Second Set of Requests for Additional Information for the Review of the Hypothetical License Amendment Application for Treatment of Dogs with Synovetin OA® Containing Sn-117m

Comment 1

The technical evaluation assumes less than 1 minute a day at 6 inches beyond the scope of the instructions for all categories. If someone's typical dog-human interactions exceed this, it is possible that they will exceed the public dose limit even if they limit this interaction during the instructional period. Therefore, a different category is needed, or the procedure needs to specify that if the normal behavior of the dog leads to direct contact interactions of more than 1 minute a day, these dogs should not be treated. In addition, as there are limitations needed for direct contact well beyond the minimum duration of personalized instructions, longer instruction should be given alerting owners that direct contact interactions should not be increased to more than 1 minute a day after the rest of the instructions expire.

Response

The evaluation has been updated to consider direct contact for all distances less than one foot and for after the end of the written instruction period. A maximum of 5 minutes of direct contact has been selected for a bounding time of direct contact after the end of the instruction period. Exubrion wishes to have only a single instruction duration period for simplicity and ease of compliance. New written instruction duration periods have been calculated to incorporate the consideration of direct contact after the expiration of the written instruction duration and to address Comment 3c.

Comment 2

Also, confirm that the instructions will prohibit direct contact activities for the duration of time that could result in exceeding the public dose limit. Please provide an example of this instruction and the duration(s).

Response

The revised analysis in response to Comments 1 and 3b results in the existing release instructions and existing limitations on direct contact being adequate. No change to the release instructions has been made other the necessary duration.

Comment 3

The current minimum duration of the instructions is currently not long enough for the three items below.

Response

The three items below are addressed individually in the respective comment responses.

Comment 3a

The current proposal sets the duration for instructions to a minimum number of weeks necessary to show that an individual will not receive 100 mrem from the release of the dog for many situations. However, the public dose limit of 100 mrem per year is a limit from all licensed

operations and is not intended to be a dose limit from a single action of a licensee, such as release of an animal. In addition, 10 CFR 20.1101(b) requires a licensee "use, to the extent practical, procedures and engineering controls based upon sound radiation protection principles to achieve occupational doses and doses to members of the public that are as low as is reasonably achievable (ALARA)." As calculations show, some durations could lead to doses approaching 100 mrem even if instructions are strictly adhered to. NRC does not agree that the current proposal provides adequate assurance that the 100 mrem limit will not be exceeded from all licensed operations. Adding additional time to the instruction duration (such as 2 weeks or 1 half-life) would provide additional assurance that the 100 mrem limit will not be exceeded, provide less reliance on "strict adherence" to the instructions, and meet the intent of 10 CFR 20.1101(b).

Response

Evaluation of additional dose pathways from the licensed operation has been added to the technical evaluation. The minimum written instruction period has been selected to be 2 weeks. This minimum period provides for compliance with the requirement to ensure a member of the public does not receive more than 2 mrem in any one hour. It also provides ALARA dose reduction for the majority of dog sizes and behavior categories. The written instruction duration period has also been chosen to ensure that the calculated dose is less than 90 mrem for the most critical group (small children), providing an even larger margin of safety for adults and larger children. It is Exubrion's opinion that these measures provide an adequate margin of safety and are consistent with ALARA principles. The procedure has been revised to encourage owners to remain ALARA for an additional two weeks after the end of the instructions.

Comment 3b

NOTE – this item may not apply depending on the response to (a) above.

The technical evaluation states that a child could exceed the 2 mrem in a few minutes following release of an animal with the maximum dose rate. By adjusting the results by the Sn-117m half-life, this evaluation gives the appearance that the 2 mrem limit could still be met in 4 minutes for a 1 year old after the instruction duration ends, approximately 5 minutes for a 5-year-old, and approximately 12 minutes for an adult. While staff notes that an adult is unlikely to exceed the 2 mrem in any one hour as this evaluation appears to have significant conservatism by placing all activity into 1 joint, that the individual's abdomen is directly touching the joint, and the pre-screening questionnaire should prohibit treatment of animals who normally have direct contact, staff does not have adequate assurance that this procedure would not result in a young child exceeding the 2 mrem in any one hour after the duration of the instructions. Therefore, either add an instruction for longer duration for households with young children or provide a detailed evaluation demonstrating the conservatisms in this dose that quantitatively shows young children would be unlikely to exceed public dose limits after the minimum duration of instructions.

