



**FINAL REPORT**

**Test Facility Study No. 185350**  
**Sponsor Reference No. ALC-NC-0552**

**A Tissue Distribution Study of a [<sup>3</sup>H]-Labelled Lipid Nanoparticle-mRNA  
Formulation Containing ALC-0315 and ALC-0159 Following  
Intramuscular Administration in Wistar Han Rats**

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**TABLE OF CONTENTS**

|              |                                                                     |           |
|--------------|---------------------------------------------------------------------|-----------|
| <b>1</b>     | <b>COMPLIANCE STATEMENT .....</b>                                   | <b>6</b>  |
| <b>2</b>     | <b>QUALITY ASSURANCE STATEMENT .....</b>                            | <b>7</b>  |
| <b>3</b>     | <b>RESPONSIBLE PERSONNEL .....</b>                                  | <b>8</b>  |
| <b>4</b>     | <b>SUMMARY .....</b>                                                | <b>9</b>  |
| <b>5</b>     | <b>INTRODUCTION.....</b>                                            | <b>11</b> |
| <b>5.1</b>   | <b>Study Location.....</b>                                          | <b>11</b> |
| <b>5.2</b>   | <b>Study Dates .....</b>                                            | <b>11</b> |
| <b>5.3</b>   | <b>Archiving.....</b>                                               | <b>12</b> |
| <b>6</b>     | <b>EXPERIMENTAL PROCEDURE.....</b>                                  | <b>12</b> |
| <b>6.1</b>   | <b>Test Item .....</b>                                              | <b>12</b> |
| <b>6.2</b>   | <b>Other Materials .....</b>                                        | <b>13</b> |
| <b>6.3</b>   | <b>Animals and Husbandry.....</b>                                   | <b>14</b> |
| <b>6.4</b>   | <b>Specific Activity.....</b>                                       | <b>14</b> |
| <b>6.5</b>   | <b>Dose Formulation .....</b>                                       | <b>14</b> |
| <b>6.6</b>   | <b>Dose Administration and Determination .....</b>                  | <b>15</b> |
| <b>6.7</b>   | <b>Collection of Biological Samples .....</b>                       | <b>15</b> |
| <b>6.8</b>   | <b>Sample Storage .....</b>                                         | <b>16</b> |
| <b>6.9</b>   | <b>Preparation of Samples for Total Radioactivity Analysis.....</b> | <b>16</b> |
| <b>6.9.1</b> | <b>Dose Formulation .....</b>                                       | <b>16</b> |
| <b>6.9.2</b> | <b>Blood and Plasma .....</b>                                       | <b>16</b> |
| <b>6.9.3</b> | <b>Tissues .....</b>                                                | <b>16</b> |
| <b>6.9.4</b> | <b>Urine, Faeces and Cage Wash.....</b>                             | <b>17</b> |
| <b>6.10</b>  | <b>Quantification of Radioactivity.....</b>                         | <b>17</b> |

|        |                                                                         |           |
|--------|-------------------------------------------------------------------------|-----------|
| 6.10.1 | <b>Liquid Scintillation Counting .....</b>                              | <b>17</b> |
| 6.10.2 | <b>Data Presentation .....</b>                                          | <b>17</b> |
| 6.11   | <b>Protocol Deviations .....</b>                                        | <b>18</b> |
| 7      | <b>RESULTS .....</b>                                                    | <b>19</b> |
| 7.1    | <b>Clinical Observations.....</b>                                       | <b>19</b> |
| 7.2    | <b>Body Weights.....</b>                                                | <b>19</b> |
| 7.3    | <b>Tissue Distribution Following Intramuscular Administration .....</b> | <b>19</b> |
| 8      | <b>CONCLUSIONS .....</b>                                                | <b>22</b> |
| 9      | <b>TABLES.....</b>                                                      | <b>23</b> |
| 10     | <b>APPENDICES .....</b>                                                 | <b>28</b> |

# **LIST OF TABLES**

|         |                                                                                                                                                                                                                   |    |
|---------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----|
| Table 1 | Mean (Sexes-Combined) Concentration and Recovery of Total Radioactivity in Whole Blood, Plasma and Tissues Following Single Intramuscular Administration of [ <sup>3</sup> H]-08-A01-C01 to Wistar Han Rats ..... | 23 |
| Table 2 | Mean Concentration of Total Radioactivity in Whole Blood, Plasma and Tissues Following Single Intramuscular Administration of [ <sup>3</sup> H]-08-A01-C01 to Wistar Han Rats .....                               | 25 |
| Table 3 | Mean Recovery of Total Radioactivity in Tissues Following Single Intramuscular Administration of [ <sup>3</sup> H]-08-A01-C01 to Wistar Han Rats .....                                                            | 27 |

# **LIST OF APPENDICES**

|            |                                                                                           |    |
|------------|-------------------------------------------------------------------------------------------|----|
| Appendix 1 | Certificates of Analysis for [ <sup>3</sup> H]-08-A01-C01 and [ <sup>3</sup> H]-CHE ..... | 28 |
| Appendix 2 | Individual Animal Dosing Summary.....                                                     | 30 |
| Appendix 3 | Urine and Faeces Sample Weights .....                                                     | 33 |
| Appendix 4 | Individual Male Concentration Data .....                                                  | 36 |
| Appendix 5 | Individual Female Concentration Data.....                                                 | 43 |
| Appendix 6 | Individual Male Recovery Data.....                                                        | 50 |
| Appendix 7 | Individual Female Recovery Data .....                                                     | 57 |
| Appendix 8 | Individual Male 100 µg mRNA data .....                                                    | 64 |

## 1 COMPLIANCE STATEMENT

### **Study Title: A Tissue Distribution Study of a [<sup>3</sup>H]-Labelled Lipid Nanoparticle-mRNA Formulation Containing ALC-0315 and ALC-0159 Following Intramuscular Administration in Wistar Han Rats**

GLP regulations are not applicable to studies of this nature therefore no claim of GLP compliance is made. Nevertheless, as Study Director, I confirm that this study was conducted in a GLP compliant facility and that the practices and procedures adopted during its conduct were consistent with the OECD Principles of Good Laboratory Practice as incorporated into the United Kingdom Statutory Instrument for GLP.

The study was conducted according to the procedures herein described and this report represents a true and accurate record of the results obtained.

|                                                                                     |
|-------------------------------------------------------------------------------------|
| DocuSigned by:                                                                      |
| (b) (4)                                                                             |
|  |
| Signer Name: (b) (4)                                                                |
| Signing Reason: I approve this document                                             |
| Signing Time: 05-Nov-2020   11:52:33 EST                                            |
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(b) (4)  
Study Director

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## 2 QUALITY ASSURANCE STATEMENT

**Study Title: A Tissue Distribution Study of a [<sup>3</sup>H]-Labelled Lipid Nanoparticle-mRNA Formulation Containing ALC-0315 and ALC-0159 Following Intramuscular Administration in Wistar Han Rats**

This study has not been subjected to any study specific Quality Assurance procedures.

