EXUBRION™
THERAPEUTICS

Authorized User/Radiation Safety Officer Training for Synovetin OA®

Module 9: Practical Use of Synovetin OA®

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Introduction

- This module begins with a review of basic radiation safety regulations and practices.
- It then focuses specifically on the use of Synovetin OA® (^{117m}Sn):
  - Pet owner interview
  - Ordering
  - Receiving
  - Measuring
  - Disposal
  - Patient release
- Assigned reading:
  - Synovetin OA® Device Label
  - Pet Owner Interview Checklist
  - Synovetin OA® Order Form
  - Package Receipt Template
  - Dose Calibrator Instructions (Capintec)
  - Dose Calibrator Instructions (Atomlab)
  - Pet Owner Precautions and Release Instructions
  - Ludlum 26-1 DOSE Specifications Sheet
  - Waste Policy
  - Daily Closeout Survey Template
  - Weekly Wipe Test Report Template

EXUBRION THERAPEUTICS

Outline

- Radioactive Materials License
- Properties of ^{117m}Sn
- Synovetin OA® Specifics:
  - Owner Interview
  - Ordering and Receiving
  - Dose Preparation, Measurement, Calibration, Safe Handling
  - Waste Disposal
  - Pet Owner Precautions / Release Instructions
  - Release Measurement
  - Organic Waste
- Daily Closeout Surveys and Weekly Wipe Tests
- Radiation Safety Reminders
- Quiz

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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
- 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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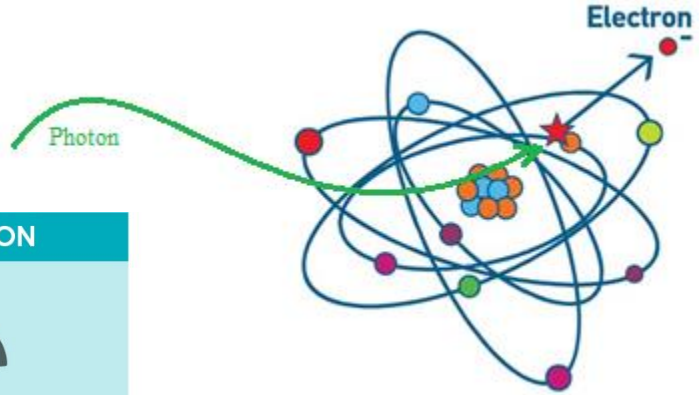
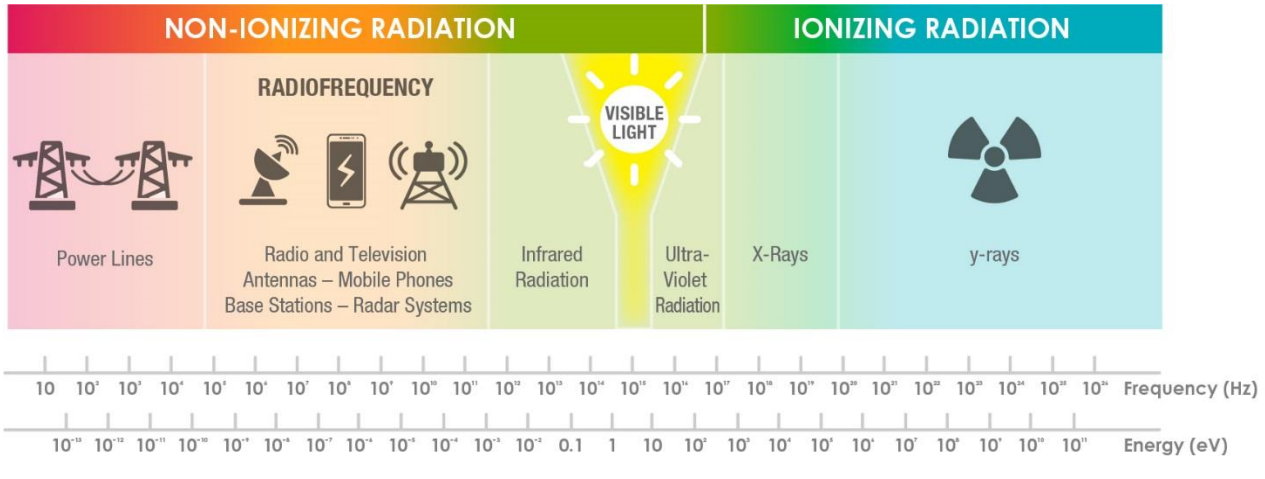
Radiation and Radioactivity

- Radiation is simply the emission and transfer of energy through space and material.
  - Radiation can take the form of kinetic energy of a particle or electromagnetic waves.
  - Radiation can be ionizing or non-ionizing.
- Ionizing radiation has enough energy to separate an electron from an atom.
- Non-ionizing radiation lacks the energy per basic unit to separate electrons from atoms.
- Radioactivity is a physical substance which emits radiation.
- Synovetin OA® contains radioactive tin-117metastable (^{117m}Sn) and has the physical form of a colloid in ammonium salt.





For more information, see Module 2.

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Radiation Units of Measurement: A Review

Radioactivity Quantity Units	
Becquerel (Bq)	Curies (Ci)
SI unit	Customary unit
Decays per second (dps)	3.7 x 10^{10} Bq

Units Describing Radiation Field		
Roentgen (R)	Radiation Absorbed Dose (rad)	Roentgen Equivalent Man (rem)
Photon ionization in air (exposure)	Amount of energy deposited in unit mass of medium	Biological effect of energy deposited by radiation in system
2.58E-4 C/kg	SI unit: Gray (Gy) = 100 rad Gray = J/kg	SI Unit: Sievert (Sv) = 100 rem Sv = Rad*QF

Mathematical Notations: Prefixes		
giga	G	10^{9}
mega	M	10^{6}
kilo	k	10^{3}
milli	m	10^{-3}
micro	μ	10^{-6}
nano	n	10^{-9}

Where:

C = Coulombs
J = Joules
QF = Quality Factor

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How To Use Various Units of Measurement: A Review

Units Describing Radiation Field		
Exposure	Contamination	Occupational Dose
Roentgen (R)	dpm/mCi/Bq	Roentgen Equivalent Man (rem)

- Use Roentgen (R) when describing an exposure in air or mR/h for exposure rate in air.
  - "Exposure" measures how much radiation is present in air.
  - Measured with an ion chamber or a GM ratemeter.
  - Used for daily surveys or release measurements.
- Use dpm when describing how much radioactivity or contamination is present.
  - Dpm is "disintegrations per minute." 1 mCi = 2.22E6 dpm; 1 Bq = 1/60 dpm
  - Use a GM ratemeter to quantify contamination on a wipe sample (See Module 7 for more details).
  - Dpm = cpm/eff; where cpm is the counts per minute on the GM ratemeter and eff is the efficiency for the isotope in question.
- Use rem or Sievert (Sv) when describing the "occupational dose," or biological effect to the human body as a system.
  - These units are used to communicate risk in terms of cancer induction probability.
  - Note, the US still recognizes the rem (1 Sv = 100 rem).
  - This is the unit you will see on your dosimetry or occupational badge report.

