THESIS

Submitted by

Meghan Marie Dieffenthaller

Department of Environmental and Radiological Health Sciences

In partial fulfillment of the requirements

For the Degree of Master of Science

Colorado State University

Fort Collins, Colorado

Spring, 2021

Master's Committee:

Advisor: Thomas Johnson

Ralf Sudowe

Michael Pagliassotti

Copyright by Meghan Marie Dieffenthaller 2021 All Rights Reserved

ABSTRACT

RADIATION DOSE TO VETERINARIANS AND VETERINARY TECHNICIANS DURING PERFORMANCE OF RADIOIODINE TREATMENT OF FELIS CATUS

The purpose of this project is to determine I-131 uptake of veterinarians or veterinary staff when radioiodine (I-131) is administered via injection to domesticated cats (*Felis catus*) with hyperthyroidism. Currently, veterinarians and staff perform a bioassay either every three months or if they have administered a cumulative 10 mCi of I-131. Veterinarians and staff undergo specific training for the handling of radioiodine injection of cats to minimize and prevent an intake. A bioassay is performed post cat injection to determine if I-131 was inhaled or absorbed. The frequency of these bioassays requires dedicated time of the veterinarians and those who must perform the bioassay. Bioassay data from veterinarians and staff at the Colorado State University Veterinary Teaching Hospital (CSU VTH) administering I-131 from the past 20 years were analyzed to ascertain if there is a correlation between the amount of time elapsed between the I-131 administration and the bioassay and the net counts resulting from the bioassay. The amount of I-131 administration and the bioassay net counts were also analyzed to determine if there was a correlation. No correlations were found, and out of 168 I-131 administrations over 20 years, only 7 bioassays showed measurable doses of I-131 of a committed dose equivalent (CDE) of 5.71 mrem (n=1), 7.53 mrem (n=2), 10.9 mrem (n=1), 20.7 mrem (n=1), and 75.1 mrem (n=2). The current precautions taken to prevent the intake of I-131 appear sufficient enough to allow for less frequent bioassays.

ACKNOWLEDGEMENTS

Thank you to Drs. Thomas Johnson, Ralf Sudowe, and Alexander Brandl who have dedicated so much time and talent to teaching health physics, especially during challenges the pandemic. Thank you especially to Dr. Johnson who has pushed me to finish my thesis before my daughter's due date. This project would also not have been possible without the aid of Jim Abraham, who was able to provide me with so much information about Colorado State University's radiation control office and the Veterinary Teaching Hospital. Thank you also to Dr. Ben Sharp who worked with me on identifying the proper statistical tests to run on the data. The Nuclear Regulatory Commission was able to provide funding to support me for three-fourths of this project, and for that I am extremely grateful. Thank you also to the other health physics graduate students in my cohort who were always ready to help with homework assignments, laboratory reports, and studying for exams.

A special thank you to my parents, who fostered a love of science and research in me from a young age, inspired me to pursue graduate school, and taught me to work hard for what I want to achieve. None of this would have been possible without my husband John Paul, who supported and loved me throughout my time in graduate school, no matter how hysterical I became while researching and writing my thesis while pregnant. Thank you to my daughter Kristin, born two days after my defense, who, though she does not know it yet, has greatly inspired me. Lastly, thanks be to God, for because of His providence my life has been so blessed.

DEDICATION

To my husband John Paul and our daughter Kristin, who are my reasons for everything.

TABLE OF CONTENTS

ABSTRACT	ii
ACKNOWLEDGEMENTS	iii
DEDICATION	iv
LIST OF TABLES	vi
LIST OF FIGURES	vii
INTRODUCTION	1
MATERIALS AND METHODS	12
RESULTS	17
DISCUSSION	32
CONCLUSION	39
REFERENCES	41
APPENDIX A	44
APPENDIX B	45
APPENDIX C	47
APPENDIX D	49
APPENDIX E	50
APPENDIX F	56
LIST OF ABBREVIATIONS	60

LIST OF TABLES

Table 1: Z-scores for net counts	50
Table 2: Total background counts, lower limit of detection, minimum detectable activity,	
predicted maximum intake of I-131, and decision level.	56

LIST OF FIGURES

Figure 1: Movement of iodine through the body
Figure 2: Sodium iodide detector set up
Figure 3: Neck phantom
Figure 4: Normal Q-Q Plot of all 168 net counts to show normality
Figure 5: Normal Q-Q Plot of Net Counts with Elimination of Counts Greater than One Standard
Deviation Below Zero
Figure 6: Histogram of All Net Counts to Show Distribution
Figure 7: Histogram of Net Counts with Elimination of Counts Greater than One Standard
Deviation Below Zero
Figure 8: Linear Regression Model of All Net Counts vs Days Elapsed Between Administration
and Bioassay
Figure 9: Histogram of Residuals from Linear Regression Model of All Net Counts vs Days
Elapsed Between Administration and Bioassay
Figure 10: Linear Regression Model of Net Counts with Elimination of Counts Greater than One
Standard Deviation Below Zero vs Days Elapsed Between Administration and Bioassay 26
Figure 11: Histogram of Residuals from Linear Regression Model of Net Counts with
Elimination of Counts Greater than One Standard Deviation Below Zero vs Days Elapsed
Between Administration and Bioassay. 27
Figure 12: Linear Regression Model of All Net Counts and Amount of I-131 Administered 28
Figure 13: Histogram of Residuals from Linear Regression Model of All Net Counts and
Amount of I-131 Administered

Figure 14: Linear Regression Model of Net Counts with Elimination of Counts Greater than Or	ne
Standard Deviation Below Zero vs Amount of I-131 Administered.	30
Figure 15: Histogram of Residuals from Linear Regression Model of Net Counts with	
Elimination of Counts Greater than One Standard Deviation Below Zero vs Amount of I-131	
Administered	31

INTRODUCTION

Thyroid Hormones and Thyroid Tumors in Cats

The thyroid is necessary for the regulation of metabolism in the body and is dependent on a source of iodine to function properly. Domesticated cats (*Felis catus*) are unable to produce iodine themselves, so they obtain it from food rich in iodine (Chung 2014). Two of the hormones the thyroid produces are reliant on iodine for their creation: the "thyroid hormones", triiodothyronine (T3) and tetraiodothyronine (T4). The level of hormones in the bloodstream is regulated by signals from the pituitary gland, signaling the thyroid gland to release either more or less hormones. T3 and T4, which increase the basal metabolic rate, are reliant on the supply of iodine in order to be created, thus causing iodine to accumulate in the thyroid in greater quantities than elsewhere in the body (IQWiG 2018).

Domesticated cats are prone to developing thyroid adenomas or carcinomas as they age. The cancerous cells in the thyroid can cause hyperthyroidism, a condition in which the thyroid produces too much T3 and T4. Signs of a cat with hyperthyroidism can include weight loss, anorexia, hyperactivity, and an abnormal coat (Barber 2007). Veterinarians can conduct bloodwork, urinalysis, and other biochemical analyses, such as checking for azotemia and hyperphosphatemia, on the cats to confirm if they have hyperthyroidism, thus indicating that they may have a thyroid adenoma or carcinoma (Mooney 2001). Another common issue with thyroid tumors in cats is that there is a high risk of metastasis, causing concern that other tumors could develop elsewhere in the body (Barber 2007).

Thyroid Tumors Treatment in Cats

When an adenoma or carcinoma forms in the thyroid, radioiodine (I-131) can be used to destroy the cells causing the tumor. Since radioiodine is chemically identical to stable iodine, the body retains and metabolizes all isotopes of iodine in the same way. While I-127, found naturally in food, is stable, I-131 undergoes beta decay. The complete decay scheme for I-131 is in Appendix A. Since hyperthyroidism, an indicator of the likely presence of a thyroid tumor, causes an increase in the production of T3 and T4, the thyroid will be using more iodine than when it is functioning properly, ensuring the uptake of the radioiodine by the thyroid (Mooney 2001). Even if the tumor is not accompanied by hyperthyroidism, the thyroid will still uptake the I-131. In addition to the thyroid preferentially uptaking iodine, the most metabolically active tissues in the thyroid, the cancer cells, will uptake more iodine than the normal cells.

The average amount of energy released by a beta particle in the decay of I-131 is 0.1916 MeV¹. The maximum range of the beta particle can be determined using Equation 5.3 from *Introduction to Health Physics*, 5th Edition.

$$R = 0.404E^{1.38} \tag{1}$$

where

 $R = \text{range of the beta particle in g/cm}^2$

E = maximum energy of the beta particle in MeV

The range of a beta particle from I-131 is approximately 0.411 g/cm². The average mass of a normal cat's thyroid is 350 mg (Cartee et al. 1993). Assuming tissue has the same density as

¹ <u>https://www.nndc.bnl.gov/nudat2/decaysearchdirect.jsp?nuc=131I&unc=nds</u> Accessed 22 December 2020.

water (1 g/cm³), the volume of the thyroid is 0.350 cm^3 , 0.04 cm is the approximate distance the beta particles will travel, so the bulk of I-131 emissions will be assumed to be absorbed in the thyroid. The average dimensions of a cat's thyroid are $19.31 \text{ mm} \times 5.42 \text{ mm} \times 3.23 \text{ mm}$, so a beta particle deposited in the middle of the thyroid would not have sufficient energy to escape (Cartee et al. 1993).

The energy deposited by the decay of I-131 is sufficient to cause single stranded breaks (SSBs) and double stranded breaks (DSBs) in the DNA of the cancerous and normal cells within the thyroid, though the normal cells outside the thyroid are spared because the majority of the dose from I-131 comes from beta decay. DNA is normally capable of repairing an SSB or DSB through homologous repair or non-homologous end joining. As the amount of SSBs and DSBs increase with the continued presence of I-131 in the thyroid, however, the DNA is less capable of keeping up with the repairs and ensuring their viability, especially if there is clustered damage, and thus induces cell death through apoptosis (Sage et al. 2017). The body is able to naturally replace the normal thyroid cells over time and normal thyroid function resumes. Radioiodine treatment is highly successful in cats and usually there is no need for a second administration (Barber 2007).

