EXUBRION™
THERAPEUTICS

Authorized User/Radiation Safety Officer Training for Synovetin OA®

Module 7: Radiation Surveys and Statistics

Chad A. Smith, PhD, CHP
F.X. Massé Associates, Inc.
www.fxmasse.com
info@fxmasse.com
978-283-4888

Introduction

- This module focuses on the practical aspects of regulations regarding:
  - Radioactive contamination
  - Surveys for radiation
  - Shipping and receiving of radioactive materials
- It also covers information regarding the use of Synovetin OA® (^{117m}Sn):
  - Pet owner interview
  - Pet owner precautions
  - Model release method for animals treated with ^{117m}Sn
- Assigned reading:
  - NRC Regulatory Guide 8.2: Administrative Practices in Radiation Surveys and Monitoring
  - NRC Regulatory Guide 8.39: Release of Patients Administered Radioactive Materials
  - Minimum Detectable Activity (MDA) and Contamination Assessment
  - Pet Owner Interview Checklist
  - Pet Owner Precautions

Outline

- Radiation Units of Measurement: A Review
- Monitoring for Contamination
  - Weekly wipe test surveys
  - Daily closeout surveys
- Department of Transportation (DOT) Regulations
- Specific Instructions for Synovetin OA®
  - Pet owner interview
  - Pet owner precautions
  - Release measurement techniques
- Quiz

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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.

Contamination

Contamination is simply unwanted radioactive materials.

- There are two categories of radioactive contamination:
  - Fixed
  - Removable
- Your radioactive materials (RAM) license sets two limits for removable contamination in the areas where you use unsealed radioactivity such as ^{117m}Sn:
  1. For a "controlled area" such as your hot lab, where access is restricted
  2. For an "uncontrolled area" such as your OR, where more people have access
- Wipe tests (see Slide 8) are taken per unit area. Here we use 100cm^2, which is about the size of a postcard.

Typical Removable Contamination Limits for ^{117m}Sn	
Controlled Area	10,000 dpm/100cm^2
Uncontrolled Area	1,000 dpm/100cm^2

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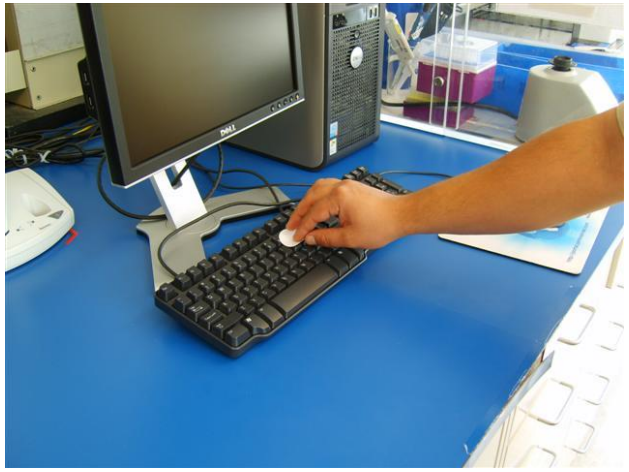
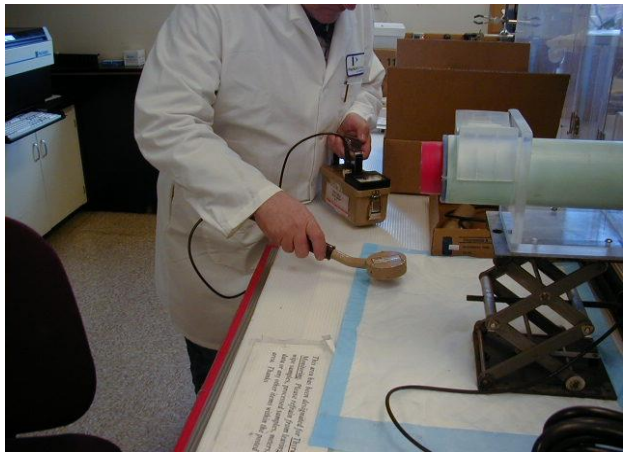
Monitoring for Contamination

- **Wipe Survey**
  - Checks for removable contamination
  - Wipe tests are required weekly for all areas of unsealed use
- **Direct Instrument Survey**
  - Checks for contamination on a surface
  - Convenient to use
  - Easily detects gross contamination
  - Uses different radiation probes connected to a survey instrument
  - Use an in-calibration instrument
  - Direct surveys are required daily in areas of unsealed use