***These units are not interchangeable.**

For more information, see Modules 2 and 4.

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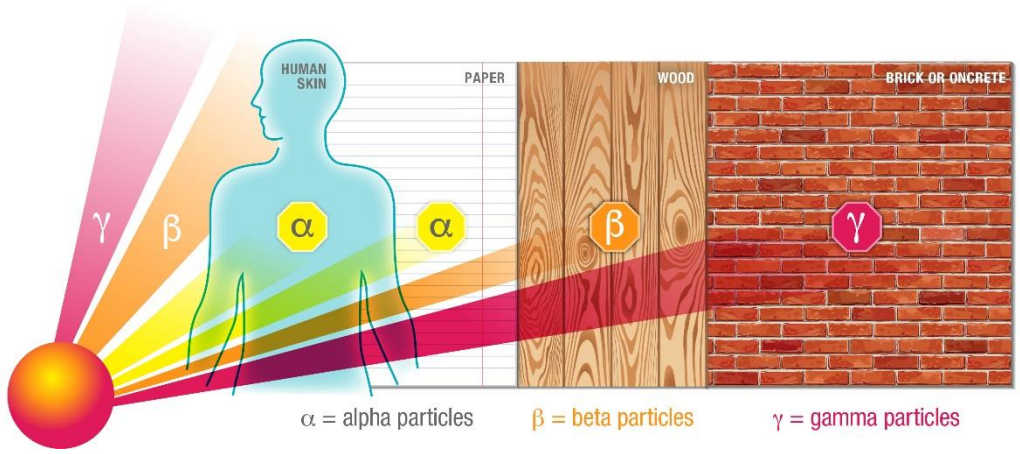
Properties of ^{117m}Sn

- ^{117m}Sn emits monoenergetic conversion electrons and gamma radiation. Once injected, these low-energy conversion electrons are absorbed in the joint and stimulate a response that reduces inflammation.
- The conversion electron is an alternative decay method competing with gamma decay. Some of the gamma rays released from the ^{117m}Sn nuclei hit the orbital electrons of the tin nucleus and eject electrons out of their orbits to become the released conversion electrons.



The conversion electrons have a maximal range in tissue of about 300 µm. The gamma photons escape the injected joint at a low rate and will decay over time.

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Properties of ^{117m}Sn *(continued)*

- The half-life of ^{117m}Sn is 14 days. This means that 3 mCi of ^{117m}Sn becomes 1.5 mCi after 14 days and 0.75 mCi after 14 more days.
- ^{117m}Sn decays by emitting internal conversion electrons and gamma rays.
  - Conversion electrons have discrete energies ranging from 127 keV to 158 keV, with a total yield of about 114%.
  - Emitted gamma rays contain three energies: 156 keV, 158.6 keV, and 314.3 keV. Of the three, 158.6 keV is the most abundant with an 86.4% yield. It can be used for diagnostic imaging and verification of an injection site.
    - Note that "decay yield" or "abundance" is the fraction of that energy in total decay. A 158.6 keV gamma ray with 86.4% abundance means that 86.4% of the time, a photon of 158.6 keV is emitted, and the other 13.6% of the time, gammas of other energies are emitted.

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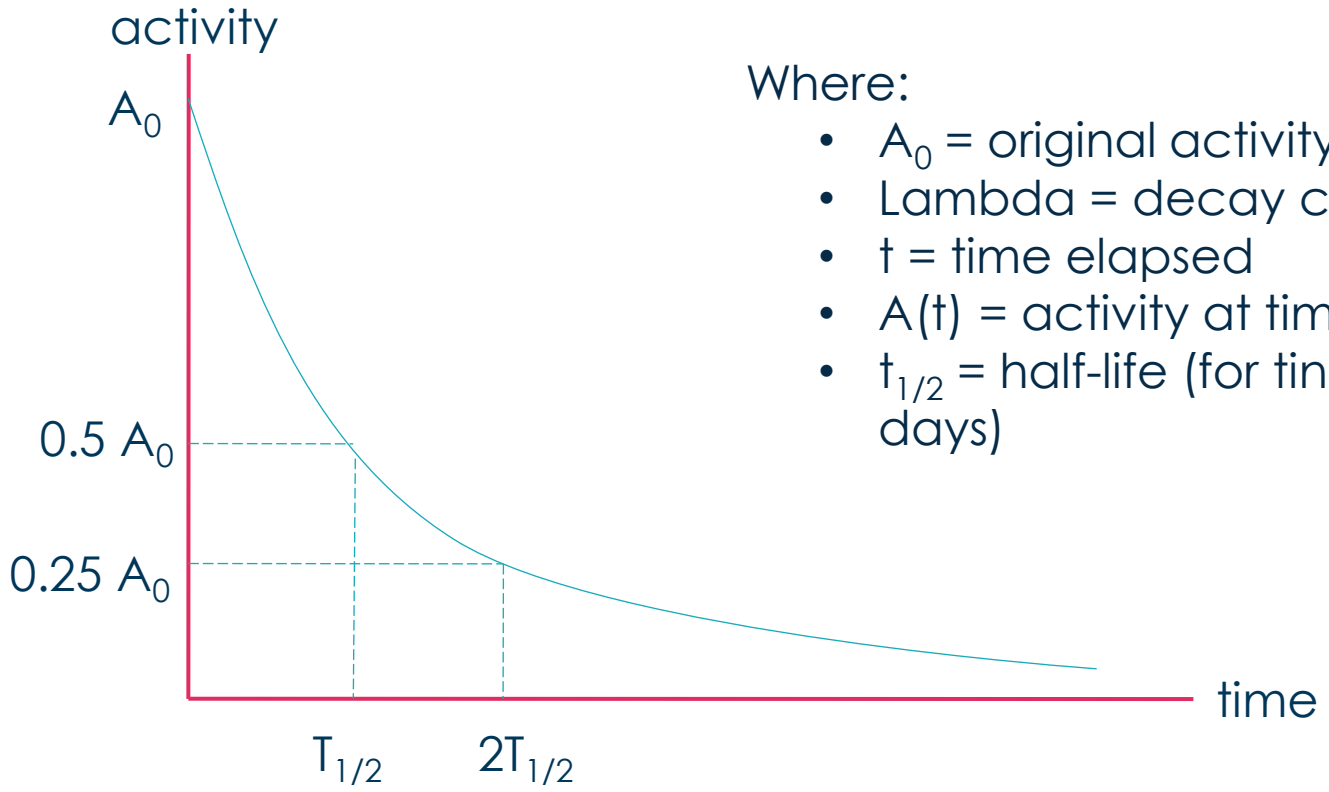
Radioactive Decay: Decay Equation

