RADIOCAT®

Centers For
The Treatment
of Feline
Hyperthyroidism

4015 E. Cactus Rd.
Phoenix, AZ 85032

1900 S. Sepulveda Blvd.
Los Angeles, CA 90025

251 N. Amphlett Blvd.
San Mateo, CA 94401

730 Randolph Rd.
Middletown, CT 06457

290 Churchmans Rd.
New Castle, DE 19720

9220 Estero Park Commons Blvd.
Suite 7
Estero, FL 33928

630 N. Cobb Parkway
Marietta, GA 30062

312 W. Northwest Highway
Arlington Heights, IL 60004

7712 Crosspoint Commons
Fisher, IN 46038

32-A Mellor Ave.
Baltimore, MD 21228

19 Main Street
Wakefield, MA 01880

207 Montgomery Road
Westfield, MA 01085

223 Siebert Rd.
Pittsburgh, PA 15237

393 Woods Lake Rd.
Greenville, SC 29607

5918 West Broad St.
Richmond, VA 23230

6651 Backlick Rd.
Springfield, VA 22150

1-800-323-9729
email
radiocat@erols.com
www.radiocat.com

March 4, 2022

Janice Nguyen
Mail Control No. 625737
USNRC, Region I
Division of Radiological Safety and Security
2100 Renaissance Boulevard, Suite 100
King of Prussia, PA 19406

RE: RADIOCAT, LLC, REQUEST FOR ADDITIONAL INFORMATION, MAIL CONTROL NO. 625737

Dear Ms Nguyen:

This is in response to your October 18, 2021, REQUEST FOR ADDITIONAL INFORMATION (RIA). For clarity, RADIOCAT's responses follow the items in the October 18, 2021 request.

1. The request provides no justification that the public dose limit of 2 mrem limit per any one hour as required by 10 CFR 20.1301(a)(2) will not be exceeded. Using the inverse square law, the exposure rate at the time of release at 1 foot would be 5.38 mR/hr and even higher on contact, such as a cat sitting in an owners lap. Therefore, additional justification is necessary to demonstrate this limit would not be exceeded following release.

Modeling has been changed to use a practical T_{eff} following release, and the instructions Radiocat provides to owners have been modified to strengthen the justification for release of patients after 48 hours after treatment.

2. The request states that a member of the public would receive 3.5 mrem or less from a cat released with an exposure rate of 0.5 mR at a meter if the individual limits time near the cat in accordance with instructions (i.e. half hour a day at 1 foot [30 cm] and 2 hours a day at 3 feet [90 cm]). However, using a point source and no decay for the first day, the calculated dose is approximately 4 mrem. Please update the value or provide further information (i.e. calculation) on how 3.5 mrem was determined.

Instructions have been modified to instruct the owner not hold the cat closer than 3 feet during the first two weeks after release.

3. The request should ensure all assumptions are justified or that the procedure includes controls to ensure assumptions are appropriate for each released cat. For example:

a. After the 14 day period, the applicants calculated TEDE assumes the cat will only sit on a person's lap for 1 hour a day. Either update this assumption to a conservative timeframe to capture all cats or describe how licensees will ensure they will only release treated cats with this type of typical behavior. In addition, provide justification for the 30 cm distance used.

Instructions have been modified to instruct the owner not hold the cat closer than three feet during the first two weeks after release.

b. After the 14 day period, the applicant calculated TEDE using the exposure rate at a distance of 30 cm. In this calculation, only dose to the gonads is considered. Provide updated values considering dose to the whole body or provide justification as to why only dose to the gonads is considered. In addition, provide justification for the 30 cm distance.

Instructions have been modified to instruct the owner not hold the cat closer than three feet during the first two weeks after release. After two weeks, when a practical T_{eff} reported in a recent presentation, "Dose Assessment for Humans Exposed to Domestic Animals Administered Radioactive Material", DM Hamby, RS Flora, RR Benke, VA Shaffer, K Tapp, IRPA North American Regional Congress, February 2022, is used, only whole body dose from close contact is considered.

c. For all quantitative assumptions, provide a range of typical cat values and justify that the values chosen in the calculation are appropriate. For example, the application assumes a feline patient receives a dose of 5 mCi and has an uptake of approximately 20%. What is the range of normal administration activities and uptake fractions? In addition, the application assumes a member of the public ingests up to 0.1% of free iodine. Provide general justification for this value.