### **3 RESPONSIBLE PERSONNEL**

Study Director:

(b) (4)

Sponsor Representative:

(b) (6)

Test Facility Management:

(b) (4)

#### 4 SUMMARY

The test item, 08-A01-C01, is an aqueous dispersion of lipid nanoparticles (LNP), comprised of a proprietary mixture of lipid components (including ALC-0315, ALC-0159, distearoylphosphatidylcholine, and cholesterol) and mRNA. The mRNA encodes a model protein (luciferase) and is not pharmacologically active. The test item contains trace amounts of radiolabelled [Cholesteryl-1,2-<sup>3</sup>H(N)]-Cholesteryl Hexadecyl Ether ([<sup>3</sup>H]-CHE), a non-exchangeable, non-metabolisable lipid marker used to monitor the disposition of the lipid nanoparticles (containing encapsulated mRNA). Once intracellular, the [<sup>3</sup>H]-CHE does not recirculate and therefore allows assessment of distribution of the particles.

The objectives of this study were to:

1. Characterise the disposition of 08-A01-C01 containing a radiolabelled lipid marker in male and female Wistar Han rats following a single intramuscular administration.
2. Determine the concentration and content of radioactivity in blood, plasma and tissues of rats (expressed as µg lipid eq/mL (or per g for tissue), and % administered (injected dose)/tissue, where appropriate).

Wistar Han rats (21 male and 21 female) each received a single intramuscular dose of [<sup>3</sup>H]-08-A01-C01 at a target mRNA total dose of 50 µg/animal (1.29 mg/animal total lipid dose). The content and concentration of total radioactivity in blood, plasma and tissues were determined at pre-defined time points following administration.

Whole blood and tissue samples were collected at 0.25, 1, 2, 4, 8, 24 and 48 hours post-dose (three animals/sex/timepoint) and plasma was subsequently separated from blood by centrifugation. The concentration of total radioactivity was measured by liquid scintillation counting (LSC).

Following intramuscular administration of [<sup>3</sup>H]-08-A01-C01 to male and female Wistar Han rats at a target dose level of 50 µg/animal (1.29 mg/animal total lipid dose), the greatest mean concentration was found remaining in the injection site at each time point in both sexes. Outside the injection site, low levels of radioactivity were detected in most tissues, with the greatest levels in plasma observed 1-4 hours post-dose. Over 48 hours, [<sup>3</sup>H]-08-A01-C01 distributed mainly to liver, adrenal glands, spleen and ovaries, with maximum concentrations observed at 8-48 hours post-dose. Total recovery (% of injected dose) of [<sup>3</sup>H]-08-A01-C01 outside the injection site was greatest in the liver (up to 21.5%) and was much less in spleen (≤1.1%), adrenal glands (≤0.1%) and ovaries (≤0.1%). The mean concentrations and tissue distribution pattern were broadly similar between the sexes.

Blood:plasma ratios were generally between 0.5-0.6, indicating that the majority of the total radioactivity is associated with the plasma fraction and that [<sup>3</sup>H]-08-A01-C01 does not undergo appreciable accumulation in red blood cells.

In conclusion, the distribution of [<sup>3</sup>H]-08-A01-C01 (monitoring the [<sup>3</sup>H]-CHE lipid label) in blood, plasma and selected tissues was determined in male and female Wistar Han rats over 48 hours after a single intramuscular injection at 50 µg mRNA/animal (1.29 mg/animal lipid dose). The concentrations of [<sup>3</sup>H]-08-A01-C01 were greatest in the injection site at all time points, with levels peaking in the plasma by 1-4 hours post-dose and distribution mainly into liver, adrenal glands, spleen and ovaries over 48 hours. Total recovery of radioactivity outside of the injection site was greatest in the liver, with much lower total recovery in spleen, and very little recovery in adrenals glands and ovaries. The mean plasma, blood and tissue concentrations and tissue distribution patterns were broadly similar between the sexes and [<sup>3</sup>H]-08-A01-C01 did not associate with red blood cells.

## 5 INTRODUCTION

The objectives of this study were to:

1. Characterise the disposition of 08-A01-C01 containing a radiolabelled lipid marker in male and female Wistar Han rats following a single intramuscular administration
2. Determine the concentration and content of radioactivity in blood, plasma and tissues of rats (expressed as  $\mu\text{g}$  lipid eq/g (or per mL for plasma) and % injected dose/tissue, where appropriate)

The Wistar Han rat was chosen as the animal model for this study as it is an accepted rodent species for preclinical toxicity testing by regulatory agencies and has been used in all regulatory toxicology studies by the Sponsor.

The study was designed to be appropriate for submission to regulatory authorities. However, it is recognised that no detailed test guidelines for the conduct of drug distribution and pharmacokinetic studies are currently available.

Initially, 21 male rats were dosed at 100  $\mu\text{g}$  mRNA/animal. Some adverse clinical signs were observed after approximately 24 hours post-dose and a subsequent review of the data showed concentrations were well detected in tissues. After discussions with the Sponsor, the target dose level was lowered to 50  $\mu\text{g}$  mRNA/animal by amendment for the remainder of the study. Reference is made to the 100  $\mu\text{g}$  mRNA /animal group in some sections of the report, however, the results are not discussed.

### 5.1 Study Location

The study was carried out at (b) (4) according to (b) (4) Protocol No. 185350 and Amendments 1 and 2.

### 5.2 Study Dates

The study was conducted according to the following timetable:

|                               |                                                             |
|-------------------------------|-------------------------------------------------------------|
| Study Initiation:             | 16 July 2020                                                |
| Experimental Start Date:      | 17 July 2020                                                |
| Experimental Completion Date: | 24 September 2020                                           |
| Study Completion Date:        | See compliance page for date of Study Director's signature. |

### 5.3 Archiving

All raw data generated and recorded during this study will be stored in the Scientific Archive of (b) (4) for 2 years after issue of the final report. After the 2-year period the Sponsor will be consulted regarding the disposal, transfer, or continued storage of the raw data. Electronic data generated by the Test Facility were archived as noted above, except reporting files stored on Shared Document Management System (SDMS), which were archived at the (b) (4)

The original signed copy of the final report will be stored indefinitely in the Scientific Archive of (b) (4)

The residual [<sup>3</sup>H]-08-A01-C01 dose (approximately 5 MBq) will be retained and stored in a fridge set to maintain 4°C at (b) (4)