- The decay equation is plotted below:
  - At one half-life, the activity drops to half of the initial activity
  - At two half-lives, the activity drops to a quarter of the initial activity

$$A(t) = A_0 e^{-\lambda t}$$

$$\lambda = \frac{\ln 2}{t_{1/2}}$$



Where:

- A_0 = original activity
- Lambda = decay constant
- t = time elapsed
- A(t) = activity at time t
- $t_{1/2}$ = half-life (for tin, this is 14 days)

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Synovetin OA® Pre-Screening Questionnaire

- Synovetin OA® contains radioactive ^{117m}Sn. Because the material is radioactive, a pre-screening questionnaire must be conducted with the pet owner to verify that they (and their family) can meet certain time and distance restrictions to maintain their radiation dose below the federally mandated public dose limit of 100 mrem/year.
  - The Pre-Screening Questionnaire checklist is part of the supplemental reading materials.
- This questionnaire must be conducted **prior to the ordering of the radioactive material**.
- There are elements which may contraindicate the therapy, such as:
  - The owner cannot maintain a distance of 2 m from the pet while sleeping
  - There are pregnant individuals in the dwelling who cannot maintain a distance of 2 m from the pet for the duration of the precautionary period.
    - Just an overall note on children and pregnant women – the annual public dose of 100 mrem applies to adults, children, pregnant women, and developing babies alike. In the Radiation Safety world, we typically take a more conservative approach with adolescent and pregnant members of the public (handle with "kid gloves").
  - The owner routinely conducts other prolonged close contact activities with the pet that they cannot or will not alter for the precautionary time frame.

EXUBRION THERAPEUTICS

Synovetin OA® Pre-Screening Questionnaire *(continued)*

- The questionnaire starts with an open-ended question where the AU needs to capture any routine close-contact behaviors of the pet owner. This information will be used in conjunction with their answers to further questions to determine whether Synovetin OA® is an appropriate treatment for their pet.
- The next section contains yes/no questions to build a pattern of behaviors and test the willingness of the owner to alter those behaviors. If the owner is not willing or able to alter close-contact behaviors for the duration of the precautionary period, other treatment options should be suggested.
- The third section provides several concepts which need to be addressed with the owner, answering any questions they may have on the way. This section is an excellent opportunity to provide the sample Release Instructions page included as the last page of the Pre-Screening Questionnaire.
- Lastly, the AU and owner sign to acknowledge that all topics, questions, and concerns have been adequately discussed.

Synovetin OA® Pre-Screening Questionnaire *(continued)*

- Below the signature area of the interview checklist is a chart of sample time and distance restrictions that should be reviewed with the owner.
    - The chart provides a measured exposure rate (see Slide 21), but for context, the highest measured exposure rate will correlate with the largest dogs receiving the highest doses of Synovetin OA® and will decrease with dog size.
- The example Release Instructions page is dog/owner-specific. The Release Instructions duration can extend if the owner has routine prolonged close-contact activities or extended duration intermediate-contact activities (for the largest dogs only).
- The Pre-Screening Questionnaire enables the AU to make an informed decision as to whether the owner is sufficiently motivated to meet the public dose limits with their behavior (changing it if necessary) to make their pet an appropriate candidate for treatment with Synovetin OA®.

Synovetin OA® Pre-Screening Questionnaire *(continued)*

- Another document included in the Supplemental Materials is the Synovetin OA® Procedure for administration. The Procedure takes a step by step approach to the Pre-Screening Questionnaire and Release Instructions.
- One of the purposes of the Pre-Screening Questionnaire is to determine which category of behavior the owners of the treated dog fits into. The categories are in the below table.

Categories of Dog/Owner distance behaviors	Time @ <1 ft per day	Time @ 1 ft per day	Time @ 3 ft per day
Common Contact	5 min	15 min	4 h
Extended intermediate contact	5 min	15 min	12 h
Extended close contact	5 min	3 h	4 h
Prolong close and intermediate contact	5 min	11 h	9 h

- Mo
- When owners spend a lot of time at intermediate contact distances (such as a dog that sits at your feet if you work at home for 8-12h per day) they would fall into the extended intermediate contact category.
- Extended close contact would include sitting in the same chair or couch as the treated dog for three hours per day.
- Prolonged close and intermediate is a combination of the two and usually involves the situation when a dog sleeps in the owner's bed.
  - The category of the dog/owner interaction is used with the below chart to prescribe the number of weeks to accompany the release instructions.
  - The next slide provides greater detail for the Release Instructions durations.

EXUBRION THERAPEUTICS

Synovetin OA® Pre-Screening Questionnaire *(continued)*

Once all of the information is gathered to complete the Pre-Screening Questionnaire, the dog/owner behavior category can be selected. If the owner typically spends more time in very close or close proximity to their dog, the number of weeks of precautions will increase.

The number at the top of the chart called "measured exposure rate" will be discussed in more detail in the following slides.

Example: Suppose the dog/owner relationship yielded an extended duration intermediate contact category because the owner was retired, and the dog spent many hours a day in the same room as the owner. After treatment, the dog's measured exposure rate was 0.3 mR/h. This would mean that 2 weeks would be prescribed on the Release Instructions.

