



# **Veterinary Use of Synovetin OA ( $^{117\text{m}}\text{Sn}$ ): Licensing, Radiation Safety, and the Future.**

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# Outline and Introductions

- “Fun” Q and A
- What is Synovetin OA?
- Currently licensed locations
- Licensing Language (Authorized Use)
- Beyond the Canine Elbow
- Clinical Effectiveness
- Adverse Events
- Publications
  - Empirical Public Dose (Smith and Krimins)
  - Anisotrophy for Other Joints (Arno Et Al)
  - Age Dependent Dose Rates (Arno Et Al)
  - Extension of Use (Arno Et Al)
- Future



Disclosure – I’ve been consulting for Exubrion since November 2017.

# Veterinary Radioactive Materials Licensing – Q/A

1. What is the most popular use of radioactivity in veterinary medicine?

$^{131}\text{I}$  for feline hyperthyroidism,  $^{99\text{m}}\text{Tc}$  for equine bone scans,  $^{117\text{m}}\text{Sn}$  for synovial joint arthritis,  $^{90}\text{Y}$  for solid tumors,  $^{90}\text{Sr}$  for plesiotherapy,  $^{18}\text{F}$  for PET scans in horses

2. T/F - The “caretaker dose” release limit is the same for animals as humans?

False – 100 mrem/y for animals...500 mrem/administration for humans (1 mSv or 5 mSv if I must)

3. Which NUREG covers veterinary licensing?

NUREG 1556 Volume 7 Rev 1 (2018)

4. Guess the percentage of people who disclose they sleep with their dog.

I think it's about 50/50

5. T/F – Radiosynoviorthesis (radiation for arthritis) has been around a long time.

True – this is en vogue in Europe using  $^{90}\text{Y}$ ,  $^{32}\text{P}$ ,  $^{169}\text{Er}$ , and  $^{186}\text{Re}$ .

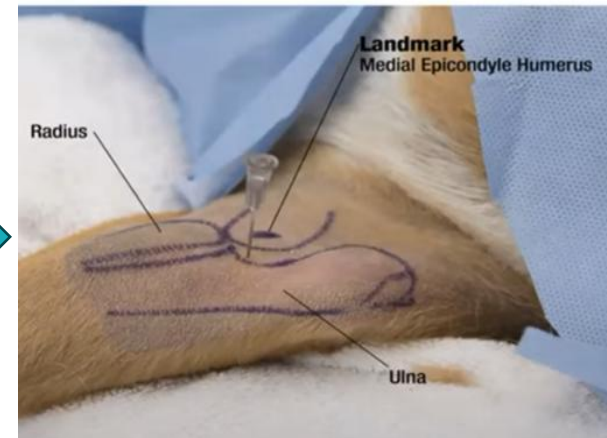
# Synovetin OA – Radiosynoviorthesis

- $^{117m}\text{Sn}$  – 13.9d half life
  - 159 keV gamma (couple other low energy x-rays too)
  - Several conversion electrons ~140 keV (these guys do “the work”)
- Form: Liquid microparticle
- Max activity administered: 6 mCi (companion animals)
- Admin: Injection into synovial joint(s)
- 99.1% of the activity stays encapsulated in the synovial joint – virtual sealed source
- Injected and released on an outpatient basis with release criteria of  $<0.45$  mR/h 1m from treated joint(s) for household animals.

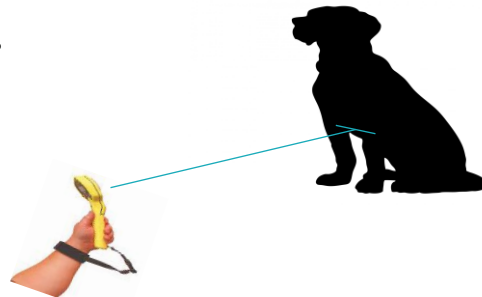
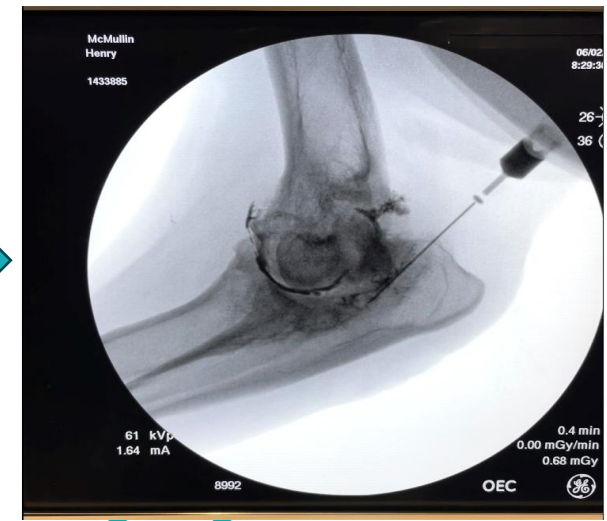
Prep →



