EXUBRION™
THERAPEUTICS

Authorized User/Radiation Safety Officer Training for Synovetin OA®

Module 1: Regulatory Overview

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Introduction

- This training course is for veterinary facilities interested in adding Synovetin OA® (tin-117metastable [tin-117m or ^{117m}Sn]) to a new or existing radioactive materials (RAM) license.
- The course consists of 8 modules related to the safe use of radioactive materials in veterinary applications. Each module includes training slides, supplemental reading material, and a short quiz. Completion of the quiz enables the trainee to move to the next module. All content is available for download.
- Upon satisfactory completion of all modules, a certificate will be generated and forwarded to the email address provided at registration.

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Outline

- Regulation of Radioactive Materials Use
- Radioactive Materials License
- Authorized Users and Radiation Safety Officers
- RAM License Amendment Process
- RAM License Conditions
- Licensee Inspections and Violations
- Supplemental Reading Material:
    1. Synovetin OA® Device Label
    2. NUREG 1556 Volume 7
    3. NRC Reg Guide 10.8
- Quiz

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Who Regulates Use of Radioactive Materials?

- US Nuclear Regulatory Commission (NRC)
  - Federal parent organization that oversees safe use of radioactive material
  - Currently 13 states (+ DC) are regulated by the NRC

- Agreement States
  - The remaining 37 states have an agreement with the NRC to manage radioactive material use at the local (state) rather than federal level
  - Agreement States have their own regulations which need to be equally stringent or more stringent than those of the NRC.

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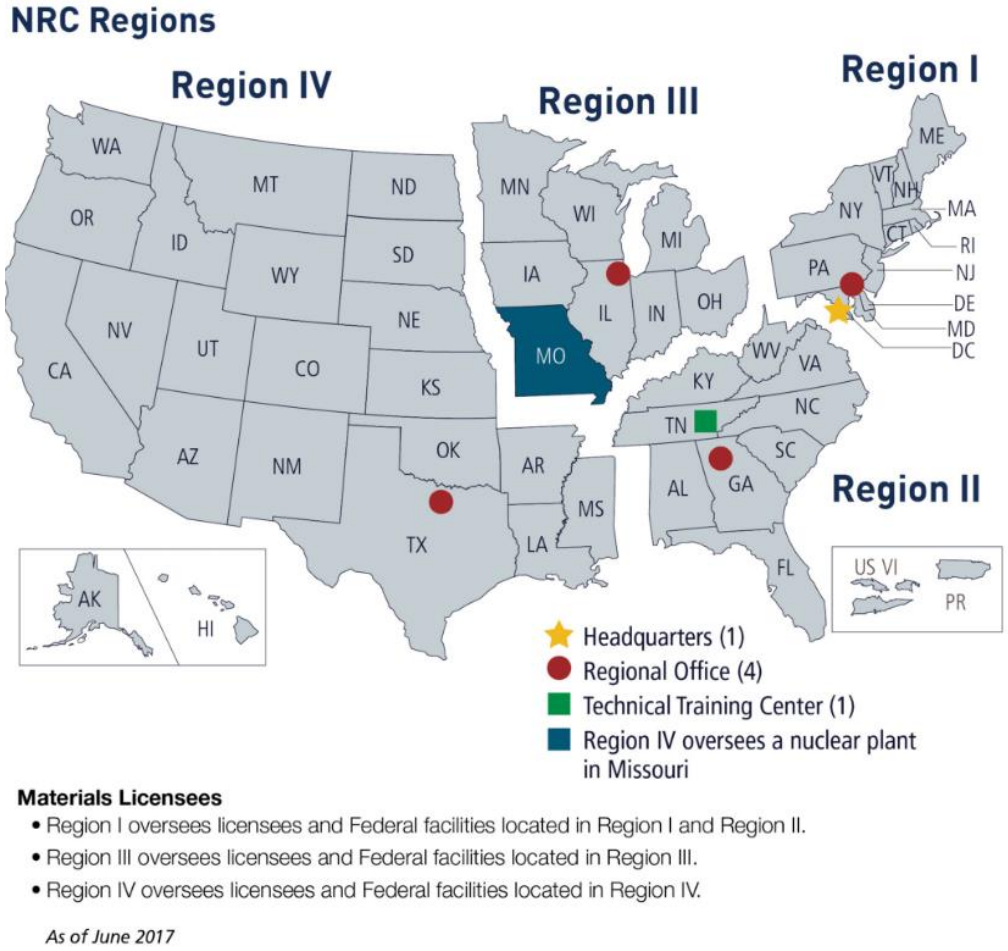
Who Regulates Your State?