Categories of Dog/Owner Distance Behaviors	Release Instructions Duration (weeks)					
Measured Exposure Rate at Release (mR/h @ 1m) [a]	0.45	0.4	0.3	0.2	0.1	0.05
Common Contact Up to 5 min/day direct contact, 15 min/day @ 1 ft and 4 h/day @ 3 ft (e.g., feeding, grooming, petting, dog walking)	2	2	2	2	2	2
Extended Duration Intermediate Contact Up to 5 min/day direct contact, 15 min/day @ 1 ft and 12 h/day @ 3 ft (e.g., dog rests at the feet of the owner etc.)	2	2	2	2	2	2
Extended Duration Close Contact Up to 5 min/day direct contact, 3 h/day @ 1 ft and 4 h/day @ 3 ft (e.g., holding dog in lap or on the couch, extended grooming, etc.)	3	3	2	2	2	2
Prolonged Close and Intermediate Contact Up to 5 min/day direct contact (e.g., joint to torso), 11 h/day @ 1ft and 9 h/day @ 3 ft (e.g., dog sleeps in the owner's bed etc.)	6	5	4	3	2	2

Measured exposure rate post therapy (slide 21)

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Pet Owner Release Instructions

Owners may show some trepidation with radiation exposure. These equivalence statistics can be used as "talking points" when discussing radiation exposure risk with pet owners:

- The maximal expected owner dose with Synovetin OA® is ~80 mrem.
- We are all exposed to ~300 mrem of natural background radiation every year. This means that the maximal expected owner dose from Synovetin OA® is approximately equivalent to 97 days of natural background radiation exposure or 69 days on the Colorado plateau as described in the table below.
- There are places in the world where natural background radiation (NBR) can be substantially higher:

Location:	NBR dose per year	Synovetin OA® max own dose equivalence
Denver, CO	420 mrem/y	69 days of NBR to reach Synovetin OA® max owner dose
Guarapari, Brazil	3500 mrem/y	8.3 days of NBR to reach Synovetin OA® max owner dose
Ramsar, Iran	26,000 mrem/y	27 **HOURS** of NBR to reach Synovetin OA® max owner dose

EXUBRION THERAPEUTICS

Pet Owner Release Instructions *(continued)*

- The perceived risk from radiation exposure is disproportionate when compared to other common activities such as driving a car, riding a bicycle, flying in an airplane, or even walking down the street:
  - An average two-view chest x-ray has a radiation dose of 10 mrem.
  - An average head CT exam has a radiation dose of 200 mrem.
  - A roundtrip flight from New York to Seattle results in a radiation dose of ~5.6 mrem.
  - 100 bananas contains enough radioactive potassium-40 to result in 1 mrem of committed effective radiation dose.
  - Going through certain airport whole-body scanners results in a radiation dose of ~0.02 mrem.
- The relative risk of receiving 10 mrem of radiation dose is approximately equivalent to driving 40 miles in a car.

Use these radiation dose equivalences and relative risks to reduce any unnecessary anxiety that an owner may exhibit due to their disproportionate fear of radiation.

Ordering Synovetin OA®

- Synovetin OA ® should be ordered **after** completing the pet owner interview checklist and determining that the owner will comply with all release instructions during the precautionary period.
- The order requires a two-week lead time and completion of the Synovetin OA ® order form (see supplemental reading materials).
- The order date is the date the order is submitted. The injection date should be no less than the order date plus two weeks.
- The weight of the dog should be the weight measured on the day of the owner interview.
- Select either one or two elbows to be injected. If two elbows will be treated, the total dose for both is delivered in one container, and the single elbow dose is volumetrically drawn according to the device label (see supplemental reading materials).
- The order should be faxed or emailed according to current order form instructions.

Dosages and Data:

Order Date: _____

Injection Date: _____

Weight of Dog: Select pounds

Dosage per elbow: 0.0 mCi

Number of elbows injected: Select

Dog name: _____

Dog Weight (lbs.)	Synovetin OA™ Dose (mCi) / Elbow Joint
10 – 19 lbs.	0.6
20 - 29 lbs.	0.9
30 - 39 lbs.	1.2
40 - 49 lbs.	1.5
50 - 59 lbs.	1.7
60 - 69 lbs.	1.9
70 - 79 lbs.	2.2
80 - 89 lbs.	2.4
90 - 99 lbs.	2.6
100 - 109 lbs.	2.8
110 lbs. and over	3

Department of Transportation (DOT) Regulations

Synovetin OA® arrives as a DOT Class 7 Type A package. It will have markings as a White I package.

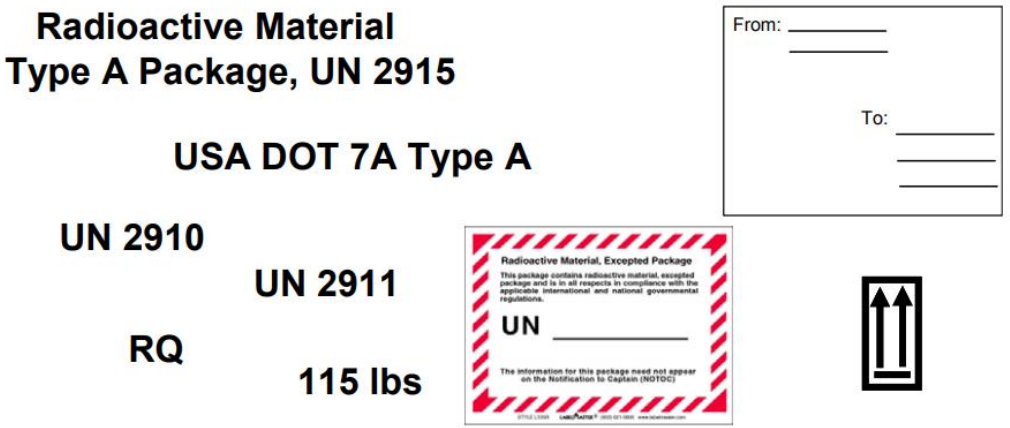

Figure-1. Examples of common radioactive package **markings**. These include proper shipping names, package types, UN numbers, and From/To addresses, orientation markers, and weights. For excepted packages, the candy-striped UN number sticker is optional; a simple sign stating the UN number can be used instead.

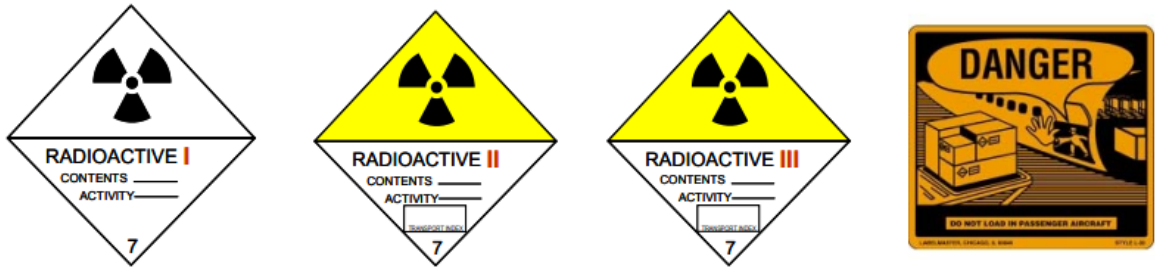

Figure-2. Examples of common radioactive package **labels.**

Specific DOT training is available through FX Massé Associates at www.fxmasse.com

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Receiving Synovetin OA ®

- After your order is submitted, the Class 7 package containing radioactive Synovetin OA® is shipped to the address listed on your radioactive materials license.
- The package must be checked in within 3 hours of receipt to meet DOT and license conditions.
- The package must be measured for exposure rate with your Ludlum 26-1 DOSE on the surface of the package and at a distance of 1 meter from the package.
- A wipe test must be taken of the outer container and the inner container.
    - All data should be captured in your package receipt documentation (see sample package receipt template in the supplemental reading material).
- If the contents are free of contamination and meet DOT exposure rate and transport index (TI) tables (see DOT training for more info), the unopened inner package must be stored in a secure location such as your hot lab.