Place aspirate →



Inject →



# Current Map of Treatment Centers



Find your state/region

This list doesn't include broadscope or terminated licenses.

Total licensed facilities since inception = 105



# Licensing Language

- Licensed in ~40 states.
- Approved use differs quite a bit.

*~40 variations*

- In all cases, the request was for what I would propose as a unified authorized use:

“Veterinary arthritis therapy”

- “For use in veterinary therapy in canines”
- “For treatment of arthritic joints of dogs”
- “For use of Synovetin OA in veterinary medical procedures”
- “As Synovetin OA for the treatment of veterinary arthritis, with the total dose not to exceed 6 mCi per treatment”
- “For possession as Synovetin OA for intra-articular injection into the synovial joints of animals”
- “Treatment of joint pain in canines”
- “For use in treatment of canine osteoarthritis in a dog’s elbow by radiosynoviorthesis”

*I like this language from NYC*

9.

Authorized Use:

(A) In companion animals (dogs) for treatment of veterinary osteoarthritis (Non-Human Use.)



# Treatments, Adverse Events, and Effectiveness

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- Licensing from limited scope licenses took off after TER published by NRC in October 2020.
- Total dogs treated = 2109
- Total number of joints treated = 3716
- There have been no reported systemic adverse events
- The product has been widely used with positive results. Effectiveness is published as “up to a year” with some commercial evidence of effectiveness in the form of retreatments:

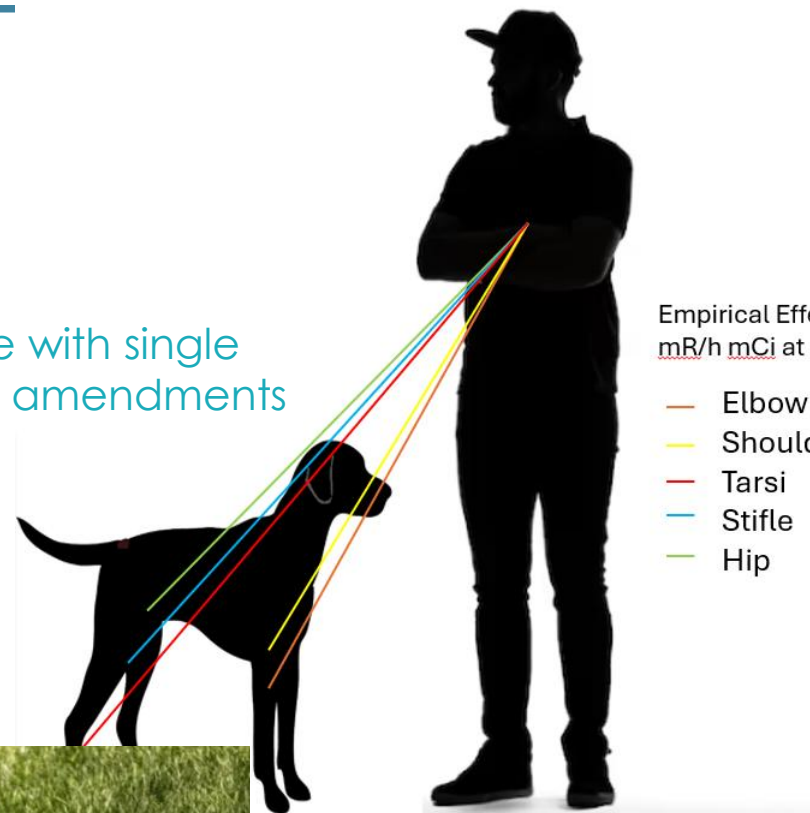
Many animals have had retreatments and 37 with a third treatment.



