Pre-Submittal Meeting with Exubrion Therapeutics

November 6, 2019

Medical Radiation Safety Team
Medical Safety and Events Assessment Branch
Division of Materials Safety, Security, State, and Tribal Programs
Office of Nuclear Material Safety and Safeguards

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Agenda

- Introductions and opening remarks
- NRC presentation
  - Process
  - Schedule
  - Necessary content for application
- NRC and Exubrion discussion
- Public comments

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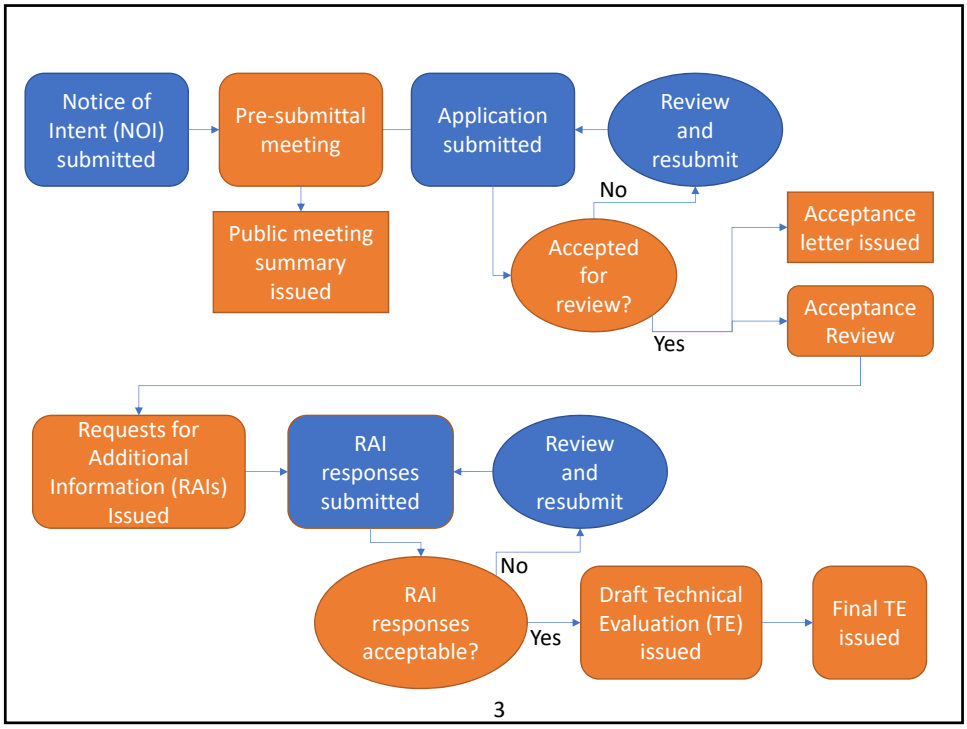

Tentative Schedule

Milestone	Tentative Date for Completion
Pre-submittal meeting held	November 6, 2019
Application received	Late November 2019
Acceptance review completed	Mid-December 2019
RAIs issued	Mid-January 2020
RAI responses received	Mid-February 2020
Draft TE issued	Mid-April 2020
Comments on Draft TE received	Late April 2020
Final TE issued	Summer 2020

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Public Dose Requirements

- **20.1301 Dose limits for individual members of the public (paraphrased)**
- (a) Each licensee shall conduct operations so that—
- (1) The total effective dose equivalent to individual members of the public from the licensed operation does not exceed 0.1 rem (1 mSv) in a year, and
- (2) The dose in any unrestricted area from external sources does not exceed 0.002 rem (0.02 millisievert) in any one hour

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Reporting Criteria

- 10 CFR 20.2203 **Reports of exposures, radiation levels, and concentrations of radioactive material exceeding the constraints or limits.**
- (a) Each licensee shall submit a written report within 30 days after learning of any of the following occurrences:
- (2) Doses in excess of any of the following:
- …..
- (iv) The limits for an individual member of the public in 10 CFR 20.1301;

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Public Dose Considerations

- These public dose limits apply to every dog, not to the average
- Licensees are responsible to ensure these dose limits are met
- Strong screening criteria are necessary to ensure public dose limits are met for proposed dose rate at time of release
- Instructions should not be relied upon as the primary way to ensuring dose limits are met

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Public Dose Considerations (cont.)

