NRC Form 313 Supplement

1. **Application**

   This is a request for an amendment of License No [*Licensee insert licensee*]

2. **Address**

   [*Licensee insert address*]

3. **Use Location**

   [*Licensee insert use location*]

4. **Contact Information**

   [*Licensee insert contact information*]

5. **Radioactive Material**

   a. Radionuclide: Tin-117m
   b. Chemical/Physical Form: Colloidal suspension
   c. Maximum Amount: 100 mCi [*Licensee modify maximum activity to suit projected workload*]

6. **Purposes for which radioactive material will be used**

   Treatment of osteoarthritis in canine elbows with Synovetin OA™. A maximum of 3 mCi per elbow (6 mCi per dog) will be used. No more than one treatment per household may be performed in a one year period.

7. **Individuals Responsible for Radiation Safety Program and their training and experience**

   [*Licensee insert name of RSO and user(s) authorized for therapeutic use on current license.*]

8. **Training**

   All personnel involved with the administration of Synovetin OA will have initial and annual refresher training including radiation safety and relevant emergency procedures. Employees preparing the administration will be users authorized on the license or appropriately trained staff members.

   Training will include the safe handling of radioactive materials in accordance with NUREG 1556 Volume 7 Appendix F. Initial training will specifically address the radiological characteristics of Sn-117m, the safe use of Synovetin OA, the patient/owner screening process

and criteria, the corresponding patient release instructions, and the reporting requirements and potential consequences if public is exceeded.

An outline of the Synovetin OA-specific training to be provided is contained in Attachment A.

9. Facilities and Equipment

- Synovetin OA is provided in patient-specific doses based on the manufacturer's weight-based protocols. The current manufacturer package insert and SDS are provided in Attachment B. The treatment will be provided on an outpatient basis although provisions will be in place to kennel dogs if necessary.

- Release exposure rates will be measured with either a calibrated pressurized ionization chamber (Ludlum 9DP or equivalent) or a calibrated Geiger-Mueller (GM) counter with energy flattening filter (Ludlum Model 44-9 with Ludlum ambient dose equivalent filter, part # 2002-1050, attached or equivalent).

- Sn-117m has a similar energy to that of Tc-99m with the addition of conversion and Auger electrons. A traditional pancake GM tube (Ludlum 44-9 or similar) will have a minimum detectable activity of <2000dpm/100cm^2. This allows the facility to complete contamination analysis without the need of a liquid scintillation counter or gamma well multi-channel analyzer.

- Radioactive Materials are secured from unauthorized removal by keeping the storage area locked at all times. [*Licensee describe area if not the same as currently used for other radioactive material.*]

- Synovetin OA is designed to be injected at any location where the patient can be appropriately stabilized. [*Licensee describe area(s) where Sn-117m will be used, including where dogs will be kenneled if necessary.*]

- Surveys will be conducted and documented post administration if the chosen injection location is outside of the currently licensed controlled areas.

10. Radiation Safety Program

a. Facility and Staff Radiation Safety

- Our existing Radiation Safety Program and Radioactive Spill Procedures will be followed [*Licensee reference procedure if needed*]. Personnel involved in the administration will wear appropriate PPE. A radioactive spill kit will available in the event of a radioactive spill.

- The existing Area Survey Procedures will be followed [*Licensee reference procedure if needed*].

- The existing personnel monitoring program will be followed [*Licensee reference procedure if needed*].

- Patient excreta monitoring is not applicable. Synovetin OA stays in the injected joint at a published rate of greater than 99.1%.[1]

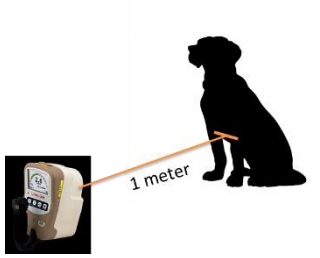
- Routine bioassay of personnel is not necessary as Synovetin OA is in an aqueous, non-volatile, colloidal solution.

- All injections will be performed by an authorized user or under the supervision of the authorized user. All personnel involved in these procedures will be appropriately trained by an authorized user and/or the radiation safety officer.

b. Public Radiation Safety

- Robust screening will be conducted to determine if the patient owner behavior pattern is suitable for the therapy. Release instructions will be provided to the owner during the screening interview to ensure the instructions can be met. Patient specific release instructions are again provided the day of the treatment and signed by the dog owner to ensure that radiation doses do not exceed federally established public dose limits.