# Beyond Canine Elbows

- Different synovial joints
- Different species
  - Cats
  - Tiger (1, another on the way)
  - Komodo Dragons (3x)
  - Other interest in Zoo Animals
  - Horses (couple of licenses)

These were done with single use temp jobsite amendments



Empirical Effective Dose Rate Constant  
 $\text{mR/h mCi}$  at distance to center of torso

— Elbow	0.075
— Shoulder	0.0583
— Tarsi	0.0736
— Stifle	0.071
— Hip	0.0524



# Publications...for $^{117m}\text{Sn}$ - Radiosynoviorthesis

Arno, Matthew G.<sup>1</sup>; Simon, Jaime<sup>2</sup>; Stevenson, Nigel<sup>3</sup>; Donecker, John<sup>3</sup> Anisotropy of the Radiation Field Following Canine Sn-117m Treatment, Health Physics: August 2021 - Volume 121 - Issue 2 - p 150-155 doi: [10.1097/HP.0000000000001428](https://doi.org/10.1097/HP.0000000000001428)

Radiation rate measurements around different joints

Arno, Matthew G.<sup>1</sup>; Smith, Chad<sup>2</sup> Age-dependent Radiation Dose Rates from Canine Sn-117m Treatments, Health Physics: August 16, 2021 - Volume - Issue - doi: [10.1097/HP.0000000000001448](https://doi.org/10.1097/HP.0000000000001448)

MCNP for different sizes of people

Smith, Chad A.<sup>1</sup>; Krimins, Rebecca A.<sup>2</sup>. External Radiation Dose to Owners of Canines Treated with ( $^{117m}\text{Sn}$ ) Radiosynoviorthesis for Osteoarthritis. Health Physics 123(2):p 128-132, August 2022. | DOI: [10.1097/HP.0000000000001579](https://doi.org/10.1097/HP.0000000000001579)

Dosimeters to owners

Arno, Matthew G.<sup>1</sup>; Stevenson, Nigel<sup>2</sup>; Smith, Chad<sup>3</sup>; Donecker, John<sup>4</sup>. Update and Extension of Release Criteria for Canine  $^{117m}\text{Sn}$  Treatments. Health Physics 124(5):p 391-396, May 2023. | DOI: [10.1097/HP.0000000000001680](https://doi.org/10.1097/HP.0000000000001680)