EXUBRION THERAPEUTICS

Dose Prep and Measurement

- Synovetin OA® comes in a concentration of 1 mL of colloid suspension with 2–4 mCi of radioactivity. The precise quantity (volume) of product needed to treat the dog will be sent to the customer.
- The material comes in a glass vial with a septum for volumetric extraction.
- The glass vial is shipped in a lead pig. Leave the glass vial contained in the lead pig when drawing the appropriate volume from the bulk glass vial.
- Be sure to follow all device label directions.
- The table at right, taken from the Synovetin OA® device label (see supplemental reading material), shows that the delivered radioactivity varies by dog weight.

Dog Weight (lbs.)	Synovetin OA® Dose per Elbow Joint (mCi)*
10–19	0.6
20–29	0.9
30–39	1.2
40–49	1.5
50–59	1.7
60–69	1.9
70–79	2.2
80–89	2.4
90–99	2.6
100–109	2.8
110 and over	3.0

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Dose Calibration

- Each dose of Synovetin OA® comes pre-calibrated for volumetric extraction and injection without the need for a dose calibrator.
- For practices that choose to use a dose calibrator, Synovetin OA® can be measured in either the bulk glass vial for a total activity measurement or in the syringe after drawing the directed volume for a single joint measurement.
  - Note that in either case, the appropriate dose calibrator channel setting must be used. The glass vial will cause the dose calibrator to underestimate the activity present depending on which channel setting is used.
  - When measuring a plastic syringe after volumetric drawing, place the syringe centrally in the dose calibrator chamber, selecting the appropriate channel for ^{117m}Sn.
  - Measuring within a plastic syringe will overestimate the actual activity.
  - Contact Exubrion Therapeutics for specific dose calibrator channel settings for common makes and models. Exubrion will provide the channel settings for both the bulk glass vial and a routine volume plastic syringe.

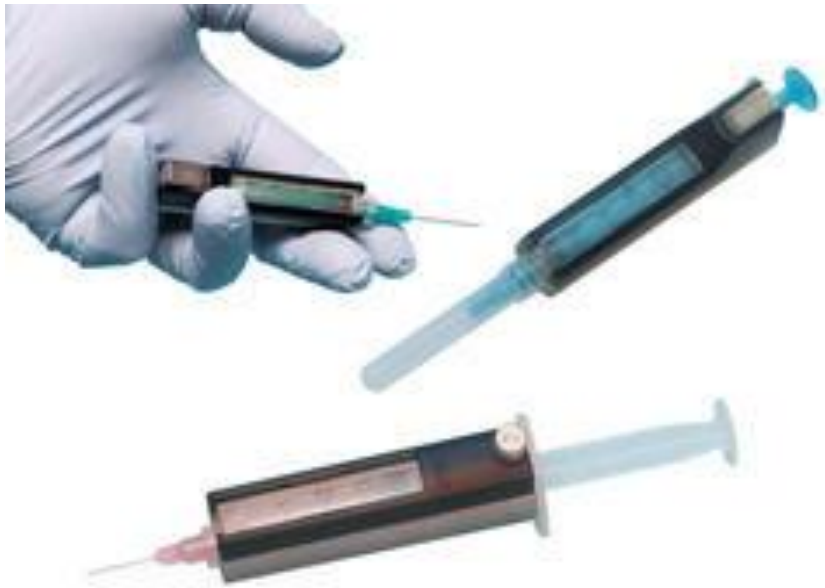
Handling

- Always use basic radiation safety principles when handling radioactivity.
- When handling unit dose syringes for prolonged periods of time, it is best to use shielding techniques such as a syringe shield.
  - If routine handling is sporadic and the handling time is short, a syringe shield is not necessary.
  - If the syringe shield impedes the delivery or extends the handling time, the AU can opt to handle the dose directly.
- Doses are typically measured in the hot lab and carried to the surgical suite where the patient is waiting.
  - Doses should be carried to the delivery location in a shielded container lined with absorbent material.
  - The shielded carrier should also be used to carry the spent syringe and contaminated tubing back to the hot lab for decay in storage.

EXUBRION THERAPEUTICS

Syringe Shield and Shielded Carrier Examples

Shielded Carrier Examples:
https://www.alimed.com/shielded-syringe-carriers.html



Syringe Shield Examples:
https://m.biodex.com/nuclear-medicine/products/syringe-vial-shields

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Post-Injection Dose Calibration

For practices with a dose calibrator, the spent syringe and contaminated tubing can be measured post-injection for residual activity to fully calculate the delivered activity:

(Initial Activity) – (Residual Activity) = Delivered Activity

Example: 2 mCi – 0.1 mCi = 1.9 mCi

RAM License Conditions: Waste Disposal

- Because most license conditions dictate that only a certain amount of radioactive material may be at a physical location at any point in time, an inventory must be kept of all radioactivity, including radioactive waste.
- When radioactive waste is disposed of, that disposal must be accounted for in the inventory and documented in a "waste log."
- Solid waste:
  - Long-lived—must be transferred for disposal.
  - Short-lived—can "decay in storage" and then be disposed of as regular waste.
    - Tin-117m (Synovetin OA®) has a half-life of 2 weeks and is categorized as "short-lived. " Therefore, all ^{117m}Sn can be disposed of as regular waste after 10 half-lives (140 days).
    - Short-lived solid waste can be further categorized as "sharps" and "non-sharps."
- Liquid waste:
  - Mixed liquid wastes must be transferred for disposal ($$$$).
  - Sink disposal is not allowed for liquid Synovetin OA®.
  - Refer to your RAM license for approved disposal methods. The supplemental reading material from Module 8 includes a Waste Policy template.