- Dogs will be surveyed prior to release. Surveys will be taken at a distance of 1 meter from the closest treated elbow in the anterior and lateral directions at the height of the dog's elbow. A maximum exposure rate in excess of 0.45 mR/h at a distance of 1 m from the injection site will preclude the immediate release of the patient. Exposure rates will be measured with either a calibrated pressurized ionization chamber or calibrated Geiger-Mueller (GM) counter with energy flattening filter. In the case where the measured exposure rate is less than 0.45 mR/h, the animal will be released to the owner after instructions have been provided.



- The procedure for performing Synovetin OA injections is contained in Attachment C.

- Release of the animals on an outpatient basis will meet local and federal public dose limitations according to NUREG 1556 Volume 7 Appendix K and the appropriate State regulations. Extensive studies have been completed demonstrating compliance with the public dose restrictions with additional layers of conservatism. The technical basis for the release criteria is contained in Attachment D.

[1] Lattimer J, et al, *Intrarticular injection of Tin-117m radisynoviorthesis agent in normal canine elbows causes no adverse effects*, Vet Radiol Ultrasound 2019; 60:567-574.

11. Waste Management

Radioactive waste will be stored in the currently listed waste room inside appropriate containers. Existing procedures for Decay-In-Storage will be followed. Separate containers will be used for Sn-177m due to the different half-life.

The radioactive waste may be held to decay-in-storage for 10 half lives or until the contact exposure rates are indistinguishable from background radiation. Once the waste contact exposure rate is no longer distinguishable from background, the solid waste will follow the typical waste stream. Background exposure rate will be determined in a non-radiation area.

12. Fees

Not applicable to license amendment.

Attachment A
Synovetin OA Training Outline

Synovetin OA Training Outline:

- Synovetin OA Practical Use and Radiation Safety
    - Radioactive Materials License
    - Authorized Users
    - Radiation Safety Officer
- Synovetin OA technical aspects
- Owner Interview and Basic Owner Precautions / Release Instructions
- Animal release regulatory requirements and consequences of public dose exceedance
- Ordering, Shipping, and Receiving
- Dose Measurement
- Syringe shield use
- Leaded carrier use
- Option to measure residual from tubing/syringe
- Decay in Storage and Sanitary Sewer
- Owner Precautions / Release Instructions
- Release Measurement
- Organic Waste
- Compliance Surveys

Attachment B
Synovetin OA Package Insert
and SDS

SAFETY DATA SHEET

Sn-117m Colloid

FILE NO.:SDS Ser002
SDS DATE: 10/25/2019

SECTION 1: IDENTIFICATION

PRODUCT NAME: Sn-117m Colloid
SYNONYMS: Synovetin OA™
PRODUCT CODES: N/A

MANUFACTURER: Theragenics Corporation
DIVISION:
ADDRESS: 5203 Bristol Industrial Way, Buford, GA 30518
EMERGENCY PHONE: 770-831-4333
CHEMTREC PHONE:
OTHER CALLS:
FAX PHONE:

CHEMICAL NAME: Hydrated tin(IV) oxide, Sn-117m enriched
CHEMICAL FAMILY:
CHEMICAL FORMULA: $Sn_XO_Y(OH)_Z$

PRODUCT USE: Veterinary Medical Device
PREPARED BY: Theragenics Corporation

SECTION 1 NOTES:

SECTION 2: HAZARD(S) IDENTIFICATION

EMERGENCY OVERVIEW: RADIOACTIVE MATERIAL. Promptly remove any contamination from the skin, eyes, or clothing. Radioactive drugs must be handled by qualified personnel in conformity with regulations appropriate to the government agency authorized to license the use of this radionuclide. The vial containing the drug should be kept within its container or within heavier shielding. Avoid contact with the radioactive contents which would cause unnecessary exposure to radiation.