Response

As suggested, the analysis has been redone to eliminate much of the conservatism. A bounding time of 5 minutes of direct contact after the end of the duration of the written instructions has been chosen to permit quantitative evaluation. Given this bounding time, the

new proposed written instruction duration periods are sufficient to ensure that the 2 mrem in any one hour criteria is not exceeded during or after the written instruction duration period.

Comment 3c

The release instructions appear to state cremation only needs to be delayed if the animal dies during the duration of the instructions while cremation will likely need to be delayed much longer. Update the instructions to inform the owners to contact the licensee if the dog dies within a justifiable duration. Update the procedure to instruct the licensee that they may need to hold a body per decay-in-storage regulations or other acceptable disposal regulations if the dog's body needs to go back to the licensee to ensure the public dose limit is not exceeded.

Response

Without requiring the dog to be returned to the licensee upon death for an inordinate period of time to determine whether there is any detectable radioactivity, Exubrion proposes that the period of concern be limited to that for which the activity is above a reasonable quantity. Sn-117m is not specifically listed in 10 CFR 30.71 and thus the exempt quantity is 0.1 µCi. However, Ba-140 and Cs-136 are listed gamma emitters with similar half-lives (12 and 13 days respectively) and that have exempt quantities of 10 µCi. Exubrion therefore proposes that the period of time be set to that which would allow the highest activity injection to decay below 10 µCi, in this case 10 half-lives or 20 weeks for the largest dogs. Within 20 weeks, the veterinarian will be notified and will delay cremation until the activity decays below 10 µCi.

No such delay is needed to bury a deceased dog.

Comment 4

The release procedure states that direct contact is when the elbow is directly in contact with an individual's torso whereas the technical evaluation calculations assumes 6 inches. When the technical basis calculation is adjusted to use the direct contact dose rate instead of dose rate at 6 inches, staff found that adults were still under 100 mrem. However, children were above 100 mrem in the Extended Duration, Close Contact and Prolonged Close and [Intermediate] Contact (Babies/Toddlers only) categories. Either increase the duration of instruction for these categories, mark in the procedure that these categories should not be used specifically if these behaviors are present in these age groups or provide additional evaluation to reduce the conservative dose values in the close contact dose.

Response

The geometric attenuation-only evaluation has been replaced with MicroShield-based calculations which refined our calculations. All interactions at a distance less than 1 foot are now treated as being on contact. The revised calculations have been performed for all the ages of concern (1,5,10, and 15 years old and adults) and the release instructions adjusted as needed to incorporate this and the changes in response to the above comments.

Comment 5

The response to RAI 11d and language in A3.6 of the procedure makes it appear that behavior modifications can be used to determine the category. However, the dose calculations assume the individual behavior is bounded by the category following the end of the duration of the instructions, not when the instructions are being used. Therefore, remove the language in A3.6

which states "or otherwise reduce interactions to fit into one of the categories listed below in A.3.7," as this implies the modifications can be used to fit into categories. Also, consider moving this step up to directly after A.3.4 as its current location made it appear that modifications should be used in the categorization.

Response

Language removed as requested. The portion of the questionnaire referenced in Step A3.5 is necessary for accurate categorization and thus needs to be conducted prior to the categorization performed in Step A3.6. Step A3.6 has been left where it is.

Comment 6

In the prescreening questionnaire, the first question should have an asterisk by the "no" because if someone is unwilling to modify their interactions for the time frames indicated on the release instructions, then the dog should not be treated. This question should also have an "N/A" for cases when modifications are not necessary to ensure the instructions are followed.

Response

Question modified as suggested. This question has been moved to be the last question asked since the other questions are behavior modifications potentially required inform the answer to this question.

Comment 7

On page 13 of the technical basis, there is a discussion that states dogs could be treated multiple times in a year. However, this conflicts with the procedure which prohibits this practice. Clarify that multiple treatments on the same elbow are not being proposed and if so, delete this statement.

Response

The statement as made is correct. However, we are not proposing to allow multiple treatments per year. The procedure and other documents submitted are clear about this. The Technical evaluation has been updated likewise.