I-131 can be delivered either subcutaneously or intravenously in doses of either 74 – 222 MBq (2-6 mCi) for adenomas or 1.11 – 1.48 GBq (30-40 mCi) for carcinomas (HICON 1971). When radioiodine is taken into the human bloodstream, 70% of it travels directly to the urinary tract and is eliminated from the body within 7 days. The other 30% is uptaken by the thyroid, metabolized by the tissues, and converted into inorganic iodine. 20% of the inorganic iodine from the thyroid is eliminated in the feces, the other 80% is brought back into the bloodstream (ICRP 1989). Figure 1 shows the pathway that iodine takes when it enters the human body.

Iodine is assumed to behave similarly in cats. The effective half-life of radioiodine is approximately 8 days in humans, and it is assumed to be similar in cats. The cat's owner's radiation dose is maintained as low as reasonably achievable (ALARA) by keeping the cat in the hospital for 96 hours (12 half lives) and releasing the cat when the measured exposure rate from 30 cm (one foot) is no more than 0.129 μ C/kg (0.5 mR/h), in accordance with the regulations Colorado State University (CSU) has from the Colorado Department of Public Health and the Environment (CDPHE) (CDPHE 2019) .

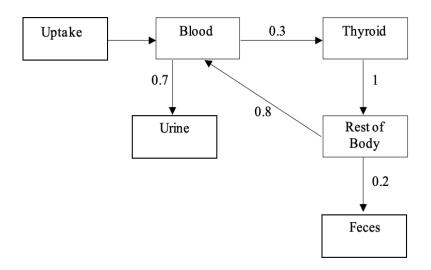


Figure 1: Movement of iodine through the body.

Chemical Form of Administered Iodine-131

The I-131 used is in a solution of sodium iodide from HICONTM. The solution has carrier-free NaI with a radioconcentration of 1,000 mCi/mL, 2 mg of diosodium edetate dihydrate USP, 4.4 mg of sodium thiosulfate pentahydrate USP, and 40 mg of dibasic sodium phosphate anhydrous USP (HICON 1971). While it is possible that the iodine could become volatilized, thus becoming an inhalation hazard to the person performing the procedure, there

have been precautionary measures taken to ensure that volatilization is unlikely. There are specific conditions that the I-131 solution must have in order to become volatilized. According to the safety data sheet (SDS), the I-131 has a low reactivity and will remain stable while stored in a dry, dark, cool, and ventilated area (Jubilant DraxImage 2017). If it is mixed with an acid or heated there may be a release of gaseous I-131. In order for the iodine to become volatile, the iodine ion (I⁻) must first become oxidized from the sodium iodide and form I₂. Potential oxidation is slowed by storing the I-131 solution in a dark, cool place. The sodium thiosulfate pentahydrate in the solution acts as a reducing agent, preventing any potential volatilization of the iodine through oxidation (Hung 1997).

CSU Procedures for Iodine-131 Administration

Colorado State University's (CSU) James L. Voss Veterinary Teaching Hospital (VTH) offers thyroid cancer treatment for domesticated cats. The administering person is required to wear personal protective equipment (PPE), which includes gloves, eye protection, a surgical mask, a lab coat, pants, and close-toed shoes².

Sodium Iodide (NaI(T1)) Detector

I-131 in the thyroid can be detected using a scintillation counter, most commonly a sodium iodide crystal with thallium "impurities" (NaI(Tl)) to act as an activator. I-131 emits a 364 keV gamma ray with an abundance of approximately 81% that can be detected outside the human body and with an NaI detector (NCHPS 2006). Within the structure of the crystal there are two discrete energy bands: the conduction band and the valence band. The two bands are

5

² From correspondence with RSO Jim Abraham.

separated by the forbidden gap. Electrons bound to the crystal are typically present in the valence band, the lower of the two. When a gamma ray interacts with the atoms of the crystal, its kinetic energy causes the electrons to become excited and ionized. As the electrons become excited, they jump from the valence band to the conduction band, leaving a hole where it left. The electron-hole pair will rejoin through the electron in the conduction band releasing a certain quantum of light to fall back to the valence band. The light is sensed by the cathode of a photomultiplier tube within the detector. Electrons are removed from the cathode and travel to a dynode. As these original electrons strike the dynode, which is a second cathode with a higher positive voltage, additional electrons are removed from the dynode. The accumulation of electrons travels to the next dynode, and the process continues for a total of about ten times, thus ultimately increasing the number of electrons proportionally to the amount of energy deposited by the gamma ray originally. The output pulse is then detected (Johnson 2017).

Bioassay of Iodine-131 Administering Personnel

A background count is always conducted before any bioassays. In order to conduct a background count, an anthropomorphic phantom is placed under the NaI(Tl) detector. The detector used at CSU is the Captus 3000 (Capintec, Inc. 2010). The materials used in the phantoms have a density that is tissue-equivalent so that radiation will interact with it in the same way it would with normal tissue (Ramos et al. 2017). The specific phantom used at CSU is the Mirion Technologies CAPTUS Neck Phantom, which is made of polymethyl methacralate (Lucite)³. Lucite has a density of 1.19 g/cm³ ⁴, which is comparable to that of soft tissue (1

³ https://capintec.com/product/neck-phantom/ Accessed 14 December 2020.

⁴ https://physics.nist.gov/cgi-bin/Star/compos.pl?matno=223 Accessed 14 December 2020.

g/cm³). The background count of the room with the phantom in it allows for subtraction of radiation that is not due to the iodine administration, increasing the precision of the background count. Figure 2 shows the NaI(Tl) detector set up, and Figure 3 shows the phantom that is used to determine the background counts.



Figure 2: Sodium iodide detector set up.



Figure 3: Neck phantom.

Prior to handling any I-131, the administering person must have a baseline bioassay performed. Under the radioactive materials license that CSU has from the CDPHE, all individuals who administer I-131 to cats and those who care for the cats post-administration must have bioassays performed within 24-72 hours of administration (CDPHE 2019). The regulations documented in the CDPHE guidelines are specifically written for the administering persons following the guidelines from NRC Regulatory Guide 8.20. Regulatory Guide 8.20 states that bioassays are necessary for people who work with a cumulative amount of at least 370 MBq (10

mCi) of I-131 over a three-month period when the I-131 is in a nonvolatile form when handled on a lab bench or in an open room. If at any point during the three-month period the cumulative amount is greater than 370 MBq (10 mCi), a bioassay must be conducted. Regulatory Guide 8.20 also lists predetermined action levels (PALs). If the administering person's thyroid contains more radioactivity than a PAL, further tests and investigations must be conducted. If the thyroid content exceeds 37 kBq (1 μ Ci), then an investigation is conducted, and measures must be taken to prevent any similar exposures. A follow up in vivo bioassay must be conducted within 24 hours of the first one, or an in vitro bioassay must be taken within two weeks of the first one. If the thyroid content exceeds 185 kBq (5 μ Ci), then a medical professional must be contacted within 2-3 hours so thyroid blocking can be evaluated and performed if necessary. Bioassay measurements at 1-week intervals must be taken until the thyroid content is less than 1 μ Ci (NRC 2014). If the dose to the vet or vet tech exceeds the whole body effective dose limit of 0.05 Sv (5 rem), or organ dose limit of 0.5 Sv (50 rem), then their work would have to be restricted from additional dose (NRC 1991).

Regulatory Limits for Iodine-131

The nonstochastic annual limit of intake (NALI) is the limit at which the incorporation of a radionuclide to an organ will not reach the threshold of causing nonstochastic effects, such as tissue necrosis or radiation sickness. The inhalation NALI of I-131 is 50 µCi, which delivers an equivalent dose of 0.5 Sv (50 rem) to the thyroid (NRC 2018). Based on the current recommendations listed in Regulatory Guide 8.20, the administering person must have a bioassay performed if they have worked with a cumulative amount of 10 mCi of I-131 during a three-month (90 day) period (10 mCi, if inhaled, is the equivalent of 10 rems to the thyroid).

If the administering person reached 10% of the NALI, equivalent to an uptake of 1.67 μCi (5 rems thyroid), the I-131 uptaken by the thyroid would still be detectable above background 55.8 days post-intake (using the CSU NaI(Tl) system), as shown in Appendix B. Regulatory Guide 8.20 states that "methods or solutions that differ from those described in this regulatory guide may be deemed acceptable if they provide sufficient basis and information for the NRC staff to verify that the proposed alternative demonstrates compliance with the appropriate NRC regulations". The intake limit of 10 mCi currently set by the regulatory guide is 20% of the NALI, meaning an uptake of 3.33 mCi of I-131, will be detectable using the CSU NaI(Tl) system for 138.6 days, as shown in Appendix C.

A previous study involving the iodination of human patients indicated that any uptakes by technicians have been well below regulatory limits (Collier 2016). If all doses to patients are 10% below the legal limits, individual monitoring of the administering person is not required by 10 CFR 20.1502. 10 CFR 20.1502 also states that no monitoring is required if all intakes of the administering person are likely to be 10% below the legal limits.

Costs Associated with Bioassay

Every time a bioassay is performed, there is a loss in productivity, both for the radiation safety officer (RSO) and administering person. The commute approximately from the CSU VTH to the RSO is approximately 8 minutes if driving, 10 minutes if biking. Each administering person must wait to ensure the RSO is free to conduct the thyroid scan. The scan lasts for a minimum of 10 minutes, with 5 minutes to count the background and 5 minutes to count the person. Then there is the 8-10-minute commute back to the CSU VTH. The RSO must also

prepare paperwork for each bioassay prior and post analysis. Overall this whole process costs a minimum of 40 - 60 minutes of the workday for two people each time a bioassay is performed.