ROUTES OF ENTRY:

POTENTIAL HEALTH EFFECTS

EYES: no data available, but some irritation is possible

SKIN: no data available, but some irritation is possible

INGESTION: no data available, though GI injury due to radiation is possible

INHALATION: no data available. In the unlikely event that the substance is inhaled, damage to airways due to radiation is possible

ACUTE HEALTH HAZARDS: no data available. Low levels of exposure are not expected to result in acute health effects.

CHRONIC HEALTH HAZARDS: The health risks associated with chronic radiation exposure (cancer, leukemia, genetic and teratogenic effects) are believed to involve levels of radiation exposure which are much higher than those permitted occupationally.

MEDICAL CONDITIONS GENERALLY AGGRAVATED BY EXPOSURE: no data available

CARCINOGENICITY

OSHA: **ACGIH:** **NTP:** **IARC:**
OTHER:

SECTION 2 NOTES:

SECTION 3: COMPOSITION/INFORMATION ON INGREDIENTS

INGREDIENT:

CAS NO.	% WT	% VOL	SARA 313 REPORTABLE
7732-18-5 (Water)	92-94		No
7790-47-8 (SnI_4)	0.4-0.8		No
57-13-6 (Urea)	2.5-3.0		No
7647-01-0 (HCl)	3.3-3.8		No
	ppm	mg/m3	

OSHA PEL-TWA: no data available
OSHA PEL STEL : no data available
OSHA PEL CEILING: no data available

ACGIH TLV-TWA: no data available
ACGIH TLV STEL: no data available
ACGIH TLV CEILING: no data available

SECTION 3 NOTES:
Urea and SnI_4 are consumed in the process. The product mixture contains hydrated tin(IV) oxide (13472-47-4), Sn-117m enriched and various ammonium salts (chloride, iodide, and bicarbonate).

SECTION 4: FIRST AID MEASURES

EYES: If a splash occurs, wash eyes with water for at least 15 minutes or until no more radioactivity can be removed. Notify radiation safety personnel.

SKIN: If skin contact occurs, wash the affected area thoroughly with soap and water until no more radioactivity can be removed. Always blot dry. Do not abrade skin. Notify radiation safety personnel.

INGESTION: Notify radiation safety personnel immediately. The amount ofSn-117m ingested should be assessed and documented. Consult a physician for proper therapy.

INHALATION: Notify radiation safety personnel immediately. The amount of material inhaled should be assessed and documented.

NOTES TO PHYSICIANS OR FIRST AID PROVIDERS: Wear proper protective equipment to avoid contact with the product.

SECTION 4 NOTES:

SECTION 5: FIRE-FIGHTING MEASURES

FLAMMABLE LIMITS IN AIR, UPPER: not determined
(% BY VOLUME) LOWER: not determined

FLASH POINT: not determined. Not considered a fire or explosion hazard.
F:
C:
METHOD USED:

AUTOIGNITION TEMPERATURE: not determined
F:
C:

NFPA HAZARD CLASSIFICATION
HEALTH: FLAMMABILITY: REACTIVITY:
OTHER:

HMIS HAZARD CLASSIFICATION
HEALTH: FLAMMABILITY: REACTIVITY:
PROTECTION:

EXTINGUISHING MEDIA: Use any means suitable for extinguishing surrounding fire.

SECTION 5: FIRE-FIGHTING MEASURES (cont'd)

SPECIAL FIRE FIGHTING PROCEDURES: In the event of a fire, wear full protective clothing and NIOSH-approved self-contained breathing apparatus with full facepiece operated in the pressure demand or other positive pressure mode.

UNUSUAL FIRE AND EXPLOSION HAZARDS: Not considered a fire or explosion hazard.

HAZARDOUS DECOMPOSITION PRODUCTS: Sn-117m-containing particles

SECTION 5 NOTES:

SECTION 6: ACCIDENTAL RELEASE MEASURES

ACCIDENTAL RELEASE MEASURES: If the product is received in a leaking condition or any loss or release of the radioactive contents occurs, notify your Radiation Safety Department and Manufacturer. All cleanup operations should be performed according to the Standard Operating Procedures (SOPs) established for your facility and by the NRC or other applicable local, state or federal regulations.