- This link (https://www.crcpd.org/mpage/Map) takes you to the Council of Radiation Control Program Directors website page showing a map of the US and contact information for each state's radiation control program.

- The map to the right identifies the regions for NRC-regulated states, and contact information for each region can be found at this link: https://www.nrc.gov/about-nrc/locations.html.



Example of an Agreement State - California's Radiation Control Program: https://www.cdph.ca.gov/Programs/CEH/DRSEM/Pages/RHB.aspx

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What Is a Radioactive Materials License?

- The US regulates the safe use of radioactive materials through the Nuclear Regulatory Commission (NRC) and Agreement States.
- A radioactive materials (RAM) license is the document that authorizes an entity to procure, possess, and manipulate sealed or unsealed radioactive materials.
- Specific regulations and procedures must be followed when handling radioactive materials, and the licensee is required to develop and maintain an approved radiation protection program.
- There are two specific roles identified on a radioactive materials license:
  - Radiation Safety Officer (RSO)
  - Authorized User (AU)

  The RSO and AU can be same person.
- For more information, refer to supplemental reading: NUREG 1556 Volume 7.

Authorized Users (AU) and Radiation Safety Officer (RSO)

- Authorized User: Licensed veterinarian who is listed on a RAM license and is trained in the safe handling and use of unsealed and sealed radioactive materials. Qualified training includes one or more of the following:
  - Fellowship in radiology and or nuclear medicine
  - Training course specific to the safe use of radioactive material
  - Preceptor attestation by an AU approved for the type of use requested
    - Authorized Users can also supervise other employees with specific, documented training. A routine example of this is a technologist trained to receive packages containing radioactivity. The technologist would be a Supervised Individual (SI).
- Radiation Safety Officer: Typically an AU or contracted consulting health or medical physicist who is trained in the state/federal regulations for the safe use of radioactive materials.
  - Responsible for the licensee's safe use of radioactive materials
  - Ensures the program is kept ALARA (staff and public exposure is maintained "as low as reasonably achievable")
  - Serves as liaison with regulators

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Amendments to Existing RAM Licenses

- Most existing veterinary RAM licensees are approved to use ^{131}I as radioiodine therapy for feline hyperthyroidism. Current licensees will already have many aspects of the radiation protection program in place.
- Before licensees are permitted to use any other radioactive material (such as tin-117m), they must submit an "amendment request" to their regulatory body for approval.
- The specific format of the amendment request will vary by state, but the content will be similar. In all cases, the most recent state-specific or federal guidance must be used.
- Amendment requests must be sent from the licensee on their letterhead and signed by a practice administrator or "responsible person" such as the RSO.

Amending an Existing RAM License to add Synovetin OA™

Minimally, each amendment request must include:

1. Existing radioactive materials license number
2. Physical address of veterinary facility and name of contact person (RSO or practice administrator)
3. Type of radioactive material to be added (tin-117m)
4. Description and purpose of use (canine osteoarthritis). Proposed wording for Synovetin OA® license amendment:
   "We are applying for an amendment for the use of tin-117m (specifically the device Synovetin OA®) to treat osteoarthritis in canine elbows. We request a possession limit of 6 millicuries (mCi) maximum per procedure and 100 millicuries (mCi) total. The treatment will be provided on an outpatient basis."
5. Training plan for staff members, both AUs and any others who will be working with RAM
6. Description of the hot lab and where the RAM will be used
7. Description of the radiation safety program (release criteria)
8. Description of the radioactive waste management program

F.X. Massé Associates has been contracted to help initiate the RAM license amendment process. Contact us at http://www.fxmasse.com/; info@fxmasse.com; or 978-283-4888.