Radiocat recognizes that it may have used estimates that are unnecessarily conservative. The normal administered activities range between 3.5 and 5 mCi. The uptake fraction is reported in to be between 15 and 25 percent in "Thyroid uptake is reported to be 21% in Thyroidal radioisotope uptake in euthyroid cats: A comparison between 131I and 99MTcO4", Lambrechts, N, Jordaan, M.M. Pilloy, WJ, Heerden, J, and Clauss, Ralf, Journal of the South African Veterinary Association, July 1997. 20% is used as the uptake fraction. The application assumed that a member of the public ingests up to 0.1% of free iodine from excreta and feces. We recognize that this may be unrealistically conservative while using it for projection of internal dose. If 0.1% is determined by the NRC to be unrealistically high, the projected uptake will be reduced.

d. The request assumes renal excretion rate from cats is the same as it is for humans to estimate excretion activity. Provide justification for that assumption using data from cats. As the application is currently using radiological half-life in external dose assessments,

this justification does not need to justify the biological half-life but should provide evidence of assumed excretion activity after 48 hours.

T_{eff}s between 1.6 and 3.4 have been reported. It is conservatively assumed that all unbound I-131 is excreted without decay.

e. The request ignores external exposure from excreted material. Provide an estimate of external exposure from excretion or provide justification for why this can be ignored.

A typical cat litter pan is 60 cm x 45 cm and is typically cleaned every day. The activity in the pan is 63 uCi or less. At 50 cm from a uniform plane containing 63 uCi, the exposure rate is 0.05 mR/hour. If an owner takes five minutes to clean the pan, the dose from excreted material, 4 µrem, is unlikely to significantly add to the owner's dose.

f. The request assumes the typical dose rates at 48 hours following administration will be less than 0.5 mrem/hr at 1 meter. Provide general information of typical dose rates at 48 hours post administration to provide justification for this assumption.

The measured value at 1 m will be 0.5 mR/hr or less. The dose rate, 0.5 mrem/hr is assumed to be numerically equal to the exposure rate, 0.5 mR/hr.

4. As stated in NUREG-1556, Volume 7, Revision 1, Appendix D, instructions should provide a margin for dose reduction but should not be relied upon as the primary way of keeping the dose to members of the public below the 1 mSv [0.1 rem or 100 mrem] public dose limit. However, your request uses instructions to ensure dose to members of the public does not exceed the public dose limit. While the procedure has the owner sign a statement saying they have been given the instructions, Radiocat's procedure does not provide a mechanism which shows that the licensee will verify that the owner will be able to meet the restrictions described in the instructions. To ensure the public dose limit will not be exceeded, the procedure must have steps which allow the licensee to ensure the owner of each released cat can and will meet instructions. Examples include a screening questionnaire and personalized instructions based on normal cat behavior and follow-up with the owner. The purpose of a follow-up after release allows the licensee to reenforce the importance of the instructions with the owner after some time has passed and to allow the licensee to learn if cat owners are able to follow instructions, allowing adjustments if necessary to the procedure and reporting if the public dose limit is expected to have been exceeded.

Radiocat screens the owner three times – when treatment is being scheduled, when the cat is admitted for treatment, and when the cat is released. The need to follow the provided instructions is reinforced when the cat is admitted and when the cat is discharged. As the NRC expects licensees to follow commitments made during licensing, Radiocat expects owners of treated cats to follow commitments made before and after treatment.

5. Please provide a dose estimate of the highest, realistic dose an individual could receive if they did not follow the instructions. This can be over the public dose limit but the release procedure should demonstrate how the licensee will prevent this scenario from happening.