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Minimum Detectable Activity and Wipe Tests

- The instrument used to monitor for contamination must be able to detect below the removable contamination limits.
  - Conservatively, the Ludlum Geiger counters recommended (26-1 Dose) can detect as low as 400 dpm/100cm^2. This is known as the **minimum detectable activity (MDA)**.
  - The calculation and basis for this is included in the supplemental reading material.
- A wipe test is taken with a plain 1-inch round filter paper, such as the Whatman® No. 1 product.
- The used filter paper is then placed on a clean lead brick with the contaminated side up for scanning.
- See next slide for more complete wipe test instructions.

Wipe Test Procedure

- Wipe an area of 100cm^2 (about the size of a postcard).
- Place the wipe on a clean lead brick with the "dirty" side up.
- Take a background reading with your GM counter in cpm (typically 100–200cpm) on the 0.1X multiplier setting.
- Place the GM ratemeter directly over the wipe.
- Allow the unit to settle and take a gross reading/measurement.
- (Gross reading – background)/efficiency = quantity of removable contamination.

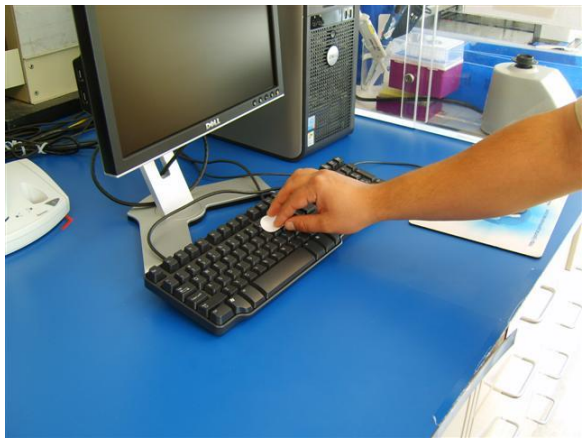
  Example:

  Gross reading = 500 cpm

  Background = 200 cpm

  Efficiency = 20% or 0.2

  (500cpm – 200cpm)/0.2 = 1500 dpm of removable contamination
- Record the result on the wipe test survey report (see next slide).



Sample Wipe Test Report

- A weekly entry is required whether or not radioactive materials were used.
- Use a gamma well or GM counter to assess if contamination is present.
- If contamination is found (>1000 dpm/100cm²):
  - Clean area
  - Re-wipe and retest
  - Record actions in comments section of report