Additionally, the failure to perform a bioassay would put the veterinary hospital and RSO in violation of written protocols, which could result in fines, or even a loss of radioactive materials licenses and the right to use radioactive materials.

Purpose of Study

The purpose of this study is to ascertain if a correlation exists between the amount of radioiodine administered to domesticated cats and iodine uptake in the thyroid of the administering person. Additionally, determination of evidence to decrease bioassay frequency will be examined. It is hypothesized that that there would be a negative correlation between the time elapsed and the net counts and a positive correlation between amount of I-131 administered and the net counts.

MATERIALS AND METHODS

This project was determined exempt by the Colorado State University Institutional Review Board. The letter documenting the exemption can be found in Appendix D.

Scans of 168 iodine bioassays from veterinarians and veterinary technicians who worked at the CSU VTH were de-identified by the RSO. The date of the radioiodine administration, amount of radioiodine administered (mCi), date of the bioassay, amount of time elapsed between administration and the bioassay (days), radioiodine background (cpm), net counts (cpm), and activity of the administering person's thyroid (mCi) were recorded in an Excel spreadsheet.

Z-score Calculation

A Z-score was calculated for all 168 net count data points, eliminating those above one standard deviation below zero using Equation 2.

$$Z = \frac{x - \mu}{\sigma} \tag{2}$$

where

x = observed value

 μ = mean of sample

 σ = standard deviation of sample

A z-score was assigned since any net counts below zero show that the administering person did not have an uptake of iodine and had blocked the detector from any background radiation more effectively than the phantom had during the background count.

Lower Limit of Detection and Minimum Detectable Activity Determination

The lower limit of detection (LLD) was calculated for background measurements using Equation 3 to show the threshold of radioactivity the detector could detect above background (Johnson 2017).

$$LLD = (4.66 \cdot \sigma_b) + 2.71 \tag{3}$$

where

 σ_b = standard deviation of the background

Equation 3 can only be used if the background and sample counting times are equal. For the thyroid bioassay counts, the background and person are each counted for five minutes.

The minimum detectable activity (MDA) was calculated for each of the background measurements to show what activity in the administering person's thyroid would be able to be detected using Equation 4.

$$MDA = \frac{LLD}{K \cdot t_g} \tag{4}$$

where

K = counter efficiency and a conversion to change transformation rate to Bq t_g = sample and background counting time

Maximum Level of Intake

The maximum level of intake that an administering person would have had was calculated using Equation 5, which is based on Equation 1.5 in NUREG 1400, to show whether a

maximum intake of I-131 by the administering person would have been detectable by the sodium iodide detector.

$$I_f = \frac{A \cdot 10^{-6}}{ALI} \tag{5}$$

where

 I_f = predicted maximum likely intake as a fraction of the ALI

A = activity administered (Ci)

ALI = annual limit of intake for radionuclide from 10 CFR 20 Appendix B

<u>Decision Level Determination</u>

The decision level (L_C) was then calculated for each background measurement using Equation 6 to determine if any of the samples required further investigation (ANSI HPS N13.30-2011). If the net counts exceed the L_C , then further investigation is required.

$$L_{\rm C} = 2.33\sqrt{n/r} \tag{6}$$

where

n= the number of background counts

r = count rate

Committed Dose Equivalent

The committed dose equivalent (CDE) was calculated for the bioassays that did show a positive result to show the dose to an administering person's thyroid over 50 years based on the activity measurement of their thyroid during the bioassay. The CDE was calculated using

Equations 7 - 12 and assuming that the uptake was 0.3 of the intake, based on ICRP 30 (ICRP 1979).

$$A = A_0 e^{-\lambda t} \tag{7}$$

where

A = activity measured at time of bioassay

 A_0 = original activity

 λ = decay constant of isotope

t = time elapsed

$$A_0 \div 0.3 = I_0 \tag{8}$$

where

 I_0 = original intake

$$I_0 \times S = \dot{D} \tag{9}$$

where

S = MIRD table S value (rad/ $\mu Ci \cdot hr$)

 $\dot{D} = \text{dose rate}$

$$D = \frac{\dot{D}}{\lambda_e} (1 - e^{-\lambda t}) \tag{10}$$

where

D = dose

 λ_e = effective half-life of isotope

t = 50 years

$$H_T = D \times w_R \tag{11}$$

where

 H_T = equivalent dose to tissue due to radiation, R

 w_R = radiation weighting factor

R Software and RStudio Version 1.3.1073 were used to perform statistical tests on the data. The Shapiro-Wilks test for normality was used to calculate the normality of the distribution of net counts both with and without the counts that were more than one standard deviation below zero to determine if removing those points increased the normality of the distribution. A one sample two-sided t-test was used to see if the net counts were equally distributed around zero. A histogram was made to further validate the results of the t-test. Linear regression was used to show if there is a correlation between the net counts and the days elapsed between administration and the bioassay. A histogram was made for the residuals of the linear regression analysis to show if the regression line was accurately fit to the data. A second linear regression model was made to show if there is a correlation between the net counts and the amount of I-131 (mCi) administered. Another histogram was made for the residuals of the linear regression analysis to show if the regression line was accurately fit to the data. The activity measured in each person was unable to statistically analyzed due to only 7 people with net counts above background.

RESULTS

Z-score Calculation

A z-score was calculated for all the net counts. The results can be found in Appendix E. 12 of the net count data points had negative standard deviations greater than one, so the data points analyze decreased from 168 to 156.

Lower Limit of Detection and Minimum Detectable Activity

The LLD was calculated to ascertain the threshold of counts the detector could distinguish above background. 101 background counts were analyzed due to the fact that not all of the bioassay reports included the background count; some only listed the overall net counts. The results are in Appendix F.

The MDA, dependent on the LLD, was calculated for each background count to show the lowest detectable activity that the NaI(Tl) detector would be able to detect above background level with Type I and Type II error at 5%. The results are in Appendix F. The radiation control office (RCO) has set up the NaI(Tl) detector so that any measurements over 40 nCi would be assumed a positive detection, and based on the calculated MDAs, the greatest MDA is 3.32 nCi, so the detector would have been able to pick up any activity in the thyroid that the RCO has indicated would be a positive detection.

Maximum Level of Intake

The maximum level of intake was calculated for the 101 I-131 administrations that included a background count in the bioassay to show the greatest amount of I-131 an

administering person could have inhaled based on the amount of I-131 they administered to the cat. This amount was then compared to the MDA to confirm that the radioactivity would have been detected. The results are in Appendix F. The fraction of I-131 uptaken by the thyroid is 0.3 of the intake, and based on the results in Appendix F, 101 are above the MDA.

Decision Level Determination

The L_C was not calculated by the RSO, but rather a value of 40 nCi was used operationally as the L_C . The L_C is used to determine if any samples would require further investigation of being a potential uptake, and assumes a Type I error of 5% and Type II error of 50%. If the net counts of the sample exceed the L_C , it is an indication that further investigation is required. The results from the calculation are in Appendix F. Based on the calculation, 11 samples (highlighted in yellow) require further investigation.

Committed Dose Equivalent

The CDE was calculated for any positive results from the bioassays so that the dose to an administering person's thyroid over 50 years could be determined in the case that the uptakes were not false positives. Eight of the 168 bioassays showed a measurable activity, all of which measured 0.001 μCi. The measurements that showed a measurable activity were taken either 0 days, 3 days, 7 days, 14 days, or 28 days post-administration. The calculated CDEs found were 5.71 mrem (n=1), 7.53 mrem (n=2), 10.9 mrem (n=1), 20.7 mrem (n=1), and 75.1 mrem (n=2), respectively.

Net Counts Normality

The Shapiro-Wilks test for normality was performed on all 168 net count data points. The null hypothesis was that there is a normal distribution of net counts, and the alternative hypothesis was that there was a non-normal distribution of net counts. The p-value from the test was 2.2×10^{-16} , which indicates that the null hypothesis is rejected, and the alternative hypothesis is accepted. A Normal Q-Q Plot of the net counts was also made and is shown below in Figure 4.

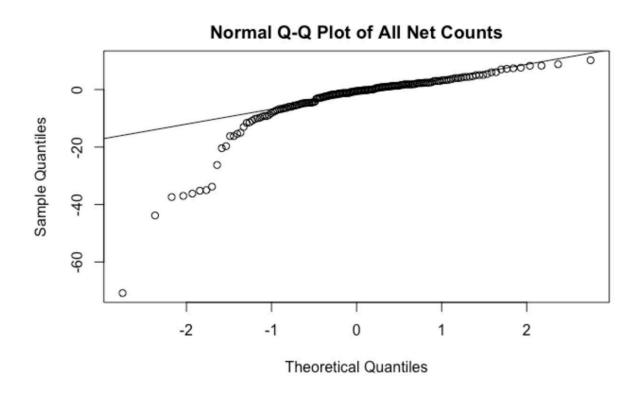


Figure 4: Normal Q-Q Plot of all 168 net counts to show normality.

A Normal Q-Q plot that shows a normal distribution of data should be completely linear with no curvature. Based on the Normal Q-Q plot in Figure 4, there is a lot of curvature, further validating the rejection of the null hypothesis.

A Z-score was calculated for all the net counts, and all negative net counts with a standard deviation greater than one were removed. This was done because negative net counts indicate that the background count was higher than the bioassay count, and so there could have been no uptake of radioiodine, and the administering person's thyroid blocked the detector from the background more than the phantom. The Shapiro-Wilks test was reperformed after removal of the negative counts. The p-value greatly increased to 0.00049. While this still indicates that the null hypothesis is rejected, thus accepting the alternative hypothesis of a non-normal distribution of net counts, the normality of the data did increase with the elimination of the net counts that were less than one standard deviation below zero. A Normal Q-Q Plot was made and is shown in Figure 5.