The highest realistic dose an individual could receive if instructions were not followed is likely to result from an owner not following the Radiocat instructions to limit exposure during the first two weeks following treatment. If an owner holds a cat against the owner's body, the dose rate at 15 cm will be 22.2 mrem per hour. This depth is assumed to be the depth of the central axis of the owner's body, representing whole body dose.

If the cat is held against the owner's body two hours per day, external whole body dose could be 115 mrem in the year following treatment, and the Total Effective Dose Equivalent will be 143 mrem. Radiocat mitigates the probability of this scenario by screening owners before accepting cats for treatment, and reinforcing the importance of instructions when the cats are admitted for treatment and when they are released to the owner's care.

Please call me at 847-965-1999 if you have any questions.

Sincerely,

Eli A. Port, CHP, P.E. (Safety Engineering)

enclosures

ec: Lisa Chicarella
David Herring
Kathy Olsen
Rand Wachsstock
Kathleen Williams

Projected Dose from Release of Patients After Two Days and When The Exposure Rate At One Meter is ≤ 0.5 mR/hr

Releasing a patient to its owners as early as possible has clear clinical advantages. Prolonged hospitalization unnecessarily stresses both the patient and the owner. Radiocat will not release an animal injected with I-131 until 48 hours after treatment and the exposure rate at 1 m is 0.5 mR/hr or less. Measurements of exposure rate will be performed by an Authorized User, by the Radiation Safety Officer, or by a trained technician under the supervision of an Authorized User or the Radiation Safety Officer.

Release after two days and at an exposure rate of 0.5 mR/hr or less at one meter achieves an ALARA balance of maintaining owner dose below the Radiation Dose Limits for Individual Members of the Public in 10 CFR 20 Subpart D and minimizing patient and owner stress. The Total Effective Dose Equivalent is less than 40 mrem in the year following treatment, 28 mrem from internal dose and 3.6 mrem from external dose. Little dose savings would be achieved from longer hospitalization that would increase stress to both owners and patients.

Radiocat provides the attached comprehensive instructions to owners. These instructions emphasize the need to restrict contact with a treated patient and are realistic for patients and owners. Pre-treatment evaluation of owners is used to determine the owners' understanding of the instructions and their willingness to comply with these instructions. The instructions have also prevented any reported incidents of waste from Radiocat patients reaching landfills.

The instructions contain the statement, "I have been given a copy of these instructions and understand that I must comply with the instructions under the conditions the US Nuclear Regulatory Commission (NRC) has set to approve the release. I understand that I am responsible for compliance with these instructions, and that failure to comply may result in enforcement action by the NRC. I also understand that Radiocat will determine when my cat reaches the radiation level required for safe release of my cat set by the NRC."

Prior to scheduling treatment, the owner are screened for commitment to compliance. The owners must sign the instructions agreeing to the conditions in the instructions when cats are being admitted for treatment. Radiocat will not treat a patient

if the owner will not sign the statement, agreeing to the conditions in the instructions. The owners must sign a similar statement before patients are release to emphasize the importance of limiting close contact during the first two weeks following release.

Uptake and excretion of I-131

It is assumed that the initial renal clearance rates for iodine in mammals, including cats, are similar to the human clearance rate. ICRP 53 specifies the renal clearance half-time for iodine as 8 hours. This value corresponds to 0.875 clearance in 24 hours. This value is used to determine free I-131 in cats at the time of release. Cats receive therapeutic doses of 3.5 mCi to 5 mCi. A conservative 5 mCi is used for modeling dose to an owner.

A cat receiving a dose of 5 mCi will typically have an uptake of approximately 20%, or 1 mCi. The remainder of the activity is excreted at the 0.875 day^{-1} clearance rate. The animal will have retained 63 µCi of free iodine after 48 hours. This free iodine is assumed to subsequently be excreted without decay.

A recent presentation, "Dose Assessment for Humans Exposed to Domestic Animals Administered Radioactive Material", DM Hamby, RS Flora, RR Benke, VA Shaffer, K Tapp, IRPA North American Regional Congress, February 2022, reported T_{eff} for I-131 in cats of 1.6 days - 1.8 days. Other studies have observed similar T_{eff}s. In the modeling of dose after release, the more conservative T_{eff} = 1.8 days is used. When T_{eff} = 1.8 days, λ_{eff} = 0.385 $days^{-1}$. These values are used in calculating external dose.

