October 26, 2020

Katherine Tapp and Irene Wu
U.S. Nuclear Regulatory Commission
Washington, DC 20555–0001

Dear Dr. Tapp and Ms. Wu:

The Executive Board of the Organization of Agreement States (Board) appreciates the modifications made to the "Technical Evaluation Report for the Exubrion Therapeutics Proposed License Application Template for the Release of Dogs Following Treatment with a Tin-117m Colloid" (TER) based on our first comment letter. Further, the Board provides the following comments for consideration as continuing concerns with the revised TER:

Technical Evaluation Report

1. The TER relies on dose rate and distance measurements that are difficult to obtain. Exubrion reported that because of movement during the equilibration time of the meter, it is hard to get a stable dose rate reading. It would be equally difficult holding a meter steady at the prescribed distance of 3.3 feet. The poor correlation of Wendt et al[1] exposure rate/weight data seems to corroborate that assertion. Exubrion should provide protocols to be added in the TER for attaining high confidence measurements to be used in guiding release decisions.

2. The Board's letter dated August 11, 2020 asked, in part, "what happens to the radiopharmaceutical if it is not injected into the correct spot, is it then excreted? Does it travel to a different physical location within the animal where the owner needs to be aware of a different radiation hazard? Is it appropriate to release the dog?" NRC responded "Exubrion stated that they saw no bio kinetic transfer to any other organs in a study evaluating impacts of missed injection sites." This satisfies the question regarding transfer to organs, but was an increase in excretion noted? If so, there is a risk of contamination and not just exposure that needs addressed.

3. The TER states that "Licensees should use the information gathered during the pre-screening evaluation and discussions with the owner, not Exubrion's evaluation of common dogs, to determine the typical time and distances the dog has with all

[1] External Radiation Exposure following Sn-117m Colloid Intra-articular Injections, R.E. Wendt III, N.R. Stevenson, J.M. Donecker, and C. Doerr.

individuals in the household. Based on the information about the interactions in the dog's household, the licensee will determine if release is appropriate for each dog following treatment and provide instructions to the household in order to have confidence that public dose limits will not be exceeded." This amounts to an individual dose assessment for each household member. Will the assessments be reviewed by the NRC during inspection and what guidelines will they use for the review? A standard license commitment to retain every household members' time studies and dose assessments should be included for each treatment.

4. NCRP Report No. 116, Limitation of Exposure to Ionizing Radiation, recommends an equivalent dose limit for the fetus of an *occupationally* exposed individual of 50 mrem (0.5 mSv) per month during the pregnancy. Excluding this treatment for households with pregnant women would seem sensible if their interactions fall within those extended and prolonged close contact categories or if individual assessments result in a dose of exceeding 50 mrem per month.

5. Under Notes to License Reviewer, the first bullet on page 18 of the TER, describes that license reviewers obtain "a commitment that the licensee will not use this procedure to release a dog whose typical behavior patterns, without instructions, do not fit into the time and distance limitations listed for one of the categories described in the procedure as these categories are the only ones evaluated." This bullet is confusing, does it intend to mean that the treatment should not be performed, or that another procedure for release should be followed?

6. Under Notes to License Reviewer, the second bullet on page 18 of the TER, states that "…the licensee will not release a dog if a child is in the house under the age of 5 who does not fit into the common contact or extended duration or immediate contact scenarios, because the other scenario is not evaluated by Exubrion's technical basis and the typical interaction patterns could exceed the public dose limits." What is "the other scenario" that was not evaluated by Exubrion? Is the objective of this point meant to restrict releasing a dog into a household with children under the age of 5 where a pre-established contact scenario does not fit with what is discovered during pre-screening or is it to reject the candidate for treatment all together?

7. The TER describes "…that licensees must investigate any public exposure where limits might have been exceeded, even if it is due to individuals not following instructions, and to report those to the NRC per 10 CFR 20.2203." The Board supports this requirement; however, concern exists over the discussion of 500 mrem being an acceptable limit to protect health and safety.

   The TER concludes that "Even if no instructions are followed, the staff determined that the highest likely exposure to a household member, who is a member of the public, would likely be below 500 mrem. As this dose will be received by someone who would likely be benefitting from the exposure and is at a level allowable by the NRC in other circumstances where individuals benefit from the exposure, such as patient release, the staff finds the risk from this dose acceptable given the licensee provides adequate instructions and means to prevent the exposure." Licensees may

lower their safety focus knowing that acceptable limits from other parts of the 10 CFR should still be upheld in worst case scenarios and ignore the need to follow up or calculate doses to adhere to 10 CFR 20.1301. An increased dose allowed to members of the public, as a consequence of patient release, is due to the life-saving or quality of life improving treatments to a human person, not an animal. The Board objects to the conclusion that an increase in dose from a treated animal is a beneficial exposure and recommends removing any discussion of other parts of regulation or the 500 mrem limit.

Procedure for Use of Synovetin OA©

8. Step A3.7 of the Procedure is confusing where it states "Note that only [one] category will apply for the entire household." If all the household members do not fit into the same category, then is the most restrictive category used? How does that reconcile with the TER where it says Exubrion's evaluation of common dogs should not be relied upon?

To summarize, the Board remains concerned about the heavy reliance on members of the public to ensure compliance with public dose limits. The procedures require pet owners and household members to provide an accurate accounting of their interaction with the dog, faithfully follow instructions and prevent certain behavior patterns. This is of particular concern in households with children. The failure of pet owners and household members to comply will result in an exceedance of the public dose limits.

As always, the Board appreciates this opportunity to be a contributing member of the National Materials Program. Please contact us if you have any questions.

Sincerely,

David Crowley, Chair
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