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Device Label: Description of Purpose and Use

Each licensee should carefully review the "Synovetin OA® Device Label" (see supplemental reading material) for important information about the product:

- Device name
- Chemical form
- Product description
- Mechanism of action
- Intended use
- Maximum individual dosage
- Warnings and precautions
- Directions and preparations for use
- Adverse reactions
- Aftercare and owner instructions
- Storage instructions

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License Conditions

- Licensees are required to safely receive and store radioactive materials in a secure location, typically using "two delay methods." This requirement can be satisfied by storing material 1) in a locked container 2) inside of a small locked room called a hot lab.
- Licensees are required to maintain areas where unsealed radioactive material is used to the specific licensed exposure rate and contamination limits. Quantification of contamination and exposure will be covered in future modules, but those measurements are typically taken with a handheld GM (Geiger-Müller) ratemeter.
- Licensees are required to maintain staff occupational radiation doses "as low as reasonably achievable" (ALARA). This can be managed by providing dosimetry (passive radiation detectors) to staff members who handle radioactive material to validate that their occupational doses do not exceed regulatory limits.
- All staff members who handle radioactive material must be provided annual radiation safety training.

License Conditions (continued)

- Licensees are required to maintain their public radiation exposure as low as reasonably achievable (ALARA) by limiting the quantity of radioactive materials injected, providing specific instructions to the pet owners, and interviewing the owners to insure they can comply with the instructions.

  The dose limit is 100 mrem/y, which is equivalent to 10 chest x-rays or 100 days of natural background radiation in the US.
- Licensees are required to safely manage their radioactive waste, typically using a "decay in storage" (DIS) method where radioactive material is set aside for a specific amount of time, then disposed of as normal waste once its radiation level is no longer distinguishable from background radiation.
- Licensees are required to maintain radiation protection program records, develop spill procedures, and annually audit the program—called the Radiation Safety Officer Audit.
- Future modules will address each condition in greater detail.

Licensee Facility Inspections

- The NRC and each Agreement State's regulators are obligated to inspect every RAM licensee. The duration between inspections varies from state to state based on the scope and type of license and the inspectors' workload.
- What to expect during a radiation control program inspection:
  - RAM licensees are subject to unannounced inspections by their state's radiation control program (typically a three-year rotation depending on previous inspection results).
  - Inspectors tour the facility, focusing on licensed areas of radioactive materials use. They typically bring their own radiation detectors and survey common use areas such as the hot lab.
  - Inspectors review license conditions and the associated records proving compliance, such as dosimetry records, patient release records, RAM receipt records, RAM disposal records, etc.

RAM License Violations

- Violations are broken down into five categories and five severity levels (I to V):
  a. Health Physics
  b. Transportation
  c. Materials Operations
  d. Miscellaneous Matters
  e. Emergency Preparedness

  Severity Levels I and II are the most severe and involve actual or high potential for impact to the public. Severity Level V reflects minor safety or environmental concerns.

  With the use of tin-117m, the primary concern is compliance with public exposure limits. This is managed through education of pet owners to provide release instructions that they must follow.
- If items of non-compliance are discovered during a facility inspection, the licensee may face:
  - Immediate suspension of license
  - Denial, modification, limitation, revocation of, or refusal to renew their license
  - Other actions that just make life hard

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RAM License Violations (continued)

- Notice of Violation
  - This is a formal notification of a violation to the applicant, licensee, or registrant. It includes the specific violation, the provision of regulation relied upon, and a reasonable period of time for correction.
  - Within 10 days of receipt of the notice of violation, a clearly delineated plan of correction must be sent back to the state or federal regulatory body.
  - The plan of action and a reasonable period of time for correction is followed by a reinspection to close the loop on the corrective actions taken.
- Administrative Hearings
  - If the license was revoked, the licensee has the procedural right to an administrative hearing.
- Civil Penalties
  - If the licensee waives the administrative hearing process, the regulatory body can impose civil penalties.

See 10 CFR Part 35 or applicable State Regulation for more information

Conclusion

- The use of radioactive material is very heavily regulated by either the Nuclear Regulatory Commission or an Agreement State, depending upon facility location.
- RAM licensees are required to designate a Radiation Safety Officer and one or more Authorized Users.
- RAM licensees must comply with the conditions listed on their license, which provide an outline for safe use of radioactive material.
- Regulators are obligated to inspect every RAM licensee to determine whether license conditions are being met.
- Although rare, violations can include civil penalties and suspension or revocation of the RAM license.

Supplemental Reading Material

Supplemental reading material for Module 1:

1. Synovetin OA® Device Label
2. NUREG 1556 Volume 7
3. NRC Reg Guide 10.8

Upon successful completion of the Module 1 quiz, you may continue to Module 2.

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