includes at least 3 cases in ordering, receiving, and unpacking radioactive materials safely, and performing the related radiation surveys using the appropriate instrumentation; preparing, implanting, and removing iodine-125 and/or palladium-103 brachytherapy sources; emergency procedures applicable to sealed sources; using

administrative controls to prevent a medical event involving this device; and maintaining running inventories of material at hand.

General surgeons, working under the supervision of an authorized user described above, who locate and remove the tissue containing the seed(s) should complete 8 hours of radiation safety training that includes: performing the related radiation surveys using appropriate instrumentation; preparing, implanting, and safely removing brachytherapy sources; and emergency procedures, including how to respond to a leaking source. This training shall be provided by the authorized user described above or the Radiation Safety Officer, as applicable.

Pathology personnel handling specimens containing radioactive material should be instructed in the radiation safety aspects of safely handling the seeds, including: use of gloves; minimizing time handling specimen; using an appropriate survey instrument to perform surveys of hands and work area following handling of the specimen; emergency procedures to be followed in the event that contamination is identified; accountability; security of the seeds post-implantation; and appropriately disposing of the seeds and/or specimens containing the seed(s).

Records

Because the iodine-125 or palladium-103 seed sources are temporarily implanted, the applicant may simplify its submission by confirming that it will:

Meet the brachytherapy requirements appropriate for a temporary implant in 10 CFR Part 35, Subpart F, "Manual Brachytherapy," Subpart L, "Record," and Subpart M, "Reports." [35.310; 35.404; 35.410; 35.406; 35.2404; 35.2406 (a) and (b); and 35.3045].

Safety Precautions and Instructions for Iodine-125 and/or Palladium-103 Seed Localization for Non-Palpable Lesions

Describe the radiation safety program for all departments involved in the RSL procedure, including the pathology laboratory, addressing: (1) safety procedures and instructions, including receipt and survey procedures; (2) specifying the individuals that must be physically present during implantation and explantation; (3) source accountability, including maintaining a record of brachytherapy source accountability, and leak testing; (4) calibration measurements of the brachytherapy sources; (5) procedures to minimize puncturing the seed(s); (6) surveys to detect leakage or lost seeds; (7) storage; (8) security; and (9) disposal. Surveys must be performed after source implant and removal [35.404 and record keeping requirements in 35.2404 and 35.2310, or equivalent Agreement State regulations]. If the licensee intends to transfer the radioactive tissue samples to an outside pathology laboratory, the licensee must submit a description of the program to ensure the samples are transferred to an NRC or Agreement State licensed laboratory authorized to receive the seeds or radioactive tissue, and the package is properly prepared for shipping.

Provide a copy of the written emergency procedures for responding to an abnormal situation to

include, (1) instructions for responding to a source ruptured (e.g. cut by scalpel) during surgical removal to include procedures for retrieval of leaking/cut sources and mitigating the I-125 uptake and decontamination of the patient and area from the ruptured source; (2) instructions to pathology personnel for responding to a leaking/cut source and decontamination of personnel and the area; (3) the process for restricting access to and posting of the implantation/explantation/pathology area in the event of an unaccounted for or ruptured source to minimize the risk of inadvertent exposure from seeds; (4) patient follow-up should they not return for explantation; and (5) names and telephone numbers of the authorized users and the Radiation Safety Officer to be contacted.

Notes to Licensees

Change in physical conditions of use.

Because the physical conditions of use exceed those reported in the Sealed Source and Device (SSD) certificate due to the sources not having been tested for puncture, the limited specific medical use licensee should request an amendment for the new conditions. Certain States will not allow variations in the physical conditions of use unless the original SSD certificate is amended or a custom evaluation is performed. Broad scope licensees should perform its own engineering and radiation safety evaluation addressing those differences. Licensees should submit documentation that addresses the safe use of the source in the normal and emergency conditions associated with this 35.1000 use. This documentation may be, but is not limited to, an engineering, historical, or scientific analysis of the surgical removal of these sources.

Revision of the iodine-125 seed localization for non-palpable lesions radiation safety programs to conform to this licensing guidance.

(Note: Requesting authorization in accordance with the following guidance will permit a licensee to make certain changes under 10 CFR 35.26, "Radiation protection program changes," or equivalent Agreement State regulations, to the iodine-125 seed localization for non-palpable lesion safety program that might otherwise require a license amendment).

The above licensing guidance may be revised as additional experience is gained regarding medical use of radioactive seed localization. A licensee already authorized to use iodine-125 and/or palladium-103 -seed for seed localization of non-palpable lesions that is committed by license condition to follow provisions in the existing guidance at the time of commitment must apply for and receive an amendment to its license in order to make changes to conform with the revised provisions.

An applicant initially applying for authorization for medical use of iodine-125 and/or palladium-103 seeds for seed localization of non-palpable lesions (or a licensee applying later for an amendment to conform with revisions in this guidance) may request authorization to allow future changes to its radiation safety program, provided the following conditions are met:

- (1) The revision is in compliance with the regulations of the NRC or Agreement State;
- (2) The revision is based on NRC's current guidance for iodine-125 seeds for seed localization of non-palpable lesions 35.1000 use posted on the NRC website;

- (3) The revision has been reviewed and approved by the licensee's Radiation Safety Officer, Radiation Safety Committee, and management;
- (4) The affected individuals are instructed on the revised program before the change is implemented;
- (5) The licensee will retain a record of each change for 5 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.

If this authorization is approved, these conditions will be incorporated as license conditions in the licensee's license.

The above guidance for changes to conform with the revised provisions does not prevent Agreement States from requiring that the licensee request an amendment for each change to its radiation safety program if that is their policy.