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Solid Waste: Decay in Storage

- Solid radioactive waste must be allowed to "decay in storage"—held until its radioactivity is not distinguishable from background radiation levels. The industry standard is to wait 10 half-lives before disposal in a regular waste stream.
- Typically a facility will have at least two solid radioactive waste containers—one to fill while the other is decaying.
- After filling a solid radioactive waste container, it is closed, dated, and left to decay.
- After the decay period is over, the waste is removed and surveyed to be sure that no radiation is detectable from the outside of the container. The survey is documented in the waste log, and the waste can be disposed of in the regular waste stream.
- The half-life of ^{117m}Sn (Synovetin OA®) is 14 days. After filling a container with ^{117m}Sn waste, close the container, date it, wait 140 days, survey with a GM counter, document the survey, then dispose as regular waste.

Above is a standard waste container labeled for radioactive waste. The solid waste from ^{117m}Sn contains such a small amount of radioactivity that the container is not required to be shielded.

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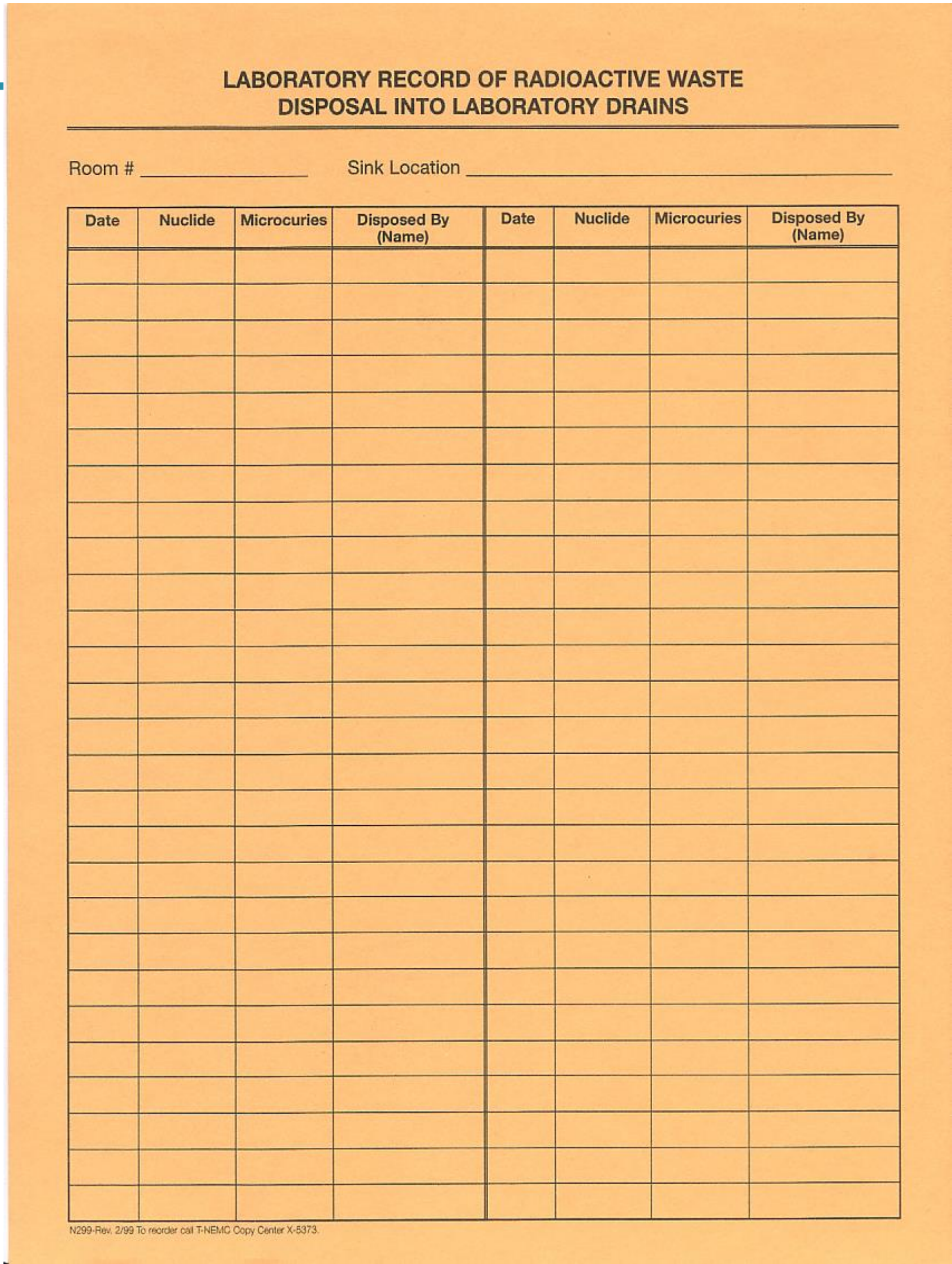
Liquid Waste: Sink Disposal

- Facilities must designate a “hot sink” for disposal of liquid radioactive waste.
- Liquid disposal activity, date, and nuclide must be documented on a disposal form or “sink log” to ensure compliance with disposal limits.
- Only water-soluble ***biologic*** radioactive solutions may be disposed of down the drain.
- Radioactive waste should never be disposed of without running the water in the sink to properly dilute/rinse the waste.
- Synovetin OA® (^{117m}Sn) does not come in a biologic aqueous form and can therefore **cannot** be disposed of in a hot sink.



LABORATORY RECORD OF RADIOACTIVE WASTE DISPOSAL INTO LABORATORY DRAINS

Room # ______________ Sink Location ______________________________

Date	Nuclide	Microcuries	Disposed By (Name)	Date	Nuclide	Microcuries	Disposed By (Name)

N299-Rev. 2/99 To reorder call T-NEMC Copy Center X-5373.

Pet Owner Release Instructions

- Once the patient has been treated with Synovetin OA® and the contaminated equipment used for injection stored for DIS in the hot lab, the Release Instructions must be reviewed with the patient's owner. (See supplemental reading materials for these instructions.)
- After this review, the exposure rate release measurement must be completed and documented. (See Module 7 for additional information.)
- The table below is from the Pre Screening Questionnaire and provides the basis for the duration of contact restrictions provided in the Release Instructions.