Biological samples generated during the course of this study were held deep frozen until issue of the final report. (b) (4) will contact the Sponsor to discuss the fate of the samples (disposal, return or retain at (b) (4)) on issue of the final report. Samples will be disposed of unless (b) (4) receives written instruction regarding shipment of the samples to the Sponsor or continued storage at (b) (4)

## 6 EXPERIMENTAL PROCEDURE

### 6.1 Test Item

|                           |                                                                         |
|---------------------------|-------------------------------------------------------------------------|
| Identification:           | [ <sup>3</sup> H]-08-A01-C01                                            |
| Supplier:                 | Acuitas Therapeutics Inc                                                |
| Lot Number:               | NC-0552-1                                                               |
| Expiration Date:          | July 7, 2021                                                            |
| Physical Description:     | White to off-white, homogenous, opalescent liquid; no foreign particles |
| Concentration (mRNA):     | 1.0 mg/mL                                                               |
| Radioactive Concentration | 0.864 mCi/mL, 1,900,000 dpm/μL                                          |

|                                |                            |
|--------------------------------|----------------------------|
| Concentration<br>(Total Lipid) | 25.7 mg/mL                 |
| Molecular weight               | Not applicable for LNP     |
| Purity:                        | 94%                        |
| Radiochemical<br>Purity        | >97%                       |
| Specific Activity<br>(mRNA):   | 0.864 mCi/mg (32.0 MBq/mg) |
| Correction Factor              | None                       |
| Storage Conditions:            | Frozen (-60°C to -90°C)    |

The test item contains trace amounts of radiolabelled [Cholesteryl-1,2-<sup>3</sup>H(N)]-Cholesteryl Hexadecyl Ether ([<sup>3</sup>H]-CHE), a non-exchangeable, non-metabolisable lipid marker used to monitor the disposition of the lipid nanoparticles (containing encapsulated mRNA). Per the manufacturer's information, the radiochemical purity of [<sup>3</sup>H]-CHE was found to be >97% and the rate of decomposition is initially 2% for 6 months from the date of purification (16 December 2019). No radiochemical purity assessments were made as part of this study.

The Certificates of Analysis for [<sup>3</sup>H]-08-A01-C01 and [<sup>3</sup>H]-CHE are presented in [Appendix 1](#).

## 6.2 Other Materials

AquaSafe 500 Plus liquid scintillation fluid was obtained from Zinsser Inc.

Monophase® was used in conjunction with the Perkin Elmer Model 307 Automatic Sample Oxidiser and was supplied by Perkin Elmer Life Science and Analytical Instruments Inc, UK.

Spec-Chec™-<sup>3</sup>H used to estimate efficiencies of combustion was also obtained from Perkin Elmer Life Science and Analytical Instruments Inc, UK.

All other materials and chemicals used were of analytical grade where available and supplied by standard commercial suppliers.

### 6.3 Animals and Husbandry

Forty-two male and 21 female Wistar Han rats (8-11 weeks and body weight 179-270 g at the time of dosing) were used in the study and were supplied by (b) (4). The animals were acclimatised to the experimental unit for at least 5 days prior to use on the study. During the acclimatisation periods, the animals were closely observed by the animal technicians to ensure that they were in good health and suitable for inclusion in the study. During the study period the animals were closely observed twice daily by the animal technicians to ensure that they were in good health.

During the study period, the rats were housed in groups in polycarbonate and stainless steel cages with wire mesh floors. Animals used for excretion collection were housed singly in all-glass metabolism cages for the separate collection of urine and faeces.

A standard laboratory diet of known formulation (SDS Rat and Rat Maintenance Diet No.1, Special Diet Services, 1 Stepfield, Witham, Essex) and domestic mains tap water were available *ad libitum*.

Holding and study areas had automatic control of light cycles and temperature. Automatic 12 hours light and 12 hours dark. Ranges of temperature and humidity measured during the study were 21-23°C and 44-67%, respectively, with the exception of 31 July 2020 where the room temperature reached a maximum of 25°C.

### 6.4 Specific Activity

The specific activity value of 1.24 MBq/mg lipid (as calculated from the 0.864 mCi/mg mRNA specific activity value supplied and converted to per mg lipid) was used to calculate the amount of [<sup>3</sup>H]-08-A01-C01 dispensed in the dose formulation.

### 6.5 Dose Formulation

[<sup>3</sup>H]-08-A01-C01 was provided in PBS/sucrose buffer at the required dose concentration (1 mg mRNA/mL). No dilutions were therefore required. Four dose formulation vials were provided (3 x 1.5 mL and 1 x 1.2 mL).

The appropriate number of vials for each dosing occasion were defrosted for at least 30 minutes prior to dosing. Prior to use, each vial was inverted 3 times to mix. Once dosing was complete, each vial was stored in a fridge within 4 hours of removal from the -80°C freezer.

The radioactive concentration of the supplied dose formulation was determined by the removal of triplicate aliquots (50 µL) prior to and after the first dosing occasion. Appropriate

dilutions of each aliquot were prepared in distilled water and duplicate aliquots of each dilution were analysed by liquid scintillation counting (LSC).

The radioactive concentration determined by LSC was within 10% of the target value provided in the supplied Certificate of Analysis and was used in the dose determination calculations.

## 6.6 Dose Administration and Determination

Each animal received a single (one site) intramuscular administration of [<sup>3</sup>H]-08-A01-C01 at either 50 or 100 µL volume for the 50 and 100 µg mRNA/animal dose groups, respectively (target doses of 1.29 or 2.57 mg total lipid/animal, respectively).

The actual dose received by each animal was determined with reference to the dose concentration, the volume of dose administered and the specific activity of [<sup>3</sup>H]-08-A01-C01 in the formulated dose. Any undosed residue was also taken in to account. The actual dose received by each animal is documented in [Appendix 2](#).

## 6.7 Collection of Biological Samples

Three male and three female rats were sacrificed at the following times:

0.25, 1, 2, 4, 8, 24 and 48 hours post dose

From each animal, a terminal blood sample (*ca.* 5-10 mL) was collected by cardiac puncture into heparinised tubes. A portion (*ca.* 0.5 mL) was retained and plasma separated from the remainder of each sample by centrifugation (3000 rpm for 10 minutes in a centrifuge set to maintain a temperature of 4°C). Blood cells were discarded.