- 10 CFR 20.1301(a)(2) – dose limit of 0.002 rem (0.02 millisievert) in any one hour
- This dose limit is not an average but for any one hour
- Distances under a foot need to be considered.
- Screening criteria maybe necessary. Instructions can support screening criteria, but cannot be the primary method which the regulation is met.

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Radiation Area

- 10 CFR 20.1003 - ***Radiation area*** means an area, accessible to individuals, in which radiation levels could result in an individual receiving a dose equivalent in excess of 0.005 rem (0.05 mSv) in 1 hour at 30 centimeters from the radiation source or from any surface that the radiation penetrates.

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Current Issues

- Justification seems to focus on averages instead of individual dogs. Public dose limit is per dog.
- Current dose release proposal of 0.5 mR/hr at a 1 meter
  - Significantly higher than recommended for Iodine-131 in cats, which has a shorter half life
  - Results in a radiation area. Proposed maximum dose rate at time of release cannot exceed this limit.
  - Very unlikely 2 mrem in any one hour could be met following dog release
  - Close contact would result in high doses very quickly, cannot be ignored

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Current Issues (cont.)

- Attenuation
  - Measurement data needed. Attenuation for different size dogs needs to be demonstrated.
  - Geometry, distances, and dose rate should be included
  - Close contact (i.e. messages, dog with legs over person, lifting the dog, etc.)
  - Assumptions need to be conservative or licensee will need strong assurance assumptions are met for each animal
- Figures to show distances would be helpful
- What about dose to a child?
- Licensees procedure if a dog cannot be released immediately

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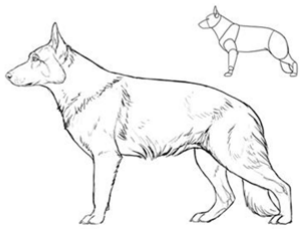
Current Issues (cont.)



Dose rates from 3 mCi dosage in 1 elbow joint at distances	Joint height, Anterior	Joint height, posterior	Joint height, left lateral	Joint height, right lateral	Standing torso height, Anterior	Standing torso height, Posterior	Standing torso height, Left lateral	Standing torso height, right lateral	dorsal
1 m									
1 foot									
contact									

Example Assumption Needing more Justification

- Additionally, in most postures of lap-sitting, the dog's body will serve as a shield for most of the human torso for radiation coming from the dog's legs or the dog would be in such a position that the average distance would be a foot or more, i.e. stretched out perpendicular to the human's legs or with the dog's legs pointed towards the human's knees. Therefore, dose rates and occupancy factors at a distance of 3 inches are not discussed further.

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Information Needed*

- Introduction
- Proposed Generic Procedures for Release
- Proposed Screening Criteria
- Proposed Generic Instructions
- Technical Basis Supporting Proposal

* Review will only consider information submitted as part of proposal.

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Introduction

- Scope
- Identify information applicants will need to provide
- Administration Limitations, i.e.
  - Maximum activity/isotope/form
  - Location of treatment
  - Minimum spacing between procedures
  - Number of dogs treated per owner/home over what time period
- Training specific to Sn-117m use

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Proposed Generic Procedures for Release

- Assumptions and limitations
- Release dose rate or method to calculate dog specific release dose rates
- Screening criteria
- Instructions
- Survey, i.e.
  - Location
  - Survey meter
  - Contamination
- Documentation
- Boarding Information

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Proposed Screening Criteria

- Define licensee's responsibility to ensure 10 CFR Part 20 is met for each individual dog within their unique circumstances.
- Describe the screening criteria you propose the licensees submit with the applications.
- Provide procedural steps on how licensees are given high-confidence that screening is sufficient to ensure public dose limits are met.
- If screening initially shows dogs behavior could result in public dose limit being exceeded, describe if and how licensees will allow owners to demonstrate dogs can meet modified behavior to allow them to be re-screened.

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Proposed Generic Instructions

- Distances
- Time lines
- What to do in the case of emergency or death
- Owner signature
- Describe dose if instructions are not followed

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Technical Basis Demonstrating Compliance

- Defend assumptions
- Provide attenuation data
- Provide dose rate data for different size animals
- Figures demonstrating distances and geometry
- Justification for expected animal behavior
- Retention studies
- Total doses for:
  - Maximum doses with instructions and screening compliance
  - Maximum dose with poor instruction compliance
  - Maximum likely dose with no instructions and screening criteria

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