Release at higher exposure rates and extended release instructions

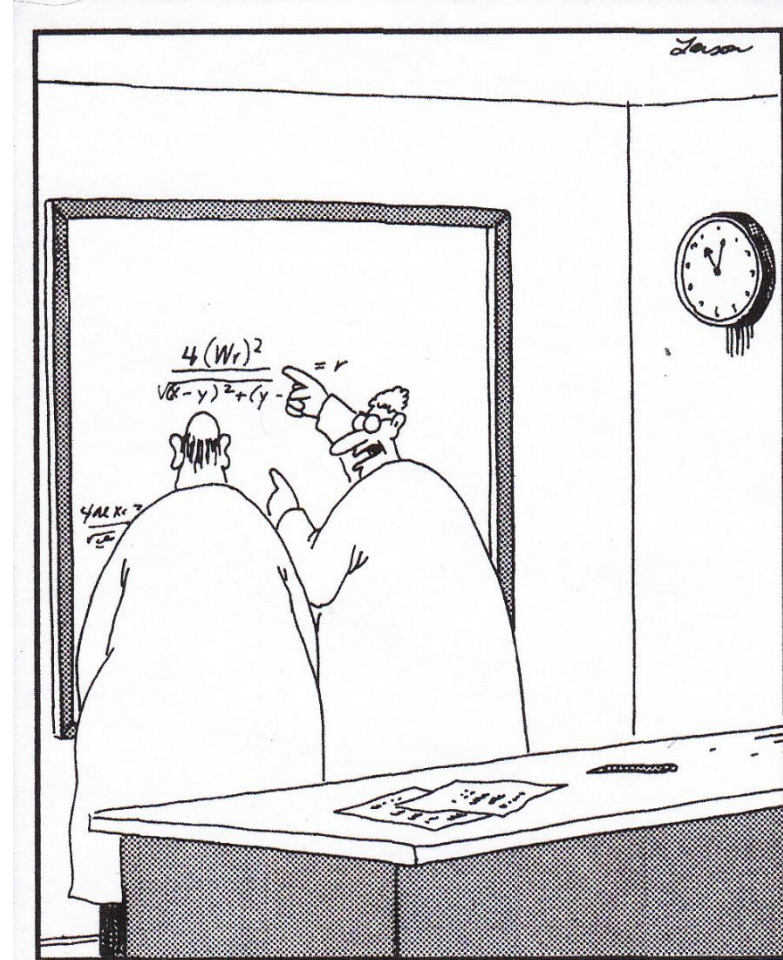
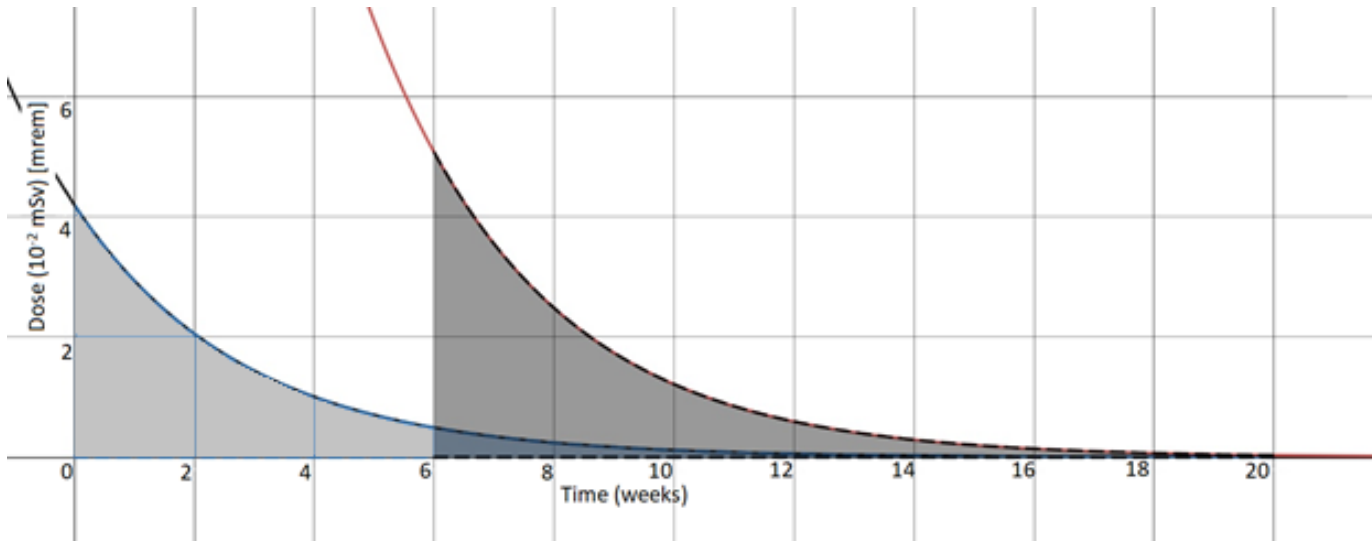
# Doses to owners – formulism

$$D_{total} = \frac{D_{ti}}{\int_0^{t_i} e^{-\lambda t} dt} \left[ \int_0^{t_{Ri}} e^{-\lambda t} dt + Occ_i \int_{t_{Ri}}^{\infty} e^{-\lambda t} dt \right] = 9 \text{ mrem average}$$

Dosimeter dose normalized for owner

Dose to owners over Prescribed restriction time

Dose to owner after restrictions



"Yes, yes, I know that, Sidney... everybody knows that!... But look: Four wrongs squared, minus two wrongs to the fourth power, divided by this formula, do make a right."

# Veterinary Simplifications

## Common Contact

Up to 5 min/day direct contact (e.g., joint to torso)  
 15 min/day @ 1 ft  
 4 h/day @ 3 ft e.g., feeding, grooming, petting, dog walking

## Extended Duration Intermediate Contact

Up to 5 min/day direct contact (e.g., joint to torso)  
 15 min/day @ 1 ft  
 12 h/day @ 3 ft e.g., dog rests at the feet of the owner etc.

## Extended Duration Close Contact

Up to 5 min/day direct contact (e.g., joint to torso)  
 3 h/day @ 1 ft e.g., holding dog in lap or on the couch, extended grooming, etc.  
 4 h/day @ 3 ft

## Prolonged Close and Intermediate Contact

Up to 5 min/day direct contact (e.g., joint to torso)  
 11 h/day @ 1ft e.g., dog sleeps in the owner's bed etc.  
 9 h/day @ 3 ft e.g., dog rests at the feet of the owner etc.