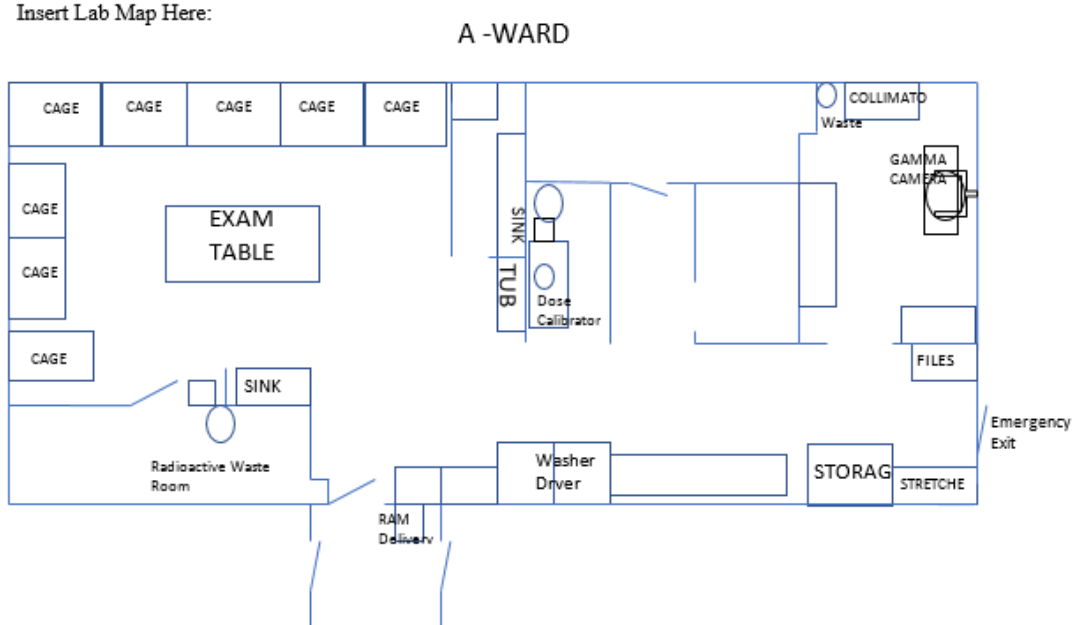
WEEKLY WIPE REPORT

DEPARTMENT: Canine Ward	LOCATION: Animal Medical Center
INSTRUMENT: Ludlum 26-1 Dose	SERIAL NUMBER: 12345

* Unless otherwise specified, measurements made with GM survey meter with results in dpm/100 cm^2.
✓ = background reading (<200 dpm/100 cm^2)
Note that Action level is 1000 dpm/100 cm^2 for an uncontrolled area and 10,000 dpm/100 cm^2 for controlled areas. Efficiency for a Ludlum 26-1 or Ludlum 44-9 is 20% for ^{117m}Sn.

Date	1	2	3	4	5	6	7	8	9	10	11	12	Survey By
4/15	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	CAS
4/16	✓	✓	✓	500	600	✓	✓	✓	✓	✓	✓	✓	CAS

Insert Lab Map Here:



Daily Closeout Surveys

- Daily closeout surveys are conducted in areas of use where you're looking for:
  - Sources or waste not appropriately shielded
  - Contaminated areas
  - Any other radiation or source of radioactivity which shouldn't be exposed
- Daily closeouts can be completed with an ion chamber or a GM ratemeter.
  - The preferred equipment for Synovetin OA® is the Ludlum 26-1 DOSE.
  - The unit should be used with the dose-flattening filter for daily closeouts and release measurements.
  - It should be used without the filter for contamination assessment.

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

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Daily Closeout Surveys *(continued)*

- Daily closeout surveys are completed with a GM ratemeter.
- Take a background reading with your GM counter in mR/h (typically 0.02–0.05 mR/h).
- Slowly move your GM probe over the surfaces which must be surveyed (areas where you used unsealed RAM).
  - You will hear the audible "clicks" using the audio function.
- (Gross rate – background rate) = net exposure rate

  Example:

  Gross reading = 0.5 mR/h

  Background = 0.05mR/h

  Net rate = 0.5 mR/h – 0.05 mR/h = 0.45 mR/h

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Sample Daily Closeout Report

- Survey is required:
  - Only in areas where RAM were used
  - Only on days when RAM were used
- If contamination is found (>0.2 mR/h):
  - Record reading
  - Clean area
  - Resurvey
  - Record action in comments section.