SECTION 6 NOTES:

SECTION 7: HANDLING AND STORAGE

HANDLING AND STORAGE: Store at 15°C to 30°C. Handling time should be kept to a minimum and appropriate shielding should be used. Handling devices such as syringe shields and tongs should be used. Storage and disposal of product should be controlled in a manner which is in compliance with the appropriate regulations of the federal or state government agency authorized to license the use of this radionuclide (Sn-117m).

OTHER PRECAUTIONS:

SECTION 7 NOTES:

SECTION 8: EXPOSURE CONTROLS/PERSONAL PROTECTION

ENGINEERING CONTROLS: shields appropriate for low-energy gamma emissions

VENTILATION : Properly sealed containers are not expected to require any special ventilation.

RESPIRATORY PROTECTION: Not expected to require personal respirator usage.

EYE PROTECTION:safety glasses or goggles

SKIN PROTECTION: Disposable plastic, latex, or rubber gloves; labcoat.

OTHER PROTECTIVE CLOTHING OR EQUIPMENT:

WORK HYGIENIC PRACTICES: No smoking, eating, or drinking should be allowed in any area where radioactive materials are handled or stored. Dispose of radioactively contaminated clothing and PPE according to regulatory requirements.

EXPOSURE GUIDELINES: no data available

SECTION 8 NOTES:

SECTION 9: PHYSICAL AND CHEMICAL PROPERTIES

APPEARANCE: cream/yellow/pale orange suspension

ODOR: none

PHYSICAL STATE: solid/liquid suspension

pH AS SUPPLIED: 6.5-9.0
pH (Other):
BOILING POINT: not determined
F:
C:
MELTING POINT: not determined
F:
C:
FREEZING POINT: not determined
F:
C:
VAPOR PRESSURE (mmHg): not determined
@
F:
C:
VAPOR DENSITY (AIR = 1): not determined
@
F:
C:
SPECIFIC GRAVITY (H2O = 1): not determined
@
F:
C:
EVAPORATION RATE: not determined

BASIS (=1):

SOLUBILITY IN WATER: The solids are insoluble. The vehicle is aqueous (miscible with water.)

PERCENT SOLIDS BY WEIGHT: ~0.5

PERCENT VOLATILE: 0
BY WT/ BY VOL @
F:
C:
VOLATILE ORGANIC COMPOUNDS (VOC):

WITH WATER: 0 LBS/GAL
WITHOUT WATER: 0 LBS/GAL

MOLECULAR WEIGHT: N/A (polymeric)
VISCOSITY: not determined
@
F:
C:

SECTION 9 NOTES:

SECTION 10: STABILITY AND REACTIVITY

STABLE **UNSTABLE**

STABILITY: Stable under ordinary conditions of use and storage.

CONDITIONS TO AVOID (STABILITY):

INCOMPATIBILITY (MATERIAL TO AVOID): anything incompatible with water (alkali metals, etc.)

HAZARDOUS DECOMPOSITION OR BY-PRODUCTS: Sn-117m-containing particles, ammonia

HAZARDOUS POLYMERIZATION: N/A

CONDITIONS TO AVOID (POLYMERIZATION): N/A

SECTION 10 NOTES:

SECTION 11: TOXICOLOGICAL INFORMATION

TOXICOLOGICAL INFORMATION: It is widely accepted by the scientific community that exposure to sufficient quantities of ionizing radiation can potentially cause harmful biological effects which include cancer, leukemia, and genetic and teratogenic effects.

SECTION 11 NOTES:

SECTION 12: ECOLOGICAL INFORMATION

ECOLOGICAL INFORMATION: Because this product is intended for use by veterinary hospital or clinic patients, it is expected to be treated by standard wastewater treatment facilities with no adverse environmental impacts.

SECTION 12 NOTES:

SECTION 13: DISPOSAL CONSIDERATIONS

WASTE DISPOSAL METHOD: Sn-117m colloids are Radioactive Waste until the activity has decayed to non-detectable levels. Radioactive waste must be handled in accordance with procedures established by your Radiation Safety Officer, NRC and other applicable regulations.