← From this to this



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 9 h/day @ 3 ft e.g., pet rests at the feet of the owner etc.

# Future...humans

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## **Preliminary Dosimetry Study of Homogeneous $^{117m}\text{Sn}$ Hydroxide Microparticles for Radiosynoviorthesis in Patients with Osteoarthritis of the Knee**

### **Protocol HTM-01**

Sponsor: Serene LLC  
21 Waterway Avenue, Suite 225  
The Woodlands, TX 77380  
USA

Start thinking about AU considerations.

It's an interesting thought puzzle, but if it's my knee - I want an orthopedist doing the joint injection, not a radiologist or rad onc.



# Human Radiosynoviorthesis

- First trial will be with 1 mCi of  $^{117m}\text{Sn}$  injected into a single knee
- So, what's the dose/risk to the patient?
  - Calculated as **0.42 mSv/mCi** for knee injection in average man
  - Scribbles to the right use Reg Guide 8.40 (EDEX)
  - It's a weird one – injected in the body, but not biodistributed, so just external dose...sortof
- OK, what about caretaker dose?
  - You don't have the benefit of attenuation of the thigh, pelvis, torso etc...
  - $D(\infty) = \mathbf{0.77 \text{ mSv/mCi at 1m}}$
  - Reg Guide 8.39 Rev 2 (Draft)...(this is a whole other discussion)

Handwritten calculations for dose to various organs:

$$D(\infty) = \frac{A_0 \cdot \Gamma \cdot t_{1/2} \cdot \Gamma}{r^2} \cdot e^{-\mu_1 x_1} \cdot e^{-\mu_2 x_2} \cdot e^{-\mu_3 x_3} \cdot e^{-\mu_4 x_4} \cdot e^{-\mu_5 x_5} \cdot f_1 \cdot f_2 \cdot e^{-\mu_6 x_6}$$

$D(\infty) = A_0 \cdot 1.44 \cdot 13.9 \cdot 40.56 \frac{\text{R}\cdot\text{cm}^2}{\text{mCi}\cdot\text{h}} \cdot 0.945 \frac{\text{Rcm}}{\text{Rcm}} \cdot 10 \frac{\text{mSv}}{\text{Rcm}}$   
 $= 402373 \frac{\text{mSv}\cdot\text{cm}^2}{\text{mCi}}$   
 $= 7672 \frac{\text{mSv}\cdot\text{cm}^2}{\text{mCi}}$

$D(\infty)_{\text{HEAD}} = \frac{7672 \frac{\text{mSv}\cdot\text{cm}^2}{\text{mCi}} \cdot e^{-\mu_1 x_1} \cdot e^{-\mu_2 x_2} \cdot e^{-\mu_3 x_3} \cdot e^{-\mu_4 x_4} \cdot e^{-\mu_5 x_5} \cdot (1 - e^{-\mu_6 x_6})}{100 \text{cm}^2}$   
 $D(\infty)_{\text{THORAX}} = \frac{7672 \frac{\text{mSv}\cdot\text{cm}^2}{\text{mCi}} \cdot e^{-\mu_1 x_1} \cdot e^{-\mu_2 x_2} \cdot e^{-\mu_3 x_3} \cdot e^{-\mu_4 x_4} \cdot (1 - e^{-\mu_5 x_5})}{75 \text{cm}^2}$   
 $D(\infty)_{\text{ABS REL}} = \frac{7672 \frac{\text{mSv}\cdot\text{cm}^2}{\text{mCi}} \cdot e^{-\mu_1 x_1} \cdot e^{-\mu_2 x_2} \cdot e^{-\mu_3 x_3} \cdot (1 - e^{-\mu_4 x_4})}{45 \text{cm}^2}$

$f_1 = 0.945 \frac{\text{Rcm}}{\text{Rcm}}$   
 $f_2 = 10 \frac{\text{mSv}}{\text{Rcm}}$   
 $\Gamma = 1.69 \frac{\text{R}\cdot\text{cm}^2}{\text{mCi}\cdot\text{h}} = 40.56 \frac{\text{R}\cdot\text{cm}^2}{\text{mCi}\cdot\text{h}}$   
 $\mu = \text{Distance from knee to AREA OF INTEREST}$   
 $\mu_i = \text{ATTENUATION COEFFICIENT. (NEAR INTERPOLATION FOR 0.159 MeV)}$