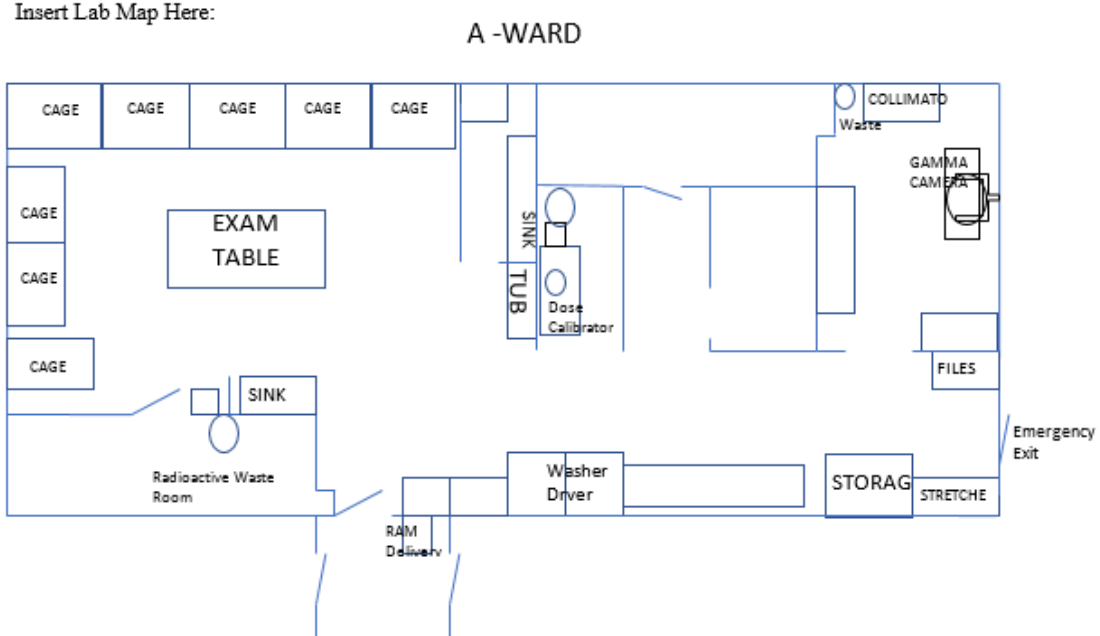
DAILY CLOSEOUT REPORT

DEPARTMENT: Canine Ward	LOCATION: Animal Medical Center
INSTRUMENT: Ludlum 26-1 Dose	SERIAL NUMBER: 12345

* Unless otherwise specified, measurements made with GM survey meter with results in mR/h.
✓ = background reading 0.02 mR/h
Note that Action level is 0.2 mR/h for an uncontrolled area and 5 mR/h for controlled areas. Daily closeout surveys are only required on days of use.

Date	1	2	3	4	5	6	7	8	9	10	11	12	Survey By
4/15	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	CAS
4/16	✓	✓	✓	0.5	0.6	✓	✓	✓	✓	✓	✓	✓	CAS

Insert Lab Map Here:



Department of Transportation (DOT) Regulations

- The Department of Transportation has regulations surrounding the shipment and receipt of radioactive materials:
  - Each package containing radioactive material will be delivered to the **secure delivery location** listed on your RAM license.
    - This is typically a lockable cabinet which can house a large box.
  - The package must be **checked in within 3 hours of receipt** and **logged on the RAM inventory** for the site.
    - A sample package check-in template is included in the supplemental reading materials.
  - The package must be **measured for exposure rate** 1 m from each side and on the surface of the exterior package.
  - A **wipe test** must be taken of the exterior and interior packaging.
  - Records must be kept for each package containing radioactive material.

DOT Regulations *(continued)*

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

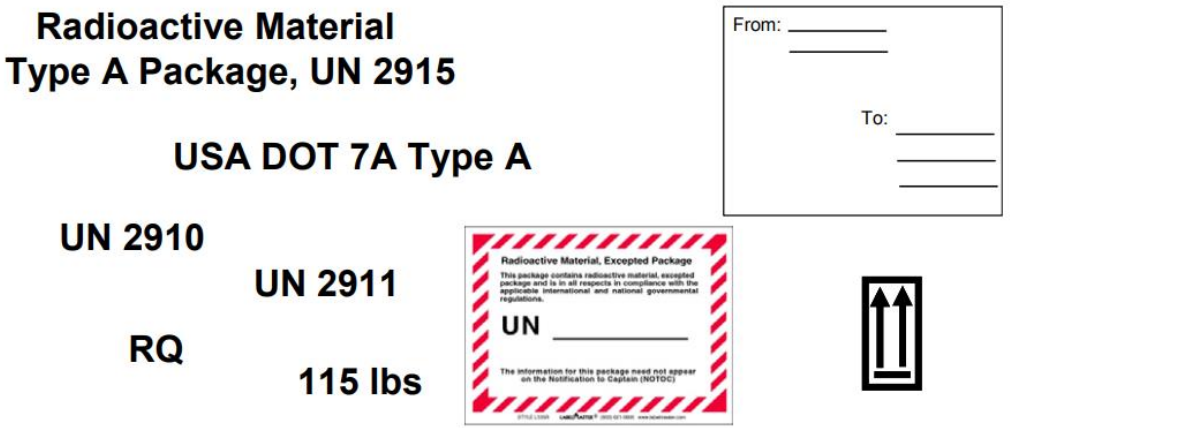


Figure-1. Examples of common radioactive package **markings**. These include proper shipping names, package types, UN numbers, and From/To addresses, orientation markers, and weights. For excepted packages, the candy-striped UN number sticker is optional; a simple sign stating the UN number can be used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