RCRA HAZARD CLASS: unknown

SECTION 13 NOTES:

SECTION 14: TRANSPORT INFORMATION

U.S. DEPARTMENT OF TRANSPORTATION
PROPER SHIPPING NAME: Radioactive Material, Type A Package
HAZARD CLASS: 7
ID NUMBER: UN2915
PACKING GROUP:
LABEL STATEMENT:

WATER TRANSPORTATION
PROPER SHIPPING NAME:
HAZARD CLASS:
ID NUMBER:

SECTION 14: TRANSPORT INFORMATION (cont'd)

PACKING GROUP:
LABEL STATEMENTS:

AIR TRANSPORTATION
PROPER SHIPPING NAME: Radioactive Material, Type A Package
HAZARD CLASS: 7
ID NUMBER: UN2915
PACKING GROUP:
LABEL STATEMENTS:

OTHER AGENCIES:

SECTION 14 NOTES:

SECTION 15: REGULATORY INFORMATION

U.S. FEDERAL REGULATIONS
TSCA (TOXIC SUBSTANCE CONTROL ACT): not currently regulated

CERCLA (COMPREHENSIVE RESPONSE COMPENSATION, AND LIABILITY ACT): not currently regulated

SARA TITLE III (SUPERFUND AMENDMENTS AND REAUTHORIZATION ACT):

311/312 HAZARD CATEGORIES: acute/chronic

313 REPORTABLE INGREDIENTS: none

STATE REGULATIONS: not currently regulated

INTERNATIONAL REGULATIONS: not currently regulated

SECTION 15 NOTES:

SECTION 16: OTHER INFORMATION

OTHER INFORMATION:

PREPARATION INFORMATION:

DISCLAIMER: Employers should use this information only as a supplement to other information gathered by them, and make independent judgment of the suitability of this information to ensure proper use, and protect the health and safety of employees. This information is furnished without warranty, and any use of the product not in conformance with this Material Safety Data Sheet, or in combination with any other product or process, is the responsibility of the user.

Synovetin OA™

[Homogeneous Tin (^{117m}Sn) Colloid]
Veterinary Device for Use in Dogs

NAME: Synovetin OA™
Tin (^{117m}Sn) stannic colloid in ammonium salt. It is supplied as a 2–4 mCi (74–148 MBq)/mL suspension for intra-articular (IA) injection.

NET QUANTITY
Vials contain a prescribed dose up to 6.0 mCi (222 MBq) at the date and time to treat one dog.

1 mL of suspension contains 2–4 mCi (74–148 MBq) of tin (^{117m}Sn) stannic colloid in ammonium salt at the date and time of end use.

PRODUCT DESCRIPTION
Synovetin OA™ is a conversion electron therapeutic veterinary device comprising a colloidal, sterile suspension with a pH between 6.5 and 9.0 where at least 90% of the particles have a size between 1.5 µm and 20 µm (HORIBA light scatter instrument). The ^{117m}Sn emits monoenergetic conversion electrons (significant energies 127–158 keV; emission probability 113%) and imageable gamma radiation (159 keV, 86% abundant). Accompanying low-energy emissions are Auger electrons (<22 keV) and X-rays (<30 keV). The half-life of ^{117m}Sn is 14 days. ^{117m}Sn decays by isomeric transition to stable ^{117}Sn.
Excipients include ammonium carbonate ($(NH_4)_2CO_3$), ammonium chloride (NH_4Cl), ammonium iodide (NH_4I), and trace tin (Sn) salts.

MECHANISM OF ACTION

Synovetin OA™ is a veterinary device consisting of a homogeneous tin colloid which emits discrete (<300 µm) low-energy conversion electrons confined to the joint space. The colloid is composed of microparticles (1.5 µm to 20 µm) that are retained in the joint space of the dog. The particles are absorbed and retained by synoviocytes and macrophages in the synovium, resulting in apoptosis and reduction of inflammatory cells. Elimination of the pro-inflammatory cells reduces inflammation of the joint synovium, thereby reducing pain associated with synovitis. The data, including radiographic evidence, supports use in Grade 1, 2, and 3 osteoarthritis (OA) of the elbow joint.

CAUTION
Federal law restricts this device to sale by or on the order of a licensed veterinarian trained in the use of radioactive veterinary medical products.

Use of this product is restricted to facilities with a compatible Radioactive Materials (RAM) license.

INTENDED USE
Synovetin OA™ is intended to reduce synovitis and associated pain of canine elbow joints afflicted with osteoarthritis.