The following tissues were collected (where relevant for sex):

|                         |                 |
|-------------------------|-----------------|
| Adipose tissue          | Ovaries         |
| Adrenal glands          | Pancreas        |
| Bladder                 | Pituitary gland |
| Bone (femur)            | Prostate        |
| Bone marrow (femur)     | Salivary glands |
| Brain                   | Skin            |
| Eyes                    | Muscle          |
| Heart                   | Small intestine |
| Injection site          | Spinal cord     |
| Kidneys                 | Spleen          |
| Large intestine         | Stomach         |
| Liver                   | Testes          |
| Lung                    | Thymus          |
| Lymph node (mandibular) | Thyroid         |

Lymph node (mesenteric)

Uterus

Additionally, for animals 043M, 045M, 046M, 048M, 051M, 052M, 055M and 058M, the tibia/fibula bone was also collected but not analysed (refer to Section 6.11).

## 6.8 Sample Storage

Samples not analysed immediately were stored frozen in a freezer set to maintain a temperature of -20°C until taken for analysis, with the exception of urine and faeces samples which were stored at -80°C. After analysis, samples were returned to storage in a freezer set to maintain a temperature of -20°C.

Samples of cage wash, dose determinations and dose residues were stored at room temperature prior to and following analysis. These samples were discarded at the Study Director's discretion following acceptance of the study results.

## 6.9 Preparation of Samples for Total Radioactivity Analysis

Volumes or weights of all samples were measured where appropriate

### 6.9.1 Dose Formulation

Duplicate aliquots (0.1 mL) of each dilution of the dose formulation were diluted with water and dissolved in scintillation fluid (Aquasafe 500 Plus, Zinsser Inc.) and analysed directly by liquid scintillation counting.

### 6.9.2 Blood and Plasma

Duplicate weighed aliquots of whole blood (2 x ca. 0.15 g) were taken and then combusted using a Perkin Elmer Model 307 Sample Oxidiser. The resultant  $^3\text{H}_2\text{O}$  generated was collected by absorption in Monophase® (15 mL).

Duplicate aliquots (100 µL) of plasma were allowed to air dry, diluted with water and dissolved in scintillation fluid (Aquasafe 500 Plus, Zinsser Inc.) and analysed directly by LSC.

### 6.9.3 Tissues

Tissue samples were finely chopped with scissors and duplicate, where appropriate, portions were combusted using a Perkin Elmer Model 307 Sample Oxidiser. Smaller tissues were aliquoted directly. The resultant  $^3\text{H}_2\text{O}$  generated was collected by absorption in Monophase® S (15 mL).

Combustion of standards showed that recovery efficiencies were in excess of 95% throughout.

#### 6.9.4 Urine, Faeces and Cage Wash

Urine, faeces and cage wash samples were collected but not analysed for total radioactivity. Urine and faeces sample weights were taken prior to storage. Urine and faeces samples were retained at -80°C for possible analysis of specific lipids by LC-MS/MS conducted and reported separately. The sample weights are presented in [Appendix 3](#).

#### 6.10 Quantification of Radioactivity

##### 6.10.1 Liquid Scintillation Counting

All samples prepared in scintillation fluid were subjected to liquid scintillation counting for 5 min, together with representative blank samples, using a Liquid Scintillation Analyser with automatic quench correction by an external standard method. Prior to analysis, samples were allowed to stabilise with regard to light and temperature. Self-normalisation and calibration (SNC) were conducted once a day. An unquenched tritium standard was used to initially calibrate the system to obtain optimal performance by adjusting the voltage on the photo-multiplier tubes. Representative blank sample values were subtracted from sample count rates to give net disintegrations per minute (dpm) per sample. A limit of reliable measurement of 30 counts per minute (cpm) above background was instituted in these laboratories. Any results arising from data below the limit of reliable measurement were noted in the Results section of the report. Sample repeat analysis were in accordance with Standard Operating Procedures.

##### 6.10.2 Data Presentation

Levels of radioactivity in all samples were quantified by LSC and the data captured into DEBRA® management software, Version 5.7 (LabLogic Ltd, UK). Plasma, blood and tissues concentrations of radioactivity in dpm/g and mass eq/g were calculated based on the measured specific activity (1.24 MBq/mg lipid) of radiolabelled test item in the dose formulation.

Individual and mean data were tabulated. The following information was reported:

- Radioactive content in tissues where a total organ weight is applicable was calculated as % administered (injected) dose
- Radioactive content in tissues, whole blood and plasma as µg equiv/g (or mL).
- Blood/plasma ratio

Data presented in results tables are computer generated in DEBRA and rounded appropriately for inclusion in the report. As a consequence, calculation of individual and mean values from data presented will, in some instances, yield slight differences from the results presented.

## 6.11 Protocol Deviations

Due to the unavailability of rats within specification at (b) (4) the rat supplier used in this study was Envigo, UK, deviating from Section 11 of the Protocol. In the opinion of the Study Director this had no impact on the study outcome since the correct age and strain of rats were used on this study.

In error, tibia/fibula bone were collected at necropsy for animals 043M, 045M, 046M, 048M, 051M, 052M, 055M, and 058M instead of femur bone, deviating from Section 14.1 of the Protocol. Once noticed, the femur bone was retrieved from the residual carcass stored in the -20°C freezer pending disposal and analysed after discussions with the Sponsor. The results appeared similar to the other animals in each timepoint and therefore this had no impact on the study outcome.

## 7 RESULTS

### 7.1 Clinical Observations

In the 100 µg mRNA male group, approximately 24 h following administration, animal 021M was noted to have decreased activity, ungroomed, brown staining on muzzle and irregular respiration. A decrease in bodyweight was noted in all remaining animals (approximately 16 g, equivalent to *ca.* 7% reduction of bodyweight) and food hoppers appeared untouched. By approximately 30 hours post-dose, animal 021M was also piloerect, hunched, and was hypersensitive to noise stimulus. Animal 021M was humanely killed and the diagnostic necropsy carried out showed one finding in the liver (prominent lobular architecture). Additionally, animals 019M and 020M were hunched and piloerect from approximately 30 h post-dose onwards.

In the 50 µg mRNA male group, following administration and for the duration of the study, no adverse effects were noted in any animal.

In the 50 µg mRNA female group, approximately 30 h following administration, animal 042F was noted to have decreased activity, and irregular respiration. At 48 h post dose animal 042F was additionally hunched and piloerect.

### 7.2 Body Weights

At the time of dosing, body weights were in the range of 217-270 g (males) and 179-224 g (females).

### 7.3 Tissue Distribution Following Intramuscular Administration

The mean (sex combined) concentration and recovery of total radioactivity in whole blood, plasma, injection site and tissues following a single intramuscular administration of [<sup>3</sup>H]-08-A01-C01 to Wistar Han rats at a target dose level of 50 µg mRNA/animal (1.29 mg/animal lipid) is presented in [Table 1](#). The mean concentration of total radioactivity in whole blood, plasma, injection site and tissues following a single intramuscular administration of [<sup>3</sup>H]-08-A01-C01 to male and female Wistar Han rats at a target dose level of 50 µg mRNA/animal (1.29 mg/animal lipid) is presented in [Table 2](#). The mean recovery in male and female individual tissues is presented in [Table 3](#).