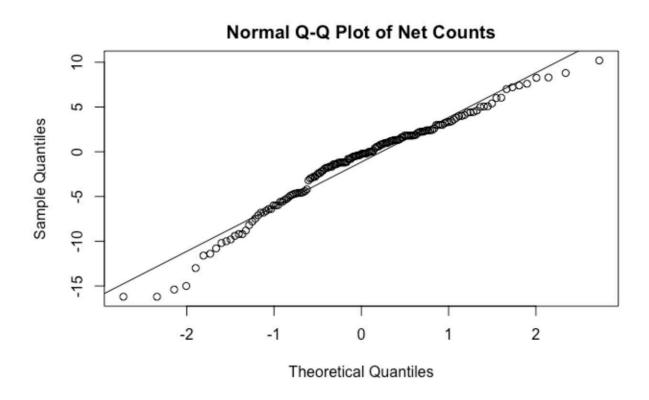


Figure 5: Normal Q-Q Plot of Net Counts with Elimination of Counts Greater than One Standard Deviation Below Zero.

The Normal Q-Q Plot of the log net counts much less curvature than the Normal Q-Q Plot shown in Figure 4, further validating the results from the Shapiro-Wilks test that the normality of the net counts did increase when they were log transformed.

Net Counts Distribution

168 net counts were then analyzed using a one-sample two-sided t-test to determine if there was an equal distribution above and below zero. The p-value given by the test was 5.8×10^{-5} . The histogram of the net counts is in Figure 6.

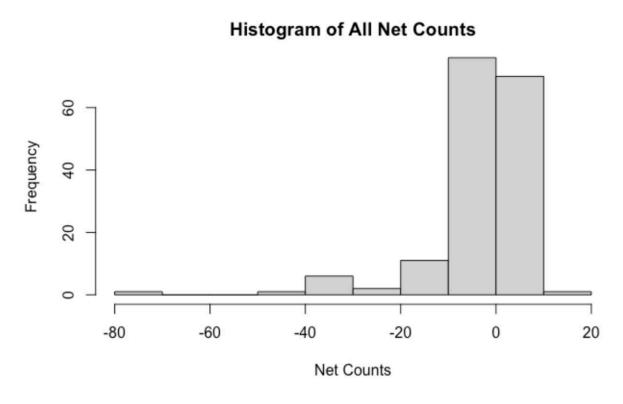


Figure 6: Histogram of All Net Counts to Show Distribution.

The null hypothesis was that there would be an equal distribution of net counts above and below zero. The alternative hypothesis was the mean of the net counts would not be equally distributed around zero. Based on the p-value, the null hypothesis was rejected, and the alternative hypothesis was accepted. In viewing the histogram, it can be visually concluded that there is a disproportional distribution of net counts below zero in comparison to those above zero, though the distribution immediately around zero is normal.

The net counts below zero indicate that the background had a higher amount of detectable radiation than the administering person's thyroid, leading to the conclusion that the person did not have an uptake of radioiodine. For this reason, the net counts greater than one standard deviation below zero were removed and the distribution of net counts around zero was analyzed again. The p-value greatly increased to 0.0095, and though this value still indicates that we reject the null hypothesis of an equal distribution around zero and conclude that it is not equally distributed, it does show that there was a great increase equality of distribution. This can also be visually concluded by the histogram in Figure 7.

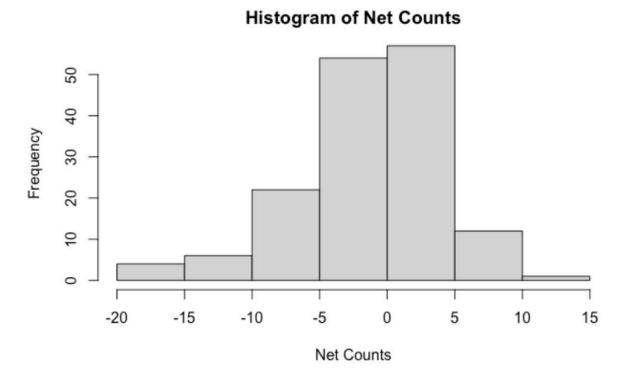


Figure 7: Histogram of Net Counts with Elimination of Counts Greater than One Standard Deviation Below Zero.

<u>Linear Regression of Net Counts and the Time Elapsed Between Administration and the Bioassay</u>

Linear regression was used to check for a correlation between the time elapsed between 168 administrations and bioassays and the net counts corresponding to each administration. The red dots on the model indicate the approximate location of the bioassays that showed a positive activity. The null hypothesis was that there was no correlation between the number of days elapsed and the net counts, and the alternative hypothesis was that there was a correlation. The p-value obtained was 0.82, indicating a failure to reject the null hypothesis. The linear regression model is shown below in Figure 8.

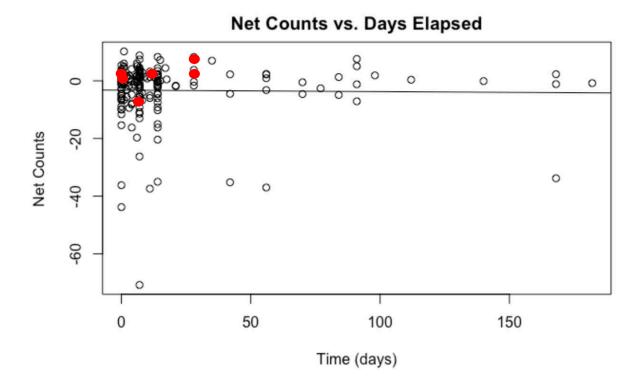


Figure 8: Linear Regression Model of All Net Counts vs Days Elapsed Between Administration and Bioassay.

To further validate the linear regression analysis, a histogram of the residuals was made to show if the line fit the data set well. A residual is the distance between each data point being analyzed and the regression line. Residuals should have a normal distribution in order for the conclusions drawn from the regression analysis to be valid. The histogram of residuals from the linear regression analysis of all the net counts and the days elapsed between I-131 administration and the bioassay is below in Figure 9.

Histogram of Residuals -60 -40 -20 0 20

Figure 9: Histogram of Residuals from Linear Regression Model of All Net Counts vs Days Elapsed Between Administration and Bioassay.

Residuals

Based on Figure 9, the residuals are not normally distributed, which shows an invalidation of the linear regression analysis of all the net counts.

When the negative net counts with a standard deviation greater than one were eliminated, the p-value decreased slightly to 0.22, but this value still indicates that the null hypothesis is rejected and we conclude that there is no correlation between the days elapsed between administration and bioassay and the net counts from each bioassay. The linear regression model for this scenario can be seen in Figure 10, and the red dots indicate the approximate location of a positive bioassay.

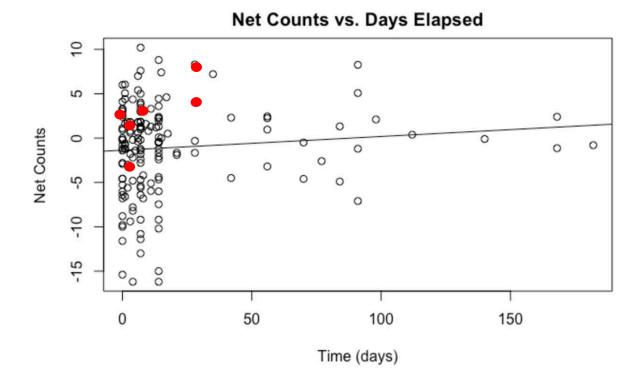


Figure 10: Linear Regression Model of Net Counts with Elimination of Counts Greater than One Standard Deviation Below Zero vs Days Elapsed Between Administration and Bioassay.

Based on the linear regression model, there is a slight positive correlation between the net counts with the elimination of the counts more than one standard deviation below zero and the amount of time elapsed between administration and bioassay, but because of the p-value, the positive slope must therefore be slight enough that it does not indicate a true correlation. A histogram of the residuals from this plot was made to indicate whether or not the linear regression analysis could be validated.

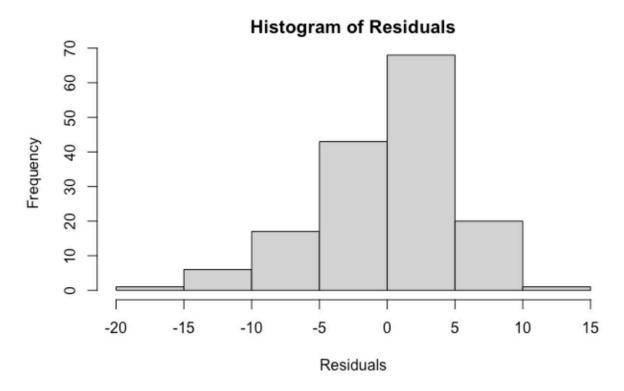


Figure 11: Histogram of Residuals from Linear Regression Model of Net Counts with Elimination of Counts Greater than One Standard Deviation Below Zero vs Days Elapsed Between Administration and Bioassay.

Based on the histogram of residuals in Figure 11, they have a much more normal distribution and therefore the linear regression analysis of the net counts without the points greater than one standard deviation below zero is validated.

Linear Regression of Net Counts and Amount of I-131 (mCi) Administered

Linear regression was used to check for a correlation between 168 values of amounts of I-131 administered the net counts corresponding to each administration. The null hypothesis was that there was no correlation between the amount of I-131 administered and the net counts, and the alternative hypothesis was that there was a correlation. The p-value obtained was 0.72,

indicating a failure to reject the null hypothesis. The linear regression model is below in Figure 12, and the red dots indicate the approximate locations of the positive bioassays.