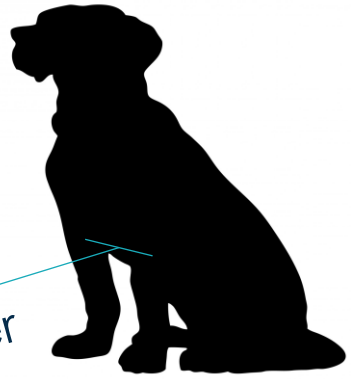
Categories of Dog/Owner Distance Behaviors

Measured Exposure Rate at Release (mR/h @ 1m) [a]	0.45	0.4	0.3	0.2	0.1	0.05
	Release Instructions Duration (weeks)					
Common Contact						
Up to 5 min/day direct contact, 15 min/day @ 1 ft and 4 h/day @ 3 ft (e.g., feeding, grooming, petting, dog walking)	**2**	**2**	**2**	**2**	**2**	**2**
Extended Duration Intermediate Contact						
Up to 5 min/day direct contact, 15 min/day @ 1 ft and 12 h/day @ 3 ft (e.g., dog rests at the feet of the owner etc.)	**2**	**2**	**2**	**2**	**2**	**2**
Extended Duration Close Contact						
Up to 5 min/day direct contact, 3 h/day @ 1 ft and 4 h/day @ 3 ft (e.g., holding dog in lap or on the couch, extended grooming, etc.)	**3**	**3**	**2**	**2**	**2**	**2**
Prolonged Close and Intermediate Contact						
Up to 5 min/day direct contact (e.g., joint to torso), 11 h/day @ 1ft and 9 h/day @ 3 ft (e.g., dog sleeps in the owner's bed etc.)	**6**	**5**	**4**	**3**	**2**	**2**

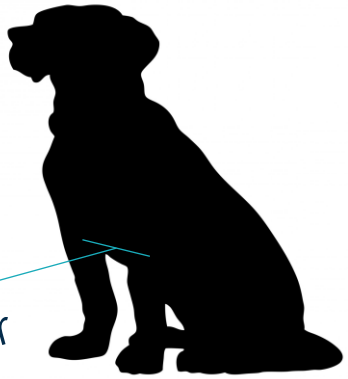
Synovetin OA® Release Measurement

- An exposure rate measurement must be made from the treated animal prior to release.
- The measurement can be completed with either an ion chamber or a GM ratemeter.
  - The preferred method is to use a Ludlum 26-1 DOSE GM ratemeter with dose-flattening filter.
- The measurement is taken 1 meter from the treatment site as seen in the diagram below:

Ludlum Model 9DP ion chamber: Positioned with the center of the chamber 1m from the elbows. Note, center of the chamber is indicated with circular indentation on the sides of the chamber.



Ludlum Model 26-1 DOSE GM rate meter with dose flattening filter: Positioned with the center of the chamber 1m from the elbows.



EXUBRION THERAPEUTICS

Pet Owner Precautions and Release Instructions *(continued)*

Below is an excerpt from the Pet Owner Precautions and Release Instructions. The AU must fill out the dog's name, treatment date, total dose administered, and release exposure rate (see next slide) and review each item thoroughly with the owner. The precautions are designed to be conservative and avoid any unnecessary radiation dose to the public, as well as minimize the potential for a radiation detector to sound an unwanted alarm, such as at airports or border crossings.

- ✓ Remember to maintain your exposure as low as reasonably achievable (ALARA).
- ✓ Do not sleep with the dog or hold the dog in or near your lap.
- ✓ Each member of the household should avoid direct contact with the treated joint(s) as much as possible. Daily direct contact should be limited to **<1** minute. **Direct** activities are those that are <1ft from the dog's treated elbow to the owner's torso (e.g., carrying the dog where the elbow is in contact or lap sitting where the elbow is directly on the torso).
- ✓ Each member of the household should limit close contact to **15** minutes and should limit intermediate contact to **4** hours. Activities such as walking or playing with your dog can continue with distance limitations maintained. **Close** activities are at 1ft (e.g., feeding, grooming, sleeping, and routine lap-sitting) and **Intermediate** activities are at 3ft (e.g., walking, jogging, and officing).
- ✓ Minimize the time that children and pregnant women spend in close contact with the dog.
- ✓ Avoid long term/daily boarding or commercial grooming of your dog for two weeks or traveling with it by air or across any international borders or very large, organized events (professional sporting events, parades, etc.). Provide a copy of this document should any questions arise.
- ✓ Minimize use of public transportation and staying in public accommodations (e.g., hotels). Transport your dog in its carrier and/or as far from passengers as is reasonable and safe for the dog.
- ✓ Follow up care is recommended where your dog received this treatment. If your dog needs emergency care, please inform the provider about its treatment with radiotherapy, and to contact (*insert contact information here*) with any questions.

Individualized behavior modifications from Pre-Screening Questionnaire:

_____

_____

_____

Remember to include the individualized behavior modifications indicated by the owner on the Pre-Screening Questionnaire

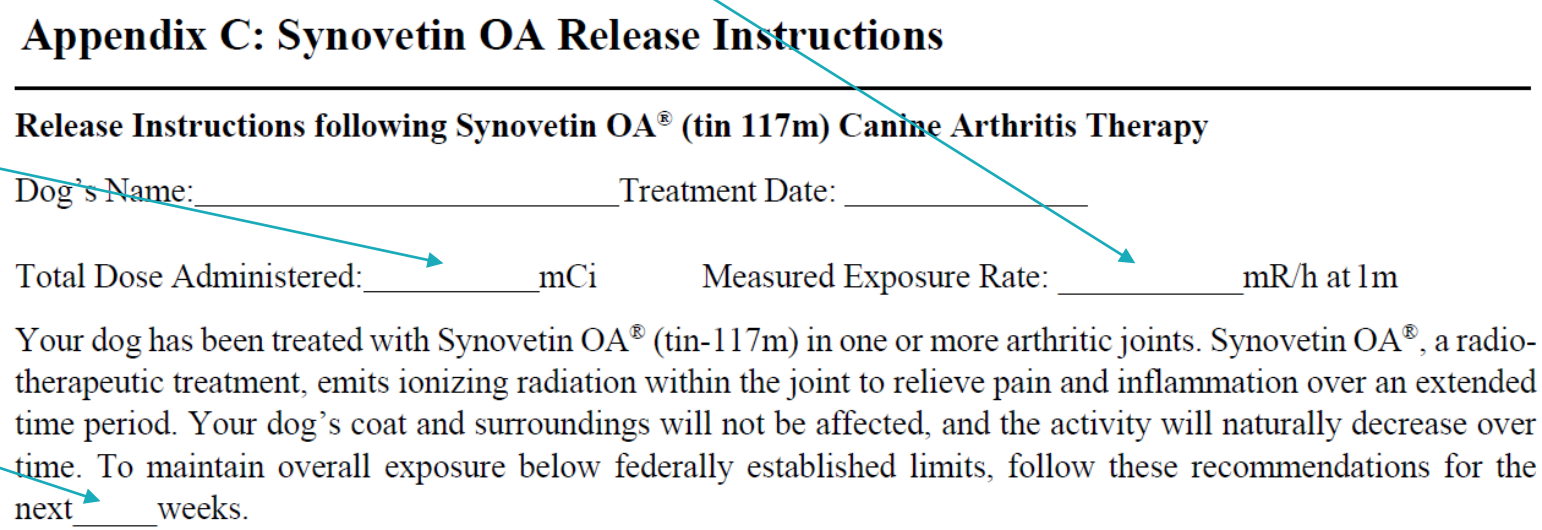
EXUBRION THERAPEUTICS

Synovetin OA® Release Measurement Completion

- The release measurement is captured on the Release Instructions document at the top right corner of the first page. A copy of the signed page is retained by the licensee, and a copy is provided to the owner.
- This measurement is a regulatory requirement and must be documented properly. The maximum exposure rate allowed is 0.45 mR/h upon release.