Individual male and female concentration data is presented in [Appendix 4](#) and [Appendix 5](#), respectively. Individual male and female recovery data is presented in [Appendix 6](#) and [Appendix 7](#), respectively. The male 100 µg data is presented in [Appendix 8](#).

When analysing the injection site, there was often high inter-animal variability in concentration and % injected dose values at each time point. This may have been due to

difficulty in collecting the entirety of this sample since the total area that the injected bolus dose migrated to within the muscle was not visible. When dosing the male 50 µg mRNA group, the injection site was circled using a marker pen to help aid dissection of the injection area. The overall injection site concentrations and % dose values were higher in males than in females. Since concentrations in other tissues were broadly similar between the sexes, it is likely that the higher injection site values in males were a result of its more consistent identification and collection in males.

Following a single intramuscular administration of [<sup>3</sup>H]-08-A01-C01, the greatest mean tissue concentration and, in most instances, % of injected dose was found remaining in the injection site at each time point in both sexes. The injection site mean concentration and equivalent % dose values are presented in the table below.

| Timepoint<br>(h) | Injection site<br>(µg equiv lipid/g) |         | Injection site<br>(% dose) |        |
|------------------|--------------------------------------|---------|----------------------------|--------|
|                  | Male                                 | Female  | Male                       | Female |
| 0.25             | 219.940                              | 36.566  | 32.887                     | 6.815  |
| 1                | 587.670                              | 199.950 | 68.829                     | 36.411 |
| 2                | 529.210                              | 93.144  | 39.053                     | 24.094 |
| 4                | 619.850                              | 56.227  | 47.710                     | 9.056  |
| 8                | 299.590                              | 125.930 | 18.731                     | 24.993 |
| 24               | 267.170                              | 122.540 | 31.957                     | 26.295 |
| 48               | 268.770                              | 61.088  | 32.823                     | 16.426 |

The highest mean recovery of total radioactivity observed was 68.8% of the administered dose at 1-hour post-dose in males.

Low levels of radioactivity were detected in most tissues from the first time point (0.25 h), with the greatest level found circulating in plasma between 1-4 hours post-dose. The plasma and blood mean concentrations and blood:plasma ratios are presented in the table below.

| Timepoint<br>(h) | Blood<br>(µg equiv lipid/g) |        | Plasma<br>(µg equiv lipid/mL) |        | Blood:plasma<br>ratio |        |
|------------------|-----------------------------|--------|-------------------------------|--------|-----------------------|--------|
|                  | Male                        | Female | Male                          | Female | Male                  | Female |
| 0.25             | 3.003                       | 0.936  | 6.035                         | 1.894  | 0.48                  | 1.15   |
| 1                | 2.809                       | 5.928  | 5.379                         | 10.884 | 0.49                  | 0.54   |
| 2                | 4.028                       | 6.773  | 8.714                         | 9.091  | 0.46                  | 0.64   |
| 4                | 3.400                       | 2.698  | 8.755                         | 4.251  | 0.42                  | 0.60   |
| 8                | 2.000                       | 0.628  | 3.573                         | 1.147  | 0.56                  | 0.55   |
| 24               | 1.274                       | 0.544  | 2.621                         | 0.945  | 0.49                  | 0.57   |
| 48               | 0.535                       | 0.305  | 1.085                         | 0.524  | 0.50                  | 0.58   |

Mean plasma concentrations peaked by 4 hours post-dose in males (8.755 µg equiv lipid/mL) and by 1 hour post-dose in females (10.884 µg equiv lipid/mL), before steadily decreasing. Concentrations were higher in plasma than in blood, with mean blood:plasma ratios generally

ca. 0.5-0.6, indicating that the majority of the total radioactivity is associated with the plasma fraction.

Over 48 hours, [<sup>3</sup>H]-08-A01-C01 distributed from the injection site to most tissues, with the majority of tissues exhibiting low levels of radioactivity. The highest mean concentrations observed, and the equivalent % dose, are presented in the tables below.

| Timepoint<br>(h) | Values expressed as µg equiv lipid/g) |        |        |        |                |        |         |
|------------------|---------------------------------------|--------|--------|--------|----------------|--------|---------|
|                  | Liver                                 |        | Spleen |        | Adrenal glands |        | Ovaries |
|                  | Male                                  | Female | Male   | Female | Male           | Female | Female  |
| 0.25             | 1.151                                 | 0.323  | 0.354  | 0.313  | 0.302          | 0.240  | 0.104   |
| 1                | 4.006                                 | 5.244  | 2.140  | 2.801  | 0.580          | 2.388  | 1.339   |
| 2                | 9.574                                 | 12.370 | 5.255  | 10.213 | 1.206          | 4.232  | 1.638   |
| 4                | 18.525                                | 14.569 | 8.945  | 11.646 | 2.569          | 3.206  | 2.341   |
| 8                | 27.916                                | 25.172 | 24.434 | 19.747 | 6.387          | 7.218  | 3.088   |
| 24               | 23.360                                | 15.119 | 22.819 | 17.341 | 19.948         | 7.595  | 5.240   |
| 48               | 18.164                                | 30.411 | 19.550 | 27.155 | 21.476         | 14.942 | 12.261  |

=Mean includes results calculated from data less than 30 cpm above background

| Timepoint<br>(h) | Liver  |        | Spleen |        | Adrenal glands |        | Ovaries |
|------------------|--------|--------|--------|--------|----------------|--------|---------|
|                  | Male   | Female | Male   | Female | Male           | Female | Female  |
| 0.25             | 0.995  | 0.209  | 0.014  | 0.011  | 0.001          | 0.001  | 0.001   |
| 1                | 2.834  | 2.907  | 0.087  | 0.098  | 0.002          | 0.012  | 0.009   |
| 2                | 7.629  | 7.030  | 0.232  | 0.418  | 0.005          | 0.015  | 0.008   |
| 4                | 15.027 | 8.699  | 0.351  | 0.419  | 0.012          | 0.018  | 0.016   |
| 8                | 21.519 | 14.580 | 1.118  | 0.845  | 0.026          | 0.043  | 0.025   |
| 24               | 19.901 | 10.977 | 0.957  | 0.685  | 0.083          | 0.049  | 0.037   |
| 48               | 13.953 | 18.357 | 0.914  | 1.146  | 0.104          | 0.108  | 0.095   |

=Mean includes results calculated from data less than 30 cpm above background

Maximum concentrations ( $C_{max}$ ) in liver and spleen were observed at 8 hours post-dose in males and 48 hours post dose in females, but were broadly similar and appeared to plateau at 8 hours post-dose when considering variability. The greatest mean concentration outside the injection site was observed in the liver, with values of 27.916 µg equiv lipid/g (equivalent to 21.5 % dose) in males and 30.411 µg equiv lipid/g (equivalent to 18.4 % dose) in females. In the spleen the highest concentrations were 24.434 µg equiv lipid/g in males and 27.155 µg equiv lipid/g (equivalent to 1.1% dose in both sexes).