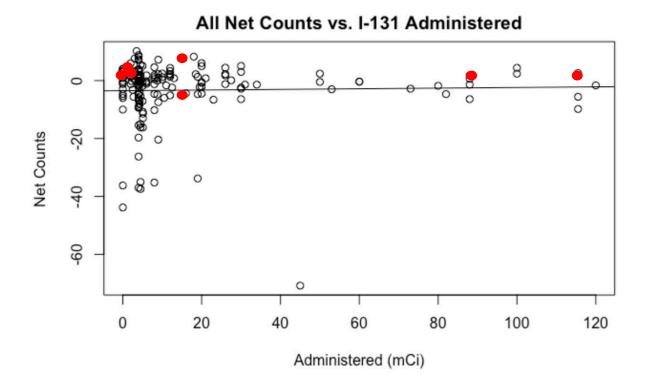


Figure 12: Linear Regression Model of All Net Counts and Amount of I-131 Administered.

Based on the linear regression model in Figure 12, there appears to be no correlation between the amount of I-131 administered and the net counts, further validating conclusion drawn from the p-value. A histogram of the residuals from this linear regression analysis was made to show whether or not the conclusions drawn from the analysis could be validated.

Histogram of Residuals Histogram of Residuals Publication of Residuals Histogram of Residuals

Figure 13: Histogram of Residuals from Linear Regression Model of All Net Counts and Amount of I-131 Administered.

Based on the histogram in Figure 13, the residuals are not normally distributed, and therefore the conclusion drawn from the linear regression analysis of all the net counts and the amount of I-131 administered cannot be validated.

When the negative net counts with a standard deviation greater than one were eliminated, the p-value increased slightly to 0.95, indicating that the null hypothesis is rejected and concluding that there is no correlation between the days elapsed between administration and bioassay and the net counts from each bioassay. A linear regression model was made and is below in Figure 14, and the red dots indicate the approximate locations of the positive bioassays.

Net Counts vs. I-131 Administered Net Counts -15

Figure 14: Linear Regression Model of Net Counts with Elimination of Counts Greater than One Standard Deviation Below Zero vs Amount of I-131 Administered.

Administered (mCi)

Based on the linear regression model plot, there is no correlation between the log of the net counts and the amount of I-131 administered, further validating the conclusion drawn from the p-value. A histogram of the residuals from this linear regression analysis was made to determine whether or not the analysis could be validated.

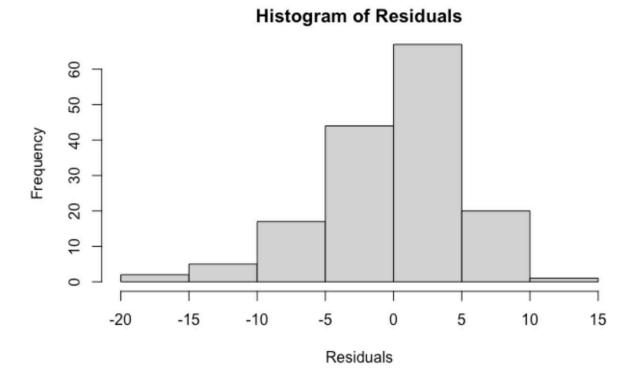


Figure 15: Histogram of Residuals from Linear Regression Model of Net Counts with Elimination of Counts Greater than One Standard Deviation Below Zero vs Amount of I-131 Administered.

Based on Figure 15, the residuals are normally distributed and therefore the conclusion drawn from the linear regression analysis of the net counts without the counts greater than one standard deviation below zero and the amount of I-131 administered is validated.

DISCUSSION

Z-score Calculation

A z-score was calculated for all the net counts, days elapsed between I-131 administration and bioassay, and amounts of I-131 administered, and data points more than three standard deviations away from the mean were eliminated. The removal of these data points caused an increase in the normality of the data.

Net count outliers could have been caused for a variety of reasons, such as a higher or lower radon background on the day of counting or the body of the administering person shielding the detector from background activity more than the phantom.

Lower Limit of Detection and Minimum Detectable Activity

The LLD was calculated for all the background counts to show the minimum amount of counts that would have been detected above background level. Determining the LLD allowed for the MDA to be calculated. The lowest MDA was $0.00126~\mu Ci$, which corresponds to when the detector was able to detect the lowest amount of activity above background level. It is four orders of magnitude below the NALI of $50~\mu Ci$. The lowest recorded activity in an administering person's thyroid was $0.001~\mu Ci$, which shows that the detector was sensitive enough to detect even low amounts of I-131 in the person's thyroid.

Maximum Level of Intake

The maximum level of intake of I-131 was calculated so that the greatest amount of I-131 an administering person could have inhaled could be determined, allowing for the maximum

uptake of I-131 by the thyroid to be calculated and compared against the MDA. A maximum intake of I-131 would have only occurred if the regulations regarding the administration of I-131 were completely disregarded by the administering person. Based on the activity measurements of the administering persons' thyroids in Appendix F, none came close to the maximum uptake, validating the effectiveness of the precautions taken by the administering persons at CSU VTH.

<u>Decision Level Determination</u>

The L_C was calculated so that potential false positives could be identified and investigated further. The calculation showed that 11 bioassay counts could have indicated a false positive. Due to the fact that the bioassay records span the past 20 years and the effective half-life of I-131 is 7.5 days, it would not be possible to go back and investigate the bioassays that were indicated to be potential false positives.

Committed Dose Equivalent

The CDE of the 7 bioassays which showed a measurable activity were at least 4 orders of magnitude below the intake regulatory limit of 10 rem set by the Regulatory Guide 8.20 and the NALI of 50 rem. Based on these results, assuming that the activity measurements were not false positives, over the 20 year span of the bioassay records, uptakes of I-131 by administering persons have been at least three orders of magnitude below regulatory limits.

Net Counts Normality

The analysis from the Shapiro-Wilks test of the 168 net count data points showed that there was still a lack of normality in the distribution of the net counts. The Normal Q-Q Plot of this data set further validated the Shapiro-Wilks test.

The analysis from the Shapiro-Wilks test of the 156 net count data points that excluded those greater than one standard deviation below zero showed that, while there was still a lack of normality, the normality did greatly increase. The linearity of the Normal Q-Q Plot also increased, further validating the Shapiro-Wilks test.

It was reasonable to remove the net counts greater than one standard deviation below zero because they indicated that the background count was higher than the bioassay count. Most likely the administering person blocked the NaI(Tl) detector from the background radiation more effectively than the phantom, causing the net counts to be negative. Based on the negative net counts, the administering person could not have had an uptake of radioiodine.

The lack of normality of net counts could be attributed to many different factors, such as background fluctuations, radon being present naturally in higher or lower quantities in the air on the day of the bioassay, the amount of I-131 that actually interacted with the NaI(Tl) detector that day, or the random nature of radioactive decay. The bioassay data used spanned over 20 years, so there is a great amount of variability in background over such an expanse of time.

Net Counts Distribution

The analysis of the mean of the 168 net counts indicated that the distribution falls below zero, meaning that overall the bioassays indicated that the administering persons had a lower I-131 count than the background measurement. This could happen for multiple reasons, one being the random nature of radioactive decay. Another reason could be that although an

anthropomorphic phantom was in the place of a human while the background was being counted, the actual person being counted was able to block more radiation from reaching the NaI(Tl) detector than the phantom. This can be seen in the histogram depicted in Figure 6. After the net counts more than one standard deviation below zero were removed, the distribution of counts around zero greatly increases in equality, as can be seen in Figure 7.

<u>Linear Regression Model of Log of the Net Counts and the Time Elapsed Between</u> Administration and the Bioassay

The linear regression model of the net count data demonstrated no correlation between the net counts and the time elapsed between I-131 administration and the bioassay, based on the p-value. The analysis of the residuals, however, indicated that these findings were invalidated due to the non-normal distribution of residuals. The linear regression model of the net counts without those greater than one standard deviation below zero demonstrated a slight positive trend between the net counts and the time elapsed between I-131 administration and the bioassay, but the p-value demonstrated that there was no statistical correlation. This was further validated by the analysis of the residuals, which showed a normal distribution. Due to the lack of correlation from this linear regression model, if an administering person waited longer than the guidelines of 24-72 hours, they would not necessarily have a higher or lower net count than a person who had a bioassay done within that timeframe, even though the effective half-life of I-131 is 7.5 days.

One area for concern with the conclusion drawn from this data is that there is a disproportionate number of bioassays from up to two weeks post-administration versus bioassays performed greater than two weeks post-administration. This causes a skew in the data set that can be seen in Figures 8 and 9. If this had been a controlled experiment rather than using historical

data, the bioassays could be performed with the same amount of I-131 administered but different lengths of time between the administration and the bioassay, aiding in removing variables and improving the skew of the data, thus making it easier to ascertain any existing trends.

<u>Linear Regression Model of Log of the Net Counts and the Time Elapsed Between</u> Administration and the Bioassay

The linear regression model of the net count data indicated that there would be no correlation between the net counts and the amount of I-131 administered, and the p-value further demonstrated no statistical correlation. This conclusion, however, was invalidated by the analysis of the residuals, which showed a non-normal distribution. The linear regression model of the net counts without those greater than one standard deviation below zero also indicated there would be no correlation between the net counts and the amount of I-131 administered, and the p-value further demonstrated that there was no correlation. This conclusion was validated by the analysis of the residuals, which showed a normal distribution. Based on the lack of correlation from this model, it is demonstrated that the amount of I-131 administered does not influence the net counts of the administering person. If a person administers a great amount of I-131, they would not necessarily have a higher net count than someone who administered less I-131.