Administered dose is entered here.

The duration of the instructions is entered here. This duration is the outcome of the release measurement and the dog/owner behaviors discovered in the Pre-Screening Questionnaire



Appendix C: Synovetin OA Release Instructions

Release Instructions following Synovetin OA® (tin 117m) Canine Arthritis Therapy

Dog's Name:_____Treatment Date: _____

Total Dose Administered:_____mCi Measured Exposure Rate: _____mR/h at 1m

Your dog has been treated with Synovetin OA® (tin-117m) in one or more arthritic joints. Synovetin OA®, a radio-therapeutic treatment, emits ionizing radiation within the joint to relieve pain and inflammation over an extended time period. Your dog's coat and surroundings will not be affected, and the activity will naturally decrease over time. To maintain overall exposure below federally established limits, follow these recommendations for the next_____weeks.

EXUBRION THERAPEUTICS

Organic Waste

- There is always a possibility that an animal treated with ^{117m}Sn could die from unrelated causes during the precautionary period post-treatment.
- If this were to occur, the animal must be returned to the licensee for decay in storage (DIS). The licensee would need to designate a freezer for DIS for the remainder of the decay period.
- After the decay period (total of 10 half-lives), the animal may be disposed of routinely.
  - Alternatively, the carcass can be measured with a calibrated GM counter. If the measurement is "not distinguishable from background" the carcass may be treated as regular waste.
- Note that the Synovetin OA® Owner Precautions document (see supplemental reading materials) instructs owners to bring their deceased animal back to the licensee for DIS if needed.

EXUBRION THERAPEUTICS

Daily Closeout Surveys and Weekly Wipe Tests

- Each RAM licensee is required to conduct **daily closeout surveys** of any area where unsealed radioactivity was handled or used. These surveys can be completed with an ion chamber or the Ludlum 26-1 DOSE GM ratemeter. If using the Ludlum 26-1, the unit is to be used in "exposure rate" mode (mR/h). The typical license limits are shown below, and a template report form is included in the supplemental reading materials.

Typical Exposure Rate Limits	
Controlled Area	5 mR/h
Uncontrolled Area	0.2 mR/h

- Each RAM licensee is required to perform **weekly wipe tests** for removable contamination. These are completed with filter paper on a known area of use typically the size of a postcard. Wipe samples are measured for ^{117m}Sn contamination, and the surveys are documented weekly. (See supplemental reading materials and Module 7 for more detail about GM efficiencies.)

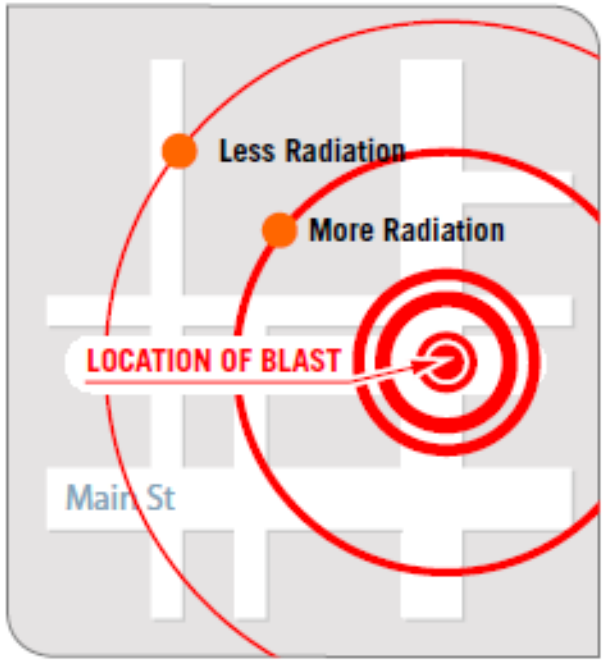
Typical Removable Contamination Limits for ^{117m}Sn	
Controlled Area	10,000 dpm/100cm^2
Uncontrolled Area	1000 dpm/100cm^2

EXUBRION THERAPEUTICS

External Radiation Exposure Reduction

There are three ways to minimize radiation dose: time, distance and shielding.

Time: Minimizing time spent exposed will also reduce your risk.



Distance: The farther away you are from the radiation the lower your exposure.

Shielding: If you have a thick shield between yourself and the radioactive materials more of the radiation will be absorbed by the thick shield, and you will be exposed to less.

EXUBRION THERAPEUTICS

As Low As Reasonably Achievable (ALARA)

- ALARA is the principle of maintaining exposure to ionizing radiation as far below the dose limits as practical, taking into account:
  - The state of technology
  - The economics of improvements in relation to the state of technology
  - The economics of improvements in relation to benefits to the public health and safety
  - Other societal and socioeconomic considerations in relation to utilization of nuclear energy and licensed materials in the public interest
- To comply, no person should conduct any operation that generates unnecessary radiation exposure

EXUBRION THERAPEUTICS

Summary of Module 9: Practical Use of Synovetin OA®

- From receipt to injection to disposal, Synovetin OA® must be used in a safe manner that meets all radioactive materials license commitments, as well as state and federal regulations.

- Exubrion Therapeutics™ has a library of FAQs available to address questions that may arise regarding the use of Synovetin OA®. Visit www.Synovetin.com to learn more.

EXUBRION THERAPEUTICS

Supplemental Reading Material

Assigned reading material for Module 9:

- Synovetin OA® Device Label
- Pre-Screening Questionnaire
- Synovetin OA® Order Form
- Package Receipt Template
- Dose Calibrator Instructions (Capintec)
- Dose Calibrator Instructions (Atomlab™)
- Release Instructions
- Synovetin OA® Procedure for Use
- Ludlum 26-1 DOSE Specifications Sheet
- Waste Policy
- Daily Closeout Survey Template
- Weekly Wipe Test Report Template

EXUBRION THERAPEUTICS