In the adrenal glands and ovaries, the highest mean concentrations were observed at 48 hours post-dose. The highest mean concentrations in the adrenal glands were 21.476 and 14.942 µg equiv lipid/g in males and females, respectively (equivalent to 0.1% dose in both sexes). The highest mean ovaries concentration was 12.261 µg equiv lipid/g (equivalent to 0.1 % dose).

## 8 CONCLUSIONS

In conclusion, the distribution of [<sup>3</sup>H]-08-A01-C01 (monitoring the [<sup>3</sup>H]-CHE lipid label) in blood, plasma and selected tissues was determined in male and female Wistar Han rats over 48 hours after a single intramuscular injection at 50 µg mRNA/animal (1.29 mg/animal lipid dose). The concentrations of [<sup>3</sup>H]-08-A01-C01 were greatest in the injection site at all time points, with levels peaking in the plasma by 1-4 hours post-dose and distribution mainly into liver, adrenal glands, spleen and ovaries over 48 hours. Total recovery of radioactivity outside of the injection site was greatest in the liver, with much lower total recovery in spleen, and very little recovery in adrenals glands and ovaries. The mean plasma, blood and tissue concentrations and tissue distribution patterns were broadly similar between the sexes and [<sup>3</sup>H]-08-A01-C01 did not associate with red blood cells.

## 9 TABLES

**Table 1 Mean (Sexes-Combined) Concentration and Recovery of Total Radioactivity in Whole Blood, Plasma and Tissues Following Single Intramuscular Administration of [<sup>3</sup>H]-08-A01-C01 to Wistar Han Rats****Target Dose Level: 50 µg mRNA/Animal; 1.29 mg Total Lipid/Animal****Results expressed as total lipid concentration (µg lipid equiv/g (mL)) and % of administered dose**

| Sample              | Total Lipid Concentration (µg lipid equiv/g (or mL)) |         |         |         |         |         |         | % of Administered Dose |        |        |        |        |        |        |
|---------------------|------------------------------------------------------|---------|---------|---------|---------|---------|---------|------------------------|--------|--------|--------|--------|--------|--------|
|                     | 0.25 min                                             | 1 h     | 2 h     | 4 h     | 8 h     | 24 h    | 48 h    | 0.25 min               | 1 h    | 2 h    | 4 h    | 8 h    | 24 h   | 48 h   |
| Adipose tissue      | 0.057                                                | 0.100   | 0.126   | 0.128   | 0.093   | 0.084   | 0.181   | -                      | -      | -      | -      | -      | -      | -      |
| Adrenal glands      | 0.271                                                | 1.484   | 2.719   | 2.888   | 6.803   | 13.772  | 18.209  | 0.001                  | 0.007  | 0.010  | 0.015  | 0.035  | 0.066  | 0.106  |
| Bladder             | 0.041                                                | 0.130   | 0.146   | 0.167   | 0.148   | 0.247   | 0.365   | 0.000                  | 0.001  | 0.001  | 0.001  | 0.001  | 0.002  | 0.002  |
| Bone (femur)        | 0.091                                                | 0.195   | 0.266   | 0.276   | 0.340   | 0.342   | 0.687   | -                      | -      | -      | -      | -      | -      | -      |
| Bone marrow (femur) | 0.479                                                | 0.960   | 1.237   | 1.236   | 1.836   | 2.492   | 3.771   | -                      | -      | -      | -      | -      | -      | -      |
| Brain               | 0.045                                                | 0.100   | 0.138   | 0.115   | 0.073   | 0.069   | 0.068   | 0.007                  | 0.013  | 0.020  | 0.016  | 0.011  | 0.010  | 0.009  |
| Eyes                | 0.010                                                | 0.035   | 0.052   | 0.067   | 0.059   | 0.091   | 0.112   | 0.000                  | 0.001  | 0.001  | 0.002  | 0.002  | 0.002  | 0.003  |
| Heart               | 0.282                                                | 1.029   | 1.402   | 0.987   | 0.790   | 0.451   | 0.546   | 0.018                  | 0.056  | 0.084  | 0.060  | 0.042  | 0.027  | 0.030  |
| Injection site      | 128.253                                              | 393.810 | 311.177 | 338.039 | 212.760 | 194.855 | 164.929 | 19.851                 | 52.620 | 31.574 | 28.383 | 21.862 | 29.126 | 24.625 |
| Kidneys             | 0.391                                                | 1.161   | 2.046   | 0.924   | 0.590   | 0.426   | 0.425   | 0.050                  | 0.124  | 0.211  | 0.109  | 0.075  | 0.054  | 0.057  |
| Large intestine     | 0.013                                                | 0.048   | 0.093   | 0.287   | 0.649   | 1.104   | 1.338   | 0.008                  | 0.025  | 0.065  | 0.192  | 0.405  | 0.692  | 0.762  |
| Liver               | 0.737                                                | 4.625   | 10.972  | 16.547  | 26.544  | 19.240  | 24.288  | 0.602                  | 2.871  | 7.330  | 11.863 | 18.050 | 15.439 | 16.155 |
| Lung                | 0.492                                                | 1.210   | 1.834   | 1.497   | 1.151   | 1.039   | 1.093   | 0.052                  | 0.101  | 0.178  | 0.169  | 0.122  | 0.101  | 0.101  |
| Lymph node (man)    | 0.064                                                | 0.189   | 0.290   | 0.408   | 0.534   | 0.554   | 0.727   | -                      | -      | -      | -      | -      | -      | -      |
| Lymph node (mes)    | 0.050                                                | 0.146   | 0.530   | 0.489   | 0.689   | 0.985   | 1.366   | -                      | -      | -      | -      | -      | -      | -      |
| Muscle              | 0.021                                                | 0.061   | 0.084   | 0.103   | 0.096   | 0.095   | 0.192   | -                      | -      | -      | -      | -      | -      | -      |
| Ovaries (females)   | 0.104                                                | 1.339   | 1.638   | 2.341   | 3.088   | 5.240   | 12.261  | 0.001                  | 0.009  | 0.008  | 0.016  | 0.025  | 0.037  | 0.095  |
| Pancreas            | 0.081                                                | 0.207   | 0.414   | 0.380   | 0.294   | 0.358   | 0.599   | 0.003                  | 0.007  | 0.014  | 0.015  | 0.015  | 0.011  | 0.019  |
| Pituitary gland     | 0.339                                                | 0.645   | 0.868   | 0.854   | 0.405   | 0.478   | 0.694   | 0.000                  | 0.001  | 0.001  | 0.001  | 0.000  | 0.000  | 0.001  |
| Prostate (males)    | 0.061                                                | 0.091   | 0.128   | 0.157   | 0.150   | 0.183   | 0.170   | 0.001                  | 0.001  | 0.002  | 0.003  | 0.003  | 0.004  | 0.003  |
| Salivary glands     | 0.084                                                | 0.193   | 0.255   | 0.220   | 0.135   | 0.170   | 0.264   | 0.003                  | 0.007  | 0.008  | 0.008  | 0.005  | 0.006  | 0.009  |
| Skin                | 0.013                                                | 0.208   | 0.159   | 0.145   | 0.119   | 0.157   | 0.253   | -                      | -      | -      | -      | -      | -      | -      |