One area for concern with the conclusion drawn from this data is that there is a disproportionate number of bioassays taken from people who administered 20 μ Ci of I-131 or less versus bioassays from people who administered more than 20 μ Ci. This causes a skew in the data set that can be seen in Figures 10 and 11. If this had been a controlled experiment rather than using historical data, the bioassays could be performed with different amounts of I-131 administered but the same length of time between the administration and the bioassay, aiding in

removing variables and improving the skew of the data, thus making it easier to ascertain any existing trends.

Analysis of Activity Measured in Administering Person

Of the 168 data points, 7 bioassays indicated an activity that was measured above 0 μ Ci. No statistical tests could be performed to ascertain the activity deposited in each administering person due to the lack of activity measured in the bioassays. The highest activity recorded in the bioassays was 0.001 μ Ci, which would indicate an inhalation of 0.003 μ Ci, and is 4 orders of magnitude smaller than the NALI of 50 μ Ci. Considering that these bioassays come from 32 different administering persons over a span of 20 years, it is remarkable that only 7 bioassays had measurable uptakes.

Future Studies

While this project was designed specifically for the CSU VTH, it would be worthwhile to review bioassays from other veterinary hospitals with the capability of administering I-131 to examine trends between the amount of I-131 administered, time elapsed between administration and bioassay, and net counts. Since this study dealt with historical data, there were some skews in the data that may have influenced the results. It would be beneficial to do a standardized study where only one variable is changed at a time and re-perform the statistical tests to check for trends in the data. It would also be useful to see if all uptakes lie within the parameters of the L_C. There is a lack of literature on studies of the effective protection of I-131 administering persons. If there are variations between veterinary hospitals in iodine uptakes, then training programs from the successful hospitals could be implemented at those that have been less successful with

protecting their staff. Reviewing all of this information could also be beneficial for hospitals that administer I-131 to treat human patients. Similar studies could also be used for other nuclear medicine techniques to test the robustness of other protection guidelines.

CONCLUSION

The use of I-131 to treat cats with thyroid tumors has been proven to be a highly effective method of treatment, but with that procedure comes the potential risk of unnecessarily exposing the administering veterinarian or veterinary technician to I-131, which could potentially be harmful. All people who will be handling the I-131 and treated the animals are required to be trained in proper handling of radioactive materials and animals. Guidelines are also in place to regulate how often and under what circumstances bioassays are necessary for the administering person. While bioassays can be extremely useful in alerting a worker if they have had an uptake, the administering persons work in a predictable environment, performing the same procedure and taking the same precautions each time. If the procedure is properly followed for each administration, there should be no risk of uptake of I-131.

It was shown through the calculation of the MDA that the NaI(Tl) detector would have been able to detect a positive bioassay during all of the measurements taken. The maximum level of I-131 that could have been uptaken by the thyroid was always above the MDA, so any activity in the thyroid should have been detected. While the calculation of the L_C indicated that 11 bioassays could have been false positives, only 7 bioassay results indicated an activity above background level. The CDEs of the activities in these bioassays were all at least 4 orders of magnitude below both the regulatory limit of intake set by Regulatory Guide 8.20 and the NALI.

It was hypothesized that there would be a negative correlation between the time elapsed between I-131 administration and the bioassay and the net counts resulting from the bioassay. It was also hypothesized that there would be a positive correlation between the amount of I-131 administered and the net counts resulting from the bioassay. After reviewing 20 years worth of

data of 168 total bioassays from 32 administering persons, no correlations could be identified between the net counts and amount of time elapsed between the administration and the bioassay. No correlation could also be found between the net counts and the amount of I-131 administered. The current guidelines that CSU VTH must follow from CDPHE and Regulatory Guide 8.20 state that bioassays are required after administration of I-131, however, this data shows that the training procedures for I-131 administration at CSU VTH are sufficient to protect the administering persons and supports bioassays to be less-frequently conducted.

REFERENCES

- American National Standards Institute. Performance Criteria for Radiobioassay. McLean, VA: Health Physics Society; 2017.
- Barber LG. Thyroid Tumors in Cats and Dogs. Veterinary Clinics of North America: Small Animal Practice; 37: 755-773; 2007. DOI: 10.1016/j.cvsm.2007.03.008.
- Capintec, Inc. CAPTUS® 3000 Thyroid Uptake System Owner's Manual. Ramsey, NJ: Capintec, Inc; 2010.
- Cartee RE, Finn Bodner ST, Gray BW. Ultrasound Examination of the Feline Thyroid. Journal of Diagnostic Medical Sonography; 9:323-326 [online]; 1993. Available at https://journals.sagepub.com/doi/pdf/10.1177/875647939300900606. Accessed 15 December 2020.
- Chung HR. Iodine and Thyroid Function. Annals of Pediatric Endocrinology and Metabolism 19: 8-12; 2014. DOI: 10.6065/apem.2014.19.1.8.
- Collier JL. Uptake and Exposure Measurements in Health Physics Technicians Associated with 131I-MIBG Patient Therapy. Cincinnati, OH: University of Cincinnati; 2016. Thesis.
- Colorado Department of Public Health and the Environment. Internal document. Denver: CDPHE; 2019.
- HICON. Kit for the Preparation of Sodium Iodine I 131 Capsules and Solution USP, Therapeutic

 Oral. Cincinatti, OH; HICON; 1971.
- Hung JC. Radioiodine Dispensing and Usage in a Centralized Hospital Nuclear Pharmacy.

 Thyroid; 7: 289-294; 1997. DOI: 10.1089/thy.1997.7.289.

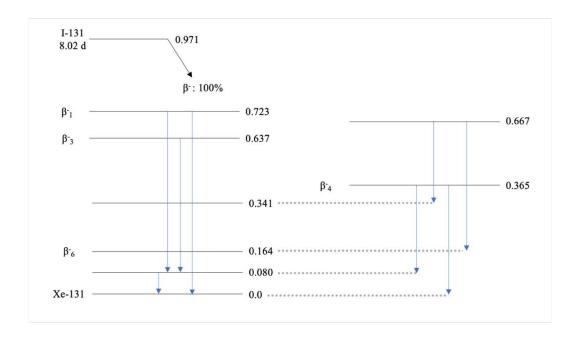
- Institute for Quality and Efficiency in Health Care (IQWiG). How Does the Thyroid Gland Work? [online]. 2018. Available at https://www.ncbi.nlm.nih.gov/books/NBK279388/. Accessed 4 November 2020.
- International Commission on Radiological Protection. Age-Dependent Doses to Members of the Public from Intake of Radionuclides: Part 1. Oxford: Pergamon Press; ICRP Publication 56; 1989.
- International Commission on Radiological Protection. Limits for Intakes of Radionuclides by Workers: Part 1. Oxford: Pergamon Press; ICRP Publication 30; 1979.
- Johnson TE. Introduction to Health Physics. New York City, NY: McGraw-Hill Education/Medical; 2017.
- Jubilant DraxImage. Safety Data Sheet HICON Kit for the Preparation of Sodium Iodine I 131 Capsules and Solution USP, Therapeutic Oral. Quebec; Jubilant DraxImage Inc; 2017.
- Mooney CT. Feline Hyperthyroidism Diagnostics Therapeutics. Veterinary Clinics of North America: Small Animal Practice; 31: 963-983; 2001. DOI: 10.1016/S0195-5616(01)50008-X.
- North Carolina Chapter of the Health Physics Society. Nuclide safety data sheet: iodine-131 [online]. 2006. Available at http://www.hpschapters.org/northcarolina/NSDS/131IPDF.pdf. Accessed 4 November 2020.
- Ramos SMO, Thomas S, Berdeguez MBT, de Sa LV, de Souza SAL. Anthropomorphic

 Phantoms Potential for More Studies and Training in Radiology. International Journal
 of Radiology and Radiation Therapy; 2: 101-104; 2017. DOI:
 10.15406/ijrrt.2017.02.00033.

- Sage E, Shikazono N. Radiation-Induced Clustered DNA Lesions: Repair and Mutagenesis. Free Radical Biology and Medicine; 107: 125-135; 2017. DOI: 10.1016/j.freeradbiomed.2016.12.008.
- U.S. Nuclear Regulatory Commission. Air Sampling in the Workplace. Washington, DC: US Government Printing Office; NUREG-1400; 1993.
- U.S. Nuclear Regulatory Commission. Annual Limits on Intakes (ALIs) and Derived Air Concentrations (DACs) of Radionuclides on Occupational Exposure; Effluent Concentrations; Concentrations for Release to Sewerage. Washington, DC: US Government Printing Office; 10 CFR 20 Appendix B; 2018.
- U.S. Nuclear Regulatory Commission. Applications for Bioassay of Radioiodine. Washington,DC: US Government Printing Office; Regulatory Guide 8.20; 2014.
- U.S. Nuclear Regulatory Commission. Occupational Dose Limits. Washington, DC: US Government Printing Office; 10 CFR 20.1201 Subpart C; 1991.
- U.S. Nuclear Regulatory Commission. Standards for Protection Against Radiation. Washington,DC: US Government Printing Office; 10 CFR 20.1502; 1998.

APPENDIX A

Decay scheme of I-131⁵.



⁵ <u>https://www.nndc.bnl.gov/nudat2/mird/</u> Accessed 2 December 2020.

APPENDIX B

Based on ICRP 30, 30% of an intake of iodine is uptaken by the thyroid. Based on the values in 10 CFR 20 Appendix B, the NALI of I-131 is equal to 50 rems in the thyroid, which is equivalent to 50 μ Ci. Reaching 10% of the NALI would mean an intake of 5 rems, or 5 μ Ci, and an intake of 1.67 μ Ci. The counting efficiency of NaI(Tl) detector used to conduct the bioassays is 0.17%, and the average background reading is 31.09 cpm.