Internal Dose

It is conservatively assumed that a member of the public inhales or ingests up to 0.1%, or 0.063 µCi of the free iodine that was excreted by the cat. The ICRP 30 committed dose to the thyroid is 1.78 rem/µCi I-131. The ingestion of 0.063 µCi would produce a 112 mrem Committed Dose Equivalent to the thyroid. The Committed Effective Dose Equivalent's contribution to the Total Effective Dose Equivalent (TEDE) would be 28 mrem.

External Dose

Radiocat will not release a patient injected with a therapeutic dose of I-131 until the exposure rate at 1 m is 0.5 mR/hour or less. Owners are instructed in writing to limit contact to no more than 2 hours at 3 feet during the first two weeks following release. The attached owner instructions emphasize the need for the owner to restrict contact with a treated cat. Dose equivalent is treated as numerically equal to exposure rate. The dose from intermittent exposure from a decaying external source is:

$$H = \int_0^T \dot{H}\, dt$$

Where: $\dot{H}_0$ is the dose received on the day of release and

$\dot{H}$ is the dose received on subsequent days, equal to $\dot{H}_0 e^{-\lambda_{eff} t}$.

λ_{eff} = 0.385/day

Owners are instructed to limit exposure to the patient during the first two weeks after release to no more than two hours at three feet (90 cm). $\dot{H}_0$ is equal to 1.23 mrem per day.

$$H = \int_0^T \dot{H}\, dt = \dot{H}_0 \int_0^T e^{-\lambda_{eff} \cdot t\ days}\, dt = 1.23\ mrem \int_0^{14} e^{-0.385/day \cdot t\ days}\, dt$$

H = 3.2 mrem when T = 14 days.

After the 14 day period, the owner' interaction with the cat is not restricted.

On day 14, $\dot{H}_{14,external}$, the external dose in 24 hours from the residual I-131 will be 0.14 mrem per day at 15 cm, the assumed the depth of the central axis of the owner's body, representing whole body dose.
$\dot{H}_{external}$ is the dose received on subsequent days, equal to $\dot{H}_{14,external}\, e^{-\lambda_{eff} t}$

$$H_{external} = \dot{H}_{external,14} \int_0^T e^{-\lambda_{eff} \cdot t}\, dt = 0.14\ mrem \int_0^{351} e^{-0.385/day \cdot t\ days}\, dt = 0.36\ \text{mrem}.$$

A typical litter box is 45 cm x 60 cm. An individual may work for up to 5 minutes per day cleaning a litter box with the individual's body 50 cm from the litter. All unbound I-131 following release is assumed deposited without decay in the litter box. The initial dose rate 50 cm from 63 µCi in a 45 cm x 60 cm plane is 0.05 mrem/hr. Servicing the litter box for five minutes contributes 0.004 mrem in a day or 0.046 mrem in the year following release if no activity is removed during servicing.

The Total Effective Dose Equivalent in the year following treatment from internal and external sources is 28 mrem + 3.2 mrem + 0.36 mrem + 0.046 mrem = 31.6 mrem.

Radiocat's goal is to maintain doses to owners as low as is reasonably achievable (ALARA), as defined in 10 CFR 20.1003, making every reasonable effort to maintain exposures to radiation as far below the dose limits in the regulations as is practical, consistent with the purpose for which the use of I-131 for the treatment of pets is undertaken, taking into account the state of technology, the economics of improvements in relation to state of technology, the economics of improvements in relation to benefits to the public health and safety, and other societal and socioeconomic considerations, and in relation to utilization I-131 in the public interest.