$w_{\text{HEAD}} = 0.1$   
 $w_{\text{THORAX}} = 0.33$   
 $w_{\text{ABS}} = 0.5$

TOTAL DOSE =  $\sum D_i \cdot w_i$

RADIONUCLIDE	COLUMN 1		COLUMN 2	
	Patient Release Threshold <sup>d</sup> $Q_{rel}$ (GBq)	(mCi)	Instruction Threshold <sup>d</sup> $Q_{ins}$ (GBq)	(mCi)
Sn-117m	0.29	7.8	0.058	1.6

# Summary

Thousands of animals have been treated successfully with Synovetin OA

While canine elbows are the most prevalent treatment location, other large synovial joints and other species can benefit from radiosynoviorthesis

Publications can be used to refine and update release criteria, confidently meeting the public dose limits

The first set of human trials has already begun in Canada, which will bring its own set of interesting licensing situations

Stop by the Exubrion Table for videos, publications, and additional lecture materials... **there's a \$10 Starbucks gift card in it for you.**



**Dr. Matt Arno**  
Analytical Framework for  
Public Dose Assessment for  
Veterinary use of Sn-117m



**Dr. Nigel Stevenson**  
Tin-117m and Synovetin OA®  
in Veterinary Science

**Scan for more brief video presentations**



# References and Questions

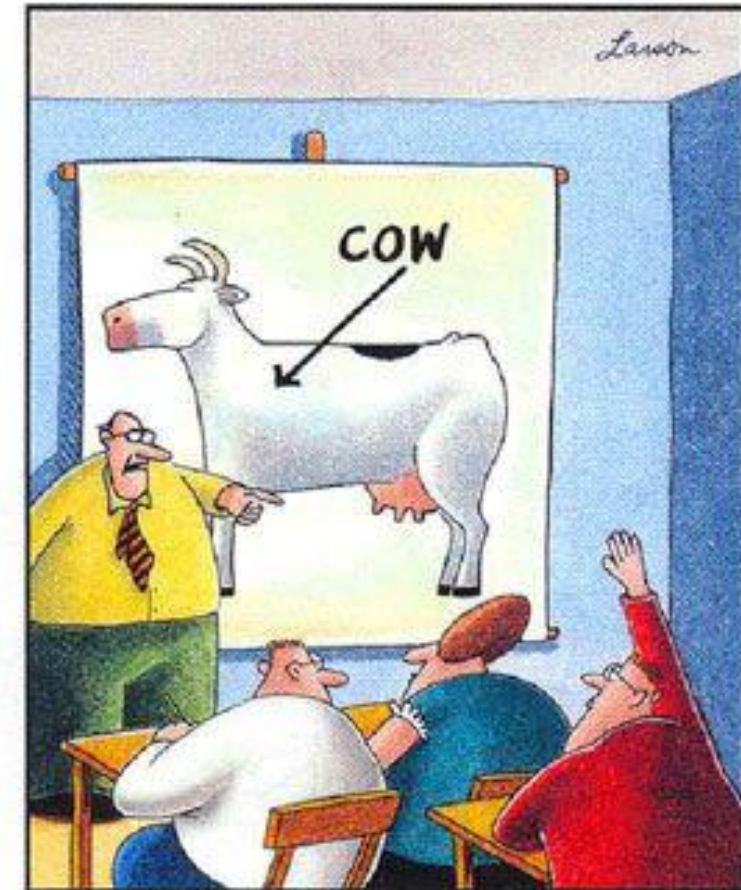
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F.X. Massé Associates, Inc.  
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## $^{117m}\text{Sn}$ Related

- Arno MG. Evaluation of potential dose to members of the public from treatment of dogs with Synovetin OA™ containing Sn-117m [online]. 2020. Available at <https://adamswebsearch2.nrc.gov/webSearch2/main.jsp?AccessionNumber=ML20142A295>. Accessed 1 October 2020.
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- <https://1350kman.com/2024/04/sunset-zoo-tiger-receives-groundbreaking-new-arthritis-treatment/>

## Far Side Related

Gary Larson – [www.thefarside.com](http://www.thefarside.com)



"Yes ... I believe there's a question in the back."