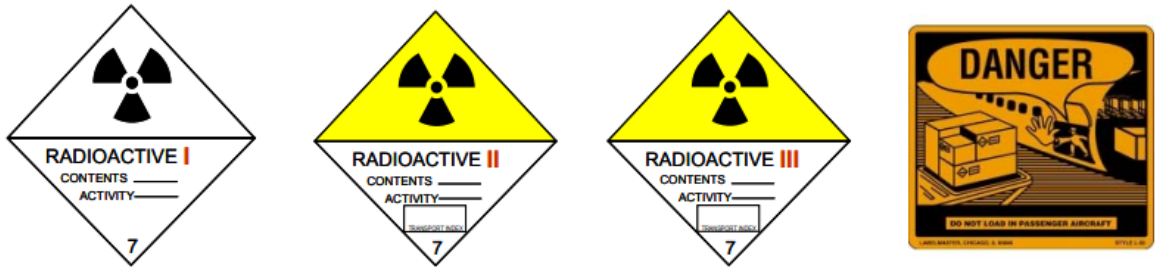


Figure-2. Examples of common radioactive package **labels.**

Specific DOT training is available through the FX Masse / Exubrion Training Course portal entitled "HazMat / DOT Training" This training course is not mandatory to send a license application or license amendment. However, most state regulatory agencies will require an individual associated with the RAM license to maintain DOT certification to oversee shipment and receipt of radioactivity.

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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.

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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
Most common	1 min	15 min	4 h
Extended intermediate contact	1 min	15 min	12 h
Extended close contact	1 min	3 h	4 h
Prolong close and intermediate contact	1 min	11 h	9 h

- Most owners and dogs will fit into the "Most common" category.
- 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.
- 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.

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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 1 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 1 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 1 min/day direct contact, 3 hr/day @ 1 ft and 4 h/day @ 3 ft e.g., holding dog in lap or on the couch, extended grooming, etc.	5	5	3	2	2	2
Prolonged Close and Intermediate Contact						
Up to 1 min/day direct contact, 11 h/day @ 1ft and 9 h/day @ 3 ft e.g., dog sleeps in the owner's bed etc.	9	8	7	5	3	2

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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

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Pet Owner Release Instructions *(continued)*

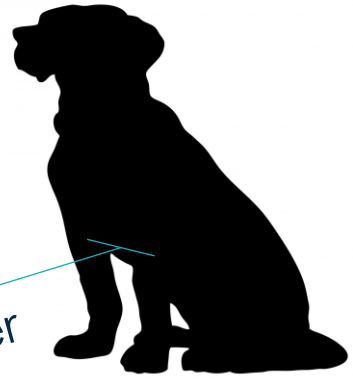
- The perceived risk from radiation exposure is disproportionate when compared to other common activities such as driving a car, riding a bicycle, flying in an airplane, or even walking down the street:
  - An average two-view chest x-ray has a radiation dose of 10 mrem.
  - An average head CT exam has 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.

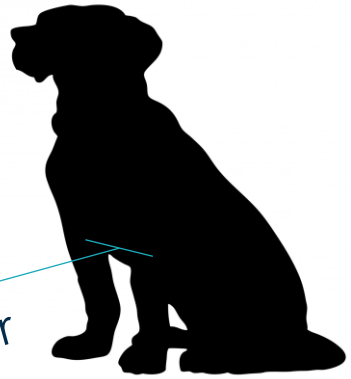
Synovetin OA® Release Measurement

- 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.