- =Partial tissue taken therefore not applicable

**Table 1**  
**(Continued)** **Mean (Sexes-Combined) Concentration of Total Radioactivity in Whole Blood, Plasma and Tissues Following Single Intramuscular Administration of [<sup>3</sup>H]-08-A01-C01 to Wistar Han Rats****Target Dose Level: 50 µg mRNA/Animal; 1.29 mg Total Lipid/Animal****Results expressed as total lipid concentration (µg lipid equiv/g (mL)) and % of administered dose**

| Sample             | Total Lipid Concentration (µg lipid equiv/g (or mL)) |       |       |        |        |        |        | % of Administered Dose |       |       |       |       |       |       |
|--------------------|------------------------------------------------------|-------|-------|--------|--------|--------|--------|------------------------|-------|-------|-------|-------|-------|-------|
|                    | 0.25 min                                             | 1 h   | 2 h   | 4 h    | 8 h    | 24 h   | 48 h   | 0.25 min               | 1 h   | 2 h   | 4 h   | 8 h   | 24 h  | 48 h  |
| Small intestine    | 0.030                                                | 0.221 | 0.476 | 0.879  | 1.279  | 1.302  | 1.472  | 0.024                  | 0.130 | 0.319 | 0.543 | 0.776 | 0.906 | 0.835 |
| Spinal cord        | 0.043                                                | 0.097 | 0.169 | 0.250  | 0.106  | 0.085  | 0.112  | 0.001                  | 0.002 | 0.002 | 0.003 | 0.001 | 0.001 | 0.001 |
| Spleen             | 0.334                                                | 2.471 | 7.734 | 10.296 | 22.091 | 20.080 | 23.353 | 0.013                  | 0.093 | 0.325 | 0.385 | 0.982 | 0.821 | 1.030 |
| Stomach            | 0.017                                                | 0.065 | 0.115 | 0.144  | 0.268  | 0.152  | 0.215  | 0.006                  | 0.019 | 0.034 | 0.030 | 0.040 | 0.037 | 0.039 |
| Testes (males)     | 0.031                                                | 0.042 | 0.079 | 0.129  | 0.146  | 0.304  | 0.320  | 0.007                  | 0.010 | 0.017 | 0.030 | 0.034 | 0.074 | 0.074 |
| Thymus             | 0.088                                                | 0.243 | 0.340 | 0.335  | 0.196  | 0.207  | 0.331  | 0.004                  | 0.007 | 0.010 | 0.012 | 0.008 | 0.007 | 0.008 |
| Thyroid            | 0.155                                                | 0.536 | 0.842 | 0.851  | 0.544  | 0.578  | 1.000  | 0.000                  | 0.001 | 0.001 | 0.001 | 0.001 | 0.001 | 0.001 |
| Uterus (females)   | 0.043                                                | 0.203 | 0.305 | 0.140  | 0.287  | 0.289  | 0.456  | 0.002                  | 0.011 | 0.015 | 0.008 | 0.016 | 0.018 | 0.022 |
| Whole blood        | 1.970                                                | 4.369 | 5.401 | 3.049  | 1.314  | 0.909  | 0.420  | -                      | -     | -     | -     | -     | -     | -     |
| Plasma             | 3.965                                                | 8.132 | 8.903 | 6.503  | 2.360  | 1.783  | 0.805  | -                      | -     | -     | -     | -     | -     | -     |
| Blood:plasma ratio | 0.815                                                | 0.515 | 0.550 | 0.510  | 0.555  | 0.530  | 0.540  | -                      | -     | -     | -     | -     | -     | -     |

- =Partial tissue taken therefore not applicable/not applicable

**Table 2 Mean Concentration of Total Radioactivity in Whole Blood, Plasma and Tissues Following Single Intramuscular Administration of [<sup>3</sup>H]-08-A01-C01 to Wistar Han Rats****Target Dose Level: 50 µg mRNA/Animal; 1.29 mg Total Lipid/Animal****Results expressed as µg lipid equiv/g (mL)**