INSTRUCTION FOR OWNERS OF CATS THAT HAVE BEEN TREATED BY RADIOCAT

After being released from therapy, your cat will still possess a small amount of I-131 that will be excreted primarily in urine, feces, and saliva. The I-131 in the cat is radioactive and is a source of radiation to members of your household and other members of the general public. You don't need to totally isolate your cat, but you must follow these safety precautions which are required by the US Nuclear Regulatory Commission (NRC) to keep doses below the NRC limits. The dose you and your family will receive is kept low by spending as little time as possible with your cat and by keeping the cat three feet from people during the first two weeks it is at home. The cat must be kept indoors and must use a litter box.

1. Put a plastic liner in the cat's litter box before adding litter. Keep the box out of occupied bedrooms and the kitchen and away from unsupervised pets and children. Wear rubber gloves when removing soiled litter from the box. Use the gloves only for this and the other tasks described in these instructions.

2. You must use flushable litter. Scoop soiled litter into toilet and flush. Follow the manufacturer's instructions on the package. The litter must be disposed of in the toilet. Do not discard the litter in trash. The radioactive material your cat excretes will set off an alarm at a waste site and may result in an investigation by the NRC or another enforcement agency.

3. If your cat vomits or urinates outside the litter box, wear the rubber gloves & use normal cleaning procedures. When possible, use flushable tissue for the cleanup. Thoroughly wash all non-flushable items before disposal.

4. Pregnant women and minors should not change the cat's litter boxes.

5. Close contact with your cat may transfer radioactive material to you, your family, or members of the general public. Do not permit the cat to lick you during the first two weeks after treatment. Avoid any snuggling, and face or hand contact with your cat's saliva & footpads.

6. Radiation dose limits may be exceeded if you do not follow these instructions. Do not permit your cat to sleep with you. Keep your cat in its crate or in an unoccupied room at night. Do not hold the cat in your lap because this increases the dose to your gonads. Wear rubber gloves to pill the cat, if needed. Limit your contact to no more than 2 hours at 3 feet. This amount of attention will satisfy your cat's emotional needs, and will keep your exposure to radiation to below one-half of the limit in NRC regulations.

7. Keep your cat away from food preparation and eating areas.

8. Instruct children to avoid the cat, and wash their hands if they touch it. Small children may not remember or understand these rules. So, take extra precautions by having them wash their hands often, especially before eating.

9. Keep the cat confined to your home. The radioactivity in the cat's urine or feces must be kept away from wildlife, neighbors and their children, and other pets. Flush any remaining soiled litter in small quantities at a time, following the manufacturer's instructions. Put on your gloves and thoroughly wash them before disposal. Your cat will have lost essentially its entire radioactivity after two weeks and it may return to its normal routines.

10. In the event your cat needs to be taken to another veterinarian, you must contact Radiocat at 1-800-323-9729 for instructions. If the cat requires emergency treatment and contacting Radiocat prior to going to another veterinarian may endanger the cat, inform the veterinarian about the treatment with I-131 and give the veterinarian a copy of these instructions.

11. Should the animal die, you must contact Radiocat at 800-323-9729 for instructions.

OWNER STATEMENT AT ADMISSION

I have been given a copy of these instructions and understand that I must comply with the instructions under the conditions the US Nuclear Regulatory Commission (NRC) has set to approve the release, and that failure to comply may result in enforcement action by the NRC. I understand that I am responsible for compliance with these instructions. I also understand that Radiocat will determine when my cat reaches the radiation level required for safe release of my cat set by the NRC.

_____ _____

Owner's Signature at Admission Date

AUTHORIZED USER STATEMENT

The owner has been interviewed and given these instructions on how to take care of their pet when at home.

_____ _____

Authorized User's Signature Prior to Treatment Date

Administration of dose: Date: __/__/__ Time: ____: ____.

RELEASE MUST BE AT LEAST 48 HOURS AFTER TREATMENT

Exposure Rate At 1 m At Release: _____mR/hr Date___/___/___ Time:___:___.

Measured by:_____

OWNER STATEMENT AT DISCHARGE

I have been given a copy of these instructions and understand that I must comply with the instructions under the conditions the US Nuclear Regulatory Commission has set to approve the release, and that failure to comply may result in enforcement action by the NRC. I understand that I am responsible for compliance with these instructions.

_____ _____

Owner's Signature at Discharge Date