WARNINGS
Do not exceed 6.0 mCi (222 MBq) of radiation activity per dog per treatment. Not for use in humans. Keep this and all medications out of reach of children. Consult a physician in case of accidental injection or ingestion by humans.

PRECAUTIONS
Injection should be performed only by a licensed veterinarian skilled in the delivery of intra-articular (IA) injections who is located at a facility that has a RAM license.

Rigorous aseptic technique must be ensured during injection.

RECTIONS FOR USE
Use the chart below to determine the appropriate dose. Doses were determined using the elbow joint.

For example, a dog weighing 25 lbs. receives an IA dose of 0.9 mCi in each elbow to be treated.

Dog Weight (lbs.)	Synovetin OA™ Dose per Elbow Joint (mCi)*
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	3.0

***Dose will be limited to 3.0 mCi/elbow joint when weight exceeds 110 lbs., with the total body dose not exceeding 6.0 mCi (i.e., two elbow joints in 110-lb. or greater-sized dogs).**

PREPARATION FOR USE
Synovetin OA™ is provided in a 3 mL glass vial within a lead cylinder. Each vial is for use with a single dog.

The product should be stored in the cardboard shipping container until needed for use. The **prescribed dose** should be **administered on the date noted** on the certificate accompanying the Synovetin OA™; however, it can be administered the day before or after if circumstances require injection on a different day. Always use proper personal protection equipment and precautions for handling radioactive medical products, including nitrile gloves, splash shield, safety goggles, back-fastening gowns, head covers, booties, and surgical masks.

STEP 1: When ready to withdraw the dose into a syringe and prior to removing the shrink wrap around the lead cylinder, gently **shake the lead cylinder for approximately 10 seconds to ensure proper mixing** of the product.

STEP 2: Remove the shrink wrap from the lead cylinder and dispose of it appropriately.

STEP 3: Remove the lead cylinder lid, but do not remove the glass vial from the lead cylinder.

STEP 4: Remove the colored flip cap from the vial and retain for placement on the vial after the dose is withdrawn.

STEP 5: Attach a plastic syringe (3 mL or other appropriate volume) to a 22-ga. needle. Where practical, use a syringe shield to maintain operator radiation doses as low as reasonably achievable and to meet existing license conditions.

STEP 6: While holding the container at an approximate 45° angle, insert the needle through the septum.

STEP 7: **Draw the prescribed volume into the syringe** for an individual elbow. **Under no circumstances should the volume be modified.** Repeat immediately for the second elbow dose. If both elbows are to be treated, both doses will be contained in a single vial. If there are any questions or concerns, contact Exubrion Therapeutics™ Customer Service at 833-942-1247.

STEP 8: The dose should be resuspended by gently inverting the syringe if more than 10 minutes has elapsed since dose was drawn into the syringe.

STEP 9: Following use of Synovetin OA™, replace the colored flip cap on the vial, then place the lid on the lead container and secure the lid with tape. Mark the vial with a tentative disposal date 5 months from the present date. After 5 months, the vial should be measured with a handheld rate meter (GM detector) to verify that radioactivity has decayed. If the vial is less than or equivalent to background radiation, it can then be disposed of as regular trash. All waste disposals should be documented according to your radioactive materials license and federal or state regulations. Do not return the vial, any packaging components, or supplies to the manufacturer.

The shielded syringe or syringes and needles that are used for administration should be placed in shielded sharps containers for radionuclides of similar half-lives (two weeks) and disposed of according to local, state, and federal regulations.

ROUTE OF ADMINISTRATION

Intra-articular injection. The product must NOT be administered by any other route. Confirmation of needle placement is recommended, whether by anatomical landmarks, fluoroscope, C-arm, ultrasound, or radiography.

DIRECTIONS FOR ADMINISTRATION

Dogs should be appropriately anesthetized or sedated prior to administration. With the canine elbow positioned at 45 degrees of flexion, inject Synovetin OA™ through a 22-ga. needle into the joint. This can be done between the lateral condyle of the humerus and the triceps tendon, but other approaches to the joint can be used. Following injection, gently flex and extend the treated joint through a range of motion to disperse the colloid throughout the joint compartments.