Decays per minute in the thyroid

$$1.67~\mu \text{Ci} \cdot \frac{1~\text{Ci}}{1~\times~10^6~\mu \text{Ci}} \cdot \frac{3.7~\times~10^{10} \text{dps}}{1~\text{Ci}} \cdot \frac{60~\text{s}}{1~\text{min}} = 3.7 \times 10^6~\text{dpm}$$

Effective half-life of I-131

$$\frac{8.05 \text{ d} \times 120 \text{ d}}{8.05 \text{ d} + 120 \text{ d}} = 7.5 \text{ d}$$

Decay constant of I-131 in the thyroid

$$\frac{\ln(2)}{7.5} = 0.092 = \lambda$$

Decays per minute of the background

$$\frac{0.17}{100} \times \frac{31.09 \text{ cpm}}{\text{dpm}} = 18288.24 \text{ dpm}$$

Standard deviation of the background

$$\sqrt{\frac{31.09 \text{ cpm}}{5 \text{ min}}} = 2.49 \text{ cpm}$$

Decays per minute of standard deviation of the background

$$\frac{0.17}{100} \cdot \frac{2.49 \text{ cpm}}{\text{dpm}} = 1464.71 \text{ dpm}$$

Decision level

$$2.33 \times 1464.71 = 3412.76 \text{ dpm}$$

Lowest background reading above decision level

$$18288.24 + 3412.76 = 21701.00 \text{ dpm}$$

Length of time for I-131 activity in thyroid to reach background counts

$$21701 = 3.7 \times 10^{6} \cdot e^{-0.092t}$$

$$0.00587 = e^{-0.092t}$$

$$\ln(0.00587) = -0.092t$$

$$-5.14 = -0.092t$$

$$t = 55.8 \text{ days}$$

APPENDIX C

Based on ICRP 30, 30% of an intake of iodine is uptaken by the thyroid. Regulatory Guide 8.20 has set the intake limit as 10 mCi, which is 20% of the NALI, meaning an uptake of 3.33 mCi of I-131. The counting efficiency of NaI(Tl) detector used to conduct the bioassays is 0.17%, and the average background reading is 31.09 cpm.

Decays per minute in the thyroid

$$3.33 \text{ mCi} \cdot \frac{1 \text{ Ci}}{1 \times 10^3 \text{ } \mu \text{Ci}} \cdot \frac{3.7 \times 10^{10} \text{dps}}{1 \text{ Ci}} \cdot \frac{60 \text{ s}}{1 \text{ min}} = 7.4 \times 10^9 \text{ dpm}$$

Effective half-life of I-131

$$\frac{8.05 \text{ d} \times 120 \text{ d}}{8.05 \text{ d} + 120 \text{ d}} = 7.5 \text{ d}$$

Decay constant of I-131 in the thyroid

$$\frac{\ln(2)}{7.5} = 0.092 = \lambda$$

Decays per minute of the background

$$\frac{0.17}{100} \times \frac{31.09 \text{ cpm}}{\text{dpm}} = 18288.24 \text{ dpm}$$

Standard deviation of the background

$$\sqrt{\frac{31.09 \text{ cpm}}{5 \text{ min}}} = 2.49 \text{ cpm}$$

Decays per minute of standard deviation of the background

$$\frac{0.17}{100} \cdot \frac{2.49 \text{ cpm}}{\text{dpm}} = 1464.71 \text{ dpm}$$

Decision level

 $2.33 \times 1464.71 = 3412.76 \text{ dpm}$

Lowest background reading above decision level

18288.24 + 3412.76 = 21701.00 dpm

Length of time for I-131 activity in thyroid to reach background counts

$$21701 = 7.4 \times 10^{9} \cdot e^{-0.092t}$$

$$2.9 \times 10^{-6} = e^{-0.092t}$$

$$\ln(2.9 \times 10^{-6}) = -0.092t$$

$$-12.8 = -0.092t$$

$$t = 138.6 \text{ days}$$

APPENDIX D



eProtocol
Office of the Vice President for Research
321 General Services Building - Campus Delivery 2011 eprotocol
TEL: (970) 491-1553

Knowledge to Go Places

DATE: August 31, 2020

TO: Johnson, Thomas, 1681 Env & Rad Health Sciences

Alexander, Bruce, 1681 Env & Rad Health Sciences, Dieffenthaller, Meghan, 1681 Env & Rad

Health Sciences

FROM: Felton-Noyle, Tammy, Senior IRB Coordinator, BMR, CSU IRB 1

PROTOCOL TITLE: Radiation Dose to Veterinarians and Veterinary Technicians During Performance of Radioiodine

Treatment of Animals

FUNDING SOURCE None
PROTOCOL NUMBER: 20-10142H
APPROVAL or
DETERMINATION PERIOD: June 18, 2020

NOTICE OF IRB REVIEW FOR HUMAN RESEARCH

Your study was reviewed and determined to be Not Human Subjects Research (NHSR) by the Colorado State University IRB (FWA0000647). As such, your activity falls outside the parameters for IRB review. You may conduct your study as described in your application without additional obligation to the IRB.

This memorandum is your record of the IRB decision related to this study. Please maintain it with your study records.

Please contact this office if you have any questions or require assistance. We appreciate your cooperation, and wish you success with your research.

Please direct any questions about the IRB's actions on this project to:

IRB Office - (970) 491-1553; RICRO_IRB@mail.Colostate.edu

Claire Chance, Senior IRB Coordinator - (970) 491-1381; Claire.Chance@Colostate.edu

Tammy Felton-Noyle, Senior IRB Coordinator - (970) 491-1655; Tammy Felton-Noyle@Colostate.edu

Felton-Noyle, Tammy

The IRB has reviewed your submitted proposal and has determined that your activity of analyzing existing, de-identified data does not meet the federal definition of human subjects research for which IRB oversight is required. We thank you for your continued communication. You have authority to conduct your research. No actions from the IRB are necessary.

None

APPENDIX E

Table 1: Z-scores for net counts.

Net	
Counts	Net Counts
(cpm)	Z-score
-70.8	-4.32
-43.8	-2.61
-37.4	-2.21
-37	-2.18
-36.2	-2.13
-36	-2.12
-36	-2.12
-36	-2.12
-35.2	-2.07
-35	-2.06
-33.8	-1.98
-26.24	-1.50
-23.8	-1.35
-23.8	-1.35
-23.8	-1.35
-23.2	-1.31
-23.2	-1.31
-20.4	-1.13
-19.69	-1.09
-16.2	-0.87
-16.2	-0.87
-15.4	-0.82
-15	-0.79
-13	-0.66
-11.8	-0.59
-11.8	-0.59
-11.6	-0.58
-11.4	-0.56
-10.8	-0.53

	I
Net	
Counts	Net Counts
(cpm)	Z-score
-10.2	-0.49
-10	-0.47
-9.8	-0.46
-9.4	-0.44
-9.2	-0.42
-9.2	-0.42
-8.8	-0.40
-8.2	-0.36
-7.8	-0.34
-7.46	-0.31
-7.1	-0.29
-6.8	-0.27
-6.8	-0.27
-6.6	-0.26
-6.4	-0.25
-6.4	-0.25
-6	-0.22
-6	-0.22
-5.96	-0.22
-5.6	-0.20
-5.6	-0.20
-5.4	-0.18
-5.28	-0.18
-5.1	-0.16
-4.9	-0.15
-4.8	-0.15
-4.7	-0.14
-4.66	-0.14
-4.6	-0.13
-4.6	-0.13
-4.575	-0.13
-4.5	-0.13
-4.4	-0.12
-4.2	-0.11
-4.2	-0.11
-3.4	-0.06
	·

Net	
Counts	Net Counts
(cpm)	Z-score
-3.4	-0.06
-3.2	-0.04
-3	-0.03
-2.92	-0.03
-2.8	-0.02
-2.8	-0.02
-2.8	-0.02
-2.6	-0.01
-2.4	0.01
-2.4	0.01
-2.2	0.02
-2.1	0.03
-1.9	0.04
-1.8	0.04
-1.8	0.04
-1.68	0.05
-1.66	0.05
-1.66	0.05
-1.4	0.07
-1.4	0.07
-1.4	0.07
-1.24	0.08
-1.22	0.08
-1.2	0.08
-1.2	0.08
-1.2	0.08
-1.2	0.08
-1.14	0.09
-0.8	0.11
-0.8	0.11
-0.8	0.11
-0.6	0.12
-0.54	0.12
-0.5	0.13
-0.46	0.13
-0.4	0.13
-	-

	I
Net	
Counts	Net Counts
(cpm)	Z-score
-0.4	0.13
-0.32	0.14
-0.2	0.15
-0.2	0.15
-0.2	0.15
-0.2	0.15
-0.1	0.15
0	0.16
0	0.16
0	0.16
0.1	0.16
0.38	0.18
0.5	0.19
0.6	0.20
0.6	0.20
0.8	0.21
0.8	0.21
0.82	0.21
0.9	0.22
0.9	0.22
0.9	0.22
0.96	0.22
1	0.22
1	0.22
1.1	0.23
1.2	0.23
1.2	0.23
1.3	0.24
1.3	0.24
1.32	0.24
1.32	0.24
1.4	0.25
1.6	0.26
1.6	0.26
1.8	0.27
1.8	0.27
	·

Net	
Counts	Net Counts
(cpm)	Z-score
1.8	0.27
1.8	0.27
1.8	0.27
1.8	0.27
1.86	0.28
1.88	0.28
2.1	0.29
2.2	0.30
2.24	0.30
2.24	0.30
2.3	0.30
2.4	0.31
2.4	0.31
2.4	0.31
2.44	0.31
2.6	0.32
2.98	0.35
3	0.35
3	0.35
3	0.35
3.2	0.36
3.3	0.37
3.32	0.37
3.4	0.37
3.6	0.39
3.8	0.40
4	0.41
4	0.41
4.1	0.42
4.362	0.43
4.4	0.44
4.44	0.44
4.6	0.45
5	0.47
5.06	0.48
5.08	0.48

Net	
Counts	Net Counts
(cpm)	Z-score
5.4	0.50
6	0.54
6.04	0.54
7	0.60
7.21	0.61
7.4	0.63
7.6	0.64
8.26	0.68
8.3	0.68
8.8	0.72
8.8	0.72
8.8	0.72
9.8	0.78
9.8	0.78
10.2	0.80
10.2	0.80
10.2	0.80
10.6	0.83
10.6	0.83
84.99	5.54
84.99	5.54
84.99	5.54
01.77	3.31

APPENDIX F

Table 2: Total background counts, lower limit of detection, minimum detectable activity, predicted maximum intake of I-131, and decision level.