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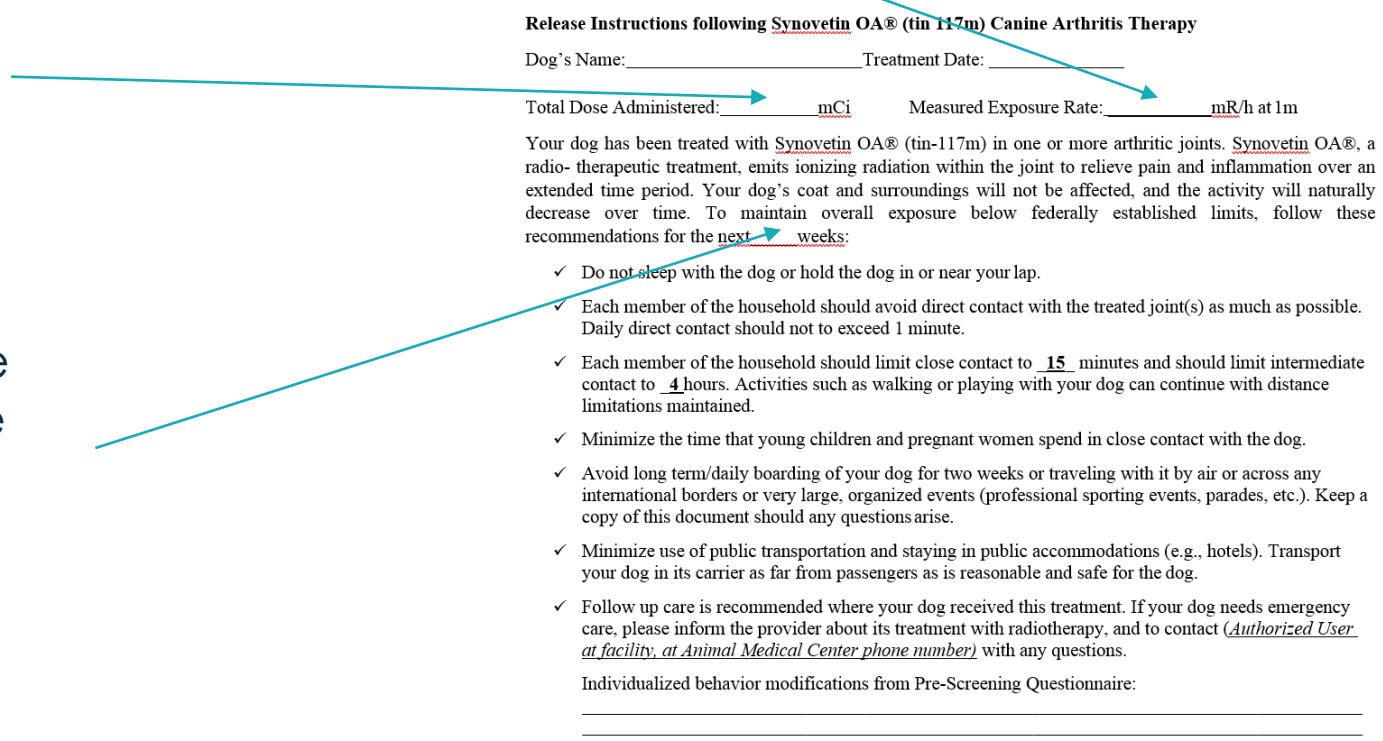
Synovetin OA® Release Measurement Completion

- 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 Interview



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:

- ✓ 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 not to exceed 1 minute.
- ✓ 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.
- ✓ Minimize the time that young children and pregnant women spend in close contact with the dog.
- ✓ Avoid long term/daily boarding 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.). Keep 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 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 (*Authorized User at facility, at Animal Medical Center phone number)* with any questions.

Individualized behavior modifications from Pre-Screening Questionnaire:

_____

_____

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Summary of Module 7: Radiation Surveys and Statistics

- RAM licensees are required to conduct weekly wipe test surveys with filter paper to assess removable contamination. This can be completed with a GM ratemeter and Ludlum model 26-1 DOSE unit.
- RAM licensees are also required to conduct daily closeout surveys with a GM ratemeter or ionization chamber to comply with license exposure limits.
- Each received package containing radioactive materials must be checked in following DOT and license requirements. This is typically completed with an exposure rate measurement at one meter, on the surface of the package, and a wipe test to quantify removable radioactivity. The receipt must be logged and added to the site inventory.
- Owners of pets to potentially be treated with Synovetin OA® must be interviewed to verify that their home life is conducive to complying with the time and distance requirements to meet federal public radiation dose limits.
- The veterinarian must review the Pet Owner Precautions sheet to instruct the owner on the time and distance requirements which follow Synovetin OA® therapy.
- Release measurements must not exceed 0.45 mR/h 1m from the treated elbow(s).
  - The treated animal cannot be released until the release measurement is equal or less than 0.45 mR/h

Supplemental Reading Material

Assigned reading material for Module 7:

- NRC Regulatory Guide 8.2: Administrative Practices in Radiation Surveys and Monitoring
- NRC Regulatory Guide 8.39: Release of Patients Administered Radioactive Materials
- MDA and Contamination Assessment
- Pre-Screening Questionnaire
- Release Instructions
- Synovetin OA® Procedure

Upon successful completion of the Module 7 quiz, you may continue to Module 8.

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