FREQUENCY OF ADMINISTRATION

If needed, Synovetin OA™ can be readministered to a previously treated elbow at least 12 months after the last treatment.

DURATION OF EFFECT FROM ADMINISTRATION

Effectiveness has been shown to last up to 12 months following a single treatment of dogs with naturally occurring OA of the elbow.

MAXIMUM ANNUAL DOSE

Total radiation dose per joint should not exceed 3.0 mCi/joint, with the total body dose not exceeding 6.0 mCi (i.e., two elbow joints during a 12-month period).

ADVERSE REACTIONS

Dogs participating in clinical studies to evaluate safety and effectiveness (n=74 dogs, 97 elbow joints) exhibited no significant adverse reactions when administered Synovetin OA™. If adverse events are observed or suspected, please report them by calling Exubrion Therapeutics™ Customer Service at 833-942-1247.

POST-INJECTION CARE

Following administration of Synovetin OA™, the dog can recover with other post-operation animals in the general clinic population. Once the dog has fully recovered, it can be discharged to go home with the approval of the facility radiation safety officer or authorized user. All treatment site policies and license requirements should be observed.

FACILITY CONTAMINATION ASSESSMENT

Removable radioactive contamination is assessed by using filter paper to wipe a known area (typically 100 cm^2), then count the number of interactions on the filter paper using a radiation detector with a known efficiency for counting the specific isotope in question. Empirical data using a Ludlum model 3 rate meter and 44-9 GM probe show the efficiency for ^{117m}Sn detection to be approximately 20% under 2D geometry. With a background rate of 100 counts per minute (cpm), this radiation detection system has a minimum detectable activity (MDA) of approximately 400 disintegrations per minute (dpm). The standard regulatory threshold for removable contamination in an unrestricted area is 2000 dpm for similar isotopes. Therefore, a Ludlum rate meter and GM is an adequate instrument to use for compliance measurements of removable contamination.

Note, ^{117m}Sn has a similar gamma emission as the commonly used medical radioisotope ^{99m}Tc along with several low-energy conversion electron emissions which would only aid in the detection efficiency of contamination.

EXPOSURE RATE MEASUREMENTS

Radioactive materials licenses require daily closeout surveys of all areas where unsealed radioactive material was used. These surveys can be completed with any rate meter capable of detecting the type of radiation emitted by the radioactivity. Further, license conditions require that release exposure rate measurements be completed prior to releasing animals who have been administered radioactivity. Most license conditions require the measurement taken not exceed 0.45 mR/h at 1 meter from the treatment site. The exposure rate release measurement and daily closeout surveys can be completed with either a standard volume ion chamber such as the Ludlum 9DP or Victoreen 451P, a Ludlum Model 3 rate meter and energy compensated GM probe 44-38, or a Ludlum 26-1 DOSE with energy flattening cover. While the ion chamber is the gold standard for exposure rate measurements, the Ludlum model 26-1 DOSE is the most practical because it can satisfy both contamination and exposure rate measurements (with dose flattening cover).

OWNER INSTRUCTIONS FOR POST-TREATMENT CARE

When the level of radiation is determined to be below the established levels for release, the dog can be discharged. The dog will, however, retain a low level of radioactivity in the treated joint(s) for a short period of time. There is no requirement for rehabilitation or restraint of the dog, and it can resume its normal level of activity. Specific written instructions based on the post-treatment radiation dosimetry for care and proximity to the treated dog will be provided by the radiation safety officer (RSO) or authorized user (AU) of a radioactive materials (RAM)-licensed veterinary hospital to the dog owner. A RAM-licensed veterinary hospital RSO or AU should contact Exubrion Therapeutics™ if there are specific questions.

MANUFACTURED BY Theragenics Corporation for Exubrion Therapeutics™

Manufacturer's contact information:
Theragenics Corporation
5203 Bristol Industrial Way
Buford, GA 30518
Customer Service Phone: 833-942-1247
info@exubrion.com

STORAGE INSTRUCTIONS

Store in the shipping container at controlled room temperature (10°–30°C or 50°–86°F) until ready to use.

EXUBRION™
THERAPEUTICS

 September 2019 EXN-SYN-057

Attachment C
Procedure for use of Synovetin OA

Attachment D
Technical Basis for Release Criteria