D 1 1			D 11 4 1	Predicted		
Background Counts		MDA	Predicted Max Intake	Max Uptake		Net
(cpm)	LLD	MDA (μCi)	wiax iiitake (μCi)	Optake (μCi)	Lc	Counts
31.4	17.6	0.00154	0.0	0.0	5.84	-10.00
28.6	16.9	0.00134	90.0	27.0	5.57	-5.40
26.8	16.5	0.00144	80.0	24.0	5.39	1.40
27.6	16.7	0.00144	80.0	24.0	5.47	1.80
26.8	16.5	0.00146	600.0	180.0	5.39	-2.80
30	17.3	0.00144	600.0	180.0	5.71	-4.20
24	15.7	0.00131	0.0	0.0	5.10	1.00
19.8	14.5	0.00137	0.0	0.0	4.64	4.00
25.8	16.2	0.00120	120.0	36.0	5.29	-0.20
25.6	16.2	0.00141	1760.0	528.0	5.27	-1.40
21	14.9	0.00111	1760.0	528.0	4.78	1.80
22	15.2	0.00123	88.0	26.4	4.89	10.60
28	16.8	0.00132	1200.0	360.0	5.51	-0.40
22	15.2	0.00117	64.0	19.2	4.89	-0.20
20.8	14.8	0.00132	54.0	16.2	4.75	-5.60
21.8	15.1	0.00123	600.0	180.0	4.87	-2.40
22.6	15.4	0.00133	45.0	13.5	4.95	-0.20
23.8	15.7	0.00136	80.0	24.0	5.08	-4.60
20.6	14.8	0.00128	56.0	16.8	4.73	0.80
25.2	16.1	0.00140	80.0	24.0	5.23	-6.00
25.2	16.1	0.00140	80.0	24.0	5.23	3.60
24.6	15.9	0.00138	0.0	0.0	5.17	-6.00
28.2	16.8	0.00147	1600.0	480.0	5.53	-1.80
22.4	15.3	0.00133	50.0	15.0	4.93	-3.20
27.4	16.6	0.00145	90.0	27.0	5.45	-0.80
40.8	19.7	0.00174	90.0	27.0	6.66	-15.00
21.8	15.1	0.00131	60.0	18.0	4.87	7.60
24.2	15.8	0.00137	60.0	18.0	5.13	3.00
22.2	15.2	0.00132	80.0	24.0	4.91	-1.20
25.8	16.2	0.00141	0.0	0.0	5.29	-0.80

				Predicted		
Background) (D)	Predicted	Max		3 .7.7
Counts (cpm)	LLD	MDA (μCi)	Max Intake (μCi)	Uptake (μCi)	Lc	Net Counts
25.6	16.2	0.00141	1760.0	(μC1) 528.0	5.27	-6.40
23.0	14.9	0.00141	1760.0	528.0	4.78	0.60
24.4	15.8	0.00129	2000.0	600.0	5.15	2.40
26.6	16.4	0.00138	0.0	0.0	5.37	3.20
25.8	16.2	0.00143	120.0	36.0	5.29	1.80
67.2	24.5	0.00141	90.0	27.0	8.54	-35.00
27.4	16.6	0.00218	85.0	25.5	5.45	10.20
74		0.00143	240.0	72.0	8.96	
86.8	25.6 27.5	0.00228	160.0	48.0	9.71	-37.00
164	36.8	0.00246	900.0	270.0	13.34	-35.20 -70.80
71	25.1	0.00332	900.0		8.78	
60.09	23.1		80.0	27.6 24.0	8.08	-36.00 -19.69
		0.00207			+	
67.2	24.5	0.00218	90.0	27.0	8.54	-37.40
42	19.9	0.00176	80.0	24.0	6.75	-9.20
34	18.2	0.00160	82.2	24.7	6.08	-2.60
72.8	25.4	0.00227	80.0	24.0	8.89	-15.40
26.8	16.5	0.00144	175.0	52.5	5.39	0.00
31.6	17.7	0.00155	84.0	25.2	5.86	-8.20
35.6	18.6	0.00163	80.0	24.0	6.22	-9.40
31.4	17.6	0.00154	89.0	26.7	5.84	-3.40
28.6	16.9	0.00148	90.0	27.0	5.57	1.60
23	15.5	0.00134	90.0	27.0	5.00	5.40
25	16.0	0.00139	80.0	24.0	5.21	0.60
26.2	16.3	0.00142	90.0	27.0	5.33	0.00
21.8	15.1	0.00131	70.0	21.0	4.87	10.20
24	15.7	0.00137	160.0	48.0	5.10	4.60
27.6	16.7	0.00146	80.0	24.0	5.47	7.00
29.4	17.1	0.00150	80.0	24.0	5.65	3.00
24.4	15.8	0.00138	600.0	180.0	5.15	7.40
26.8	16.5	0.00144	80.0	24.0	5.39	-6.40
30	17.3	0.00151	80.0	24.0	5.71	-1.20
24.2	15.8	0.00137	40.0	12.0	5.13	8.80
27.8	16.7	0.00146	40.0	12.0	5.49	6.00
21.8	15.1	0.00131	0.0	0.0	4.87	1.60
24.6	15.9	0.00138	80.0	24.0	5.17	-1.20

				Predicted		
Background		100	Predicted	Max		37
Counts	IID	MDA	Max Intake	Uptake	T.a	Net
(cpm)	LLD 15.4	(μCi)	(μCi)	(μCi)	Lc	Counts
22.8	16.0	0.00134	80.0	24.0 75.0	4.98	4.00
		0.00139	250.0		5.21	-1.80
27.8	16.7	0.00146	0.0	0.0	5.49	-2.40
67.8	24.6	0.00219	86.0	25.8	8.58	-43.80
29.4	17.1	0.00150	60.0	18.0	5.65	-6.80
24.2	15.8	0.00137	80.0	24.0	5.13	3.40
24.4	15.8	0.00138	0.0	0.0	5.15	0.00
65.8	24.3	0.00216	180.0	54.0	8.45	-36.20
63.8	24.0	0.00213	90.0	27.0	8.32	-20.40
40.8	19.7	0.00174	160.0	48.0	6.66	-16.20
39.6	19.4	0.00171	80.0	24.0	6.56	-10.20
35.8	18.6	0.00164	160.0	48.0	6.23	-9.20
24	15.7	0.00137	89.0	26.7	5.10	1.20
31.4	17.6	0.00154	86.0	25.8	5.84	-11.80
23	15.5	0.00134	80.0	24.0	5.00	-0.40
26.2	16.3	0.00142	89.4	26.8	5.33	1.80
29.4	17.1	0.00150	86.0	25.8	5.65	-4.20
21.8	15.1	0.00131	0.0	0.0	4.87	2.40
26.2	16.3	0.00142	93.4	28.0	5.33	8.80
54	22.3	0.00197	186.0	55.8	7.66	-23.80
60.09	23.3	0.00207	80.0	24.0	8.08	-26.24
39	19.3	0.00170	102.0	30.6	6.51	-13.00
34.8	18.4	0.00162	102.0	30.6	6.15	-11.40
26.8	16.5	0.00144	175.0	52.5	5.39	-4.80
34	18.2	0.00160	82.2	24.7	6.08	-8.80
72.8	25.4	0.00227	80.0	24.0	8.89	-6.80
26.2	16.3	0.00142	93.4	28.0	5.33	9.80
54	22.3	0.00197	84.0	25.2	7.66	-23.20
39	19.3	0.00170	102.0	30.6	6.51	-16.20
34.8	18.4	0.00162	102.0	30.6	6.15	-10.80
31.6	17.7	0.00155	84.0	25.2	5.86	-7.80
34	18.2	0.00160	0.0	0.0	6.08	-11.60
24.97	16.0	0.00139	0.0	0.0	5.21	-4.58
20.2	14.7	0.00127	120.0	36.0	4.68	-0.60
22.4	15.3	0.00133	40.0	12.0	4.93	-1.20

				Predicted		
Background			Predicted	Max		
Counts		MDA	Max Intake	Uptake		Net
(cpm)	LLD	(μCi)	(μCi)	(μCi)	Lc	Counts
90.6	28.0	0.00251	380.0	114.0	9.92	-33.80

LIST OF ABBREVIATIONS

ABBREVIATON

DESCRIPTION

ALARA As low as reasonably achievable CDE Committed Dose Equivalent

CDPHE Colorado Department of Health and the Environment

CSU Colorado State University
DSB Double stranded break

L_C Decision level

LLD Lower limit of detection
NALI Nonstochastic limit of intake
PAL Predetermined action level
PPE Personal protective equipment

SDS Safety data sheet
SSB Single stranded break
RCO Radiation Control Office
RSO Radiation Safety Officer
VTH Veterinary Teaching Hospital