| Sample              | 0.25 min |        | 1 h     |         | 2 h     |        | 4 h     |        | 8 h     |         | 24 h    |         | 48 h    |        |
|---------------------|----------|--------|---------|---------|---------|--------|---------|--------|---------|---------|---------|---------|---------|--------|
|                     | Male     | Female | Male    | Female  | Male    | Female | Male    | Female | Male    | Female  | Male    | Female  | Male    | Female |
| Adipose tissue      | 0.040    | °0.073 | 0.050   | 0.149   | 0.070   | 0.182  | 0.093   | 0.163  | 0.116   | 0.069   | 0.126   | 0.042   | 0.129   | 0.232  |
| Adrenal glands      | 0.302    | °0.240 | 0.580   | 2.388   | 1.206   | 4.232  | 2.569   | 3.206  | 6.387   | 7.218   | 19.948  | 7.595   | 21.476  | 14.942 |
| Bladder             | 0.049    | °0.033 | 0.095   | 0.165   | 0.137   | 0.155  | 0.227   | 0.106  | 0.211   | 0.085   | 0.323   | 0.171   | 0.340   | 0.389  |
| Bone (femur)        | 0.126    | 0.056  | 0.148   | 0.241   | 0.235   | 0.296  | 0.335   | 0.217  | 0.502   | 0.177   | 0.504   | 0.180   | 0.520   | 0.854  |
| Bone marrow (femur) | 0.761    | °0.196 | 0.910   | 1.010   | 1.136   | 1.337  | 1.557   | 0.915  | 2.397   | 1.274   | 3.579   | 1.405   | 3.690   | 3.851  |
| Brain               | 0.073    | °0.016 | 0.083   | 0.117   | 0.143   | 0.133  | 0.155   | 0.075  | 0.101   | 0.045   | 0.090   | 0.047   | 0.083   | 0.052  |
| Eyes                | 0.014    | °0.006 | 0.027   | 0.043   | 0.046   | 0.058  | 0.095   | 0.038  | 0.088   | 0.030   | 0.129   | 0.052   | 0.127   | 0.097  |
| Heart               | 0.419    | °0.144 | 0.631   | 1.426   | 1.122   | 1.682  | 1.049   | 0.925  | 1.189   | 0.391   | 0.583   | 0.318   | 0.672   | 0.420  |
| Injection site      | 219.940  | 36.566 | 587.670 | 199.950 | 529.210 | 93.144 | 619.850 | 56.227 | 299.590 | 125.930 | 267.170 | 122.540 | 268.770 | 61.088 |
| Kidneys             | 0.511    | 0.271  | 0.630   | 1.692   | 1.124   | 2.967  | 1.033   | 0.814  | 0.837   | 0.342   | 0.504   | 0.348   | 0.482   | 0.368  |
| Large intestine     | 0.017    | °0.008 | 0.031   | 0.065   | 0.080   | 0.106  | 0.350   | 0.224  | 0.690   | 0.608   | 1.741   | 0.466   | 1.426   | 1.249  |
| Liver               | 1.151    | 0.323  | 4.006   | 5.244   | 9.574   | 12.370 | 18.525  | 14.569 | 27.916  | 25.172  | 23.360  | 15.119  | 18.164  | 30.411 |
| Lung                | 0.737    | 0.247  | 0.845   | 1.574   | 1.594   | 2.074  | 1.772   | 1.222  | 1.674   | 0.628   | 1.316   | 0.762   | 1.288   | 0.898  |
| Lymph node (man)    | 0.090    | °0.038 | 0.154   | 0.223   | 0.217   | 0.362  | 0.424   | 0.391  | 0.695   | 0.372   | 0.744   | 0.363   | 0.820   | 0.633  |
| Lymph node (mes)    | 0.052    | °0.048 | 0.095   | 0.196   | 0.229   | 0.831  | 0.441   | 0.536  | 0.649   | 0.729   | 1.106   | 0.863   | 1.057   | 1.675  |
| Muscle              | °0.029   | 0.012  | 0.039   | 0.082   | 0.067   | 0.100  | 0.075   | 0.130  | 0.101   | 0.091   | 0.098   | 0.092   | 0.280   | 0.104  |
| Ovaries (females)   | -        | °0.104 | -       | 1.339   | -       | 1.638  | -       | 2.341  | -       | 3.088   | -       | 5.240   | -       | 12.261 |
| Pancreas            | 0.125    | 0.037  | 0.153   | 0.261   | 0.423   | 0.404  | 0.361   | 0.398  | 0.349   | 0.239   | 0.396   | 0.320   | 0.587   | 0.611  |
| Pituitary gland     | 0.537    | °0.141 | 0.446   | 0.844   | 0.781   | 0.955  | 1.249   | 0.458  | 0.669   | 0.141   | 0.656   | 0.300   | 0.543   | 0.845  |
| Prostate (males)    | 0.061    | -      | 0.091   | -       | 0.128   | -      | 0.157   | -      | 0.150   | -       | 0.183   | -       | 0.170   | -      |
| Salivary glands     | 0.114    | °0.054 | 0.148   | 0.237   | 0.214   | 0.295  | 0.270   | 0.169  | 0.176   | 0.094   | 0.243   | 0.096   | 0.297   | 0.231  |
| Skin                | °0.016   | 0.010  | 0.028   | 0.387   | 0.054   | 0.263  | 0.085   | 0.204  | 0.122   | 0.116   | 0.195   | 0.118   | 0.209   | 0.297  |

°=Mean includes results calculated from data less than 30 cpm above background

**Table 2      Mean Concentration of Total Radioactivity in Whole Blood, Plasma and Tissues Following Single  
(Continued)      Intramuscular Administration of [<sup>3</sup>H]-08-A01-C01 to Wistar Han Rats****Target Dose Level: 50 µg mRNA/Animal; 1.29 mg Total Lipid/Animal****Results expressed as µg lipid equiv/g (mL)**

| Sample             | 0.25 min |        | 1 h   |        | 2 h   |        | 4 h   |        | 8 h    |        | 24 h   |        | 48 h   |        |
|--------------------|----------|--------|-------|--------|-------|--------|-------|--------|--------|--------|--------|--------|--------|--------|
|                    | Male     | Female | Male  | Female | Male  | Female | Male  | Female | Male   | Female | Male   | Female | Male   | Female |
| Small intestine    | 0.038    | °0.021 | 0.194 | 0.247  | 0.471 | 0.481  | 0.919 | 0.838  | 1.525  | 1.033  | 1.878  | 0.726  | 1.630  | 1.314  |
| Spinal cord        | 0.061    | °0.024 | 0.072 | 0.122  | 0.166 | 0.172  | 0.375 | 0.124  | 0.168  | 0.044  | 0.121  | 0.048  | 0.162  | 0.062  |
| Spleen             | 0.354    | °0.313 | 2.140 | 2.801  | 5.255 | 10.213 | 8.945 | 11.646 | 24.434 | 19.747 | 22.819 | 17.341 | 19.550 | 27.155 |
| Stomach            | 0.018    | °0.015 | 0.039 | 0.091  | 0.104 | 0.126  | 0.186 | 0.101  | 0.410  | 0.126  | 0.222  | 0.081  | 0.235  | 0.195  |
| Testes (males)     | 0.031    | -      | 0.042 | -      | 0.079 | -      | 0.129 | -      | 0.146  | -      | 0.304  | -      | 0.320  | -      |
| Thymus             | 0.106    | °0.069 | 0.187 | 0.298  | 0.220 | 0.459  | 0.461 | 0.209  | 0.292  | 0.100  | 0.255  | 0.159  | 0.296  | 0.366  |
| Thyroid            | 0.217    | °0.093 | 0.391 | 0.680  | 0.575 | 1.109  | 1.097 | 0.604  | 0.781  | 0.307  | 0.820  | 0.335  | 1.344  | 0.655  |
| Uterus (females)   | -        | °0.043 | -     | 0.203  | -     | 0.305  | -     | 0.140  | -      | 0.287  | -      | 0.289  | -      | 0.456  |
| Whole Blood        | 3.003    | 0.936  | 2.809 | 5.928  | 4.028 | 6.773  | 3.400 | 2.698  | 2.000  | 0.628  | 1.274  | 0.544  | 0.535  | 0.305  |
| Plasma             | 6.035    | 1.894  | 5.379 | 10.884 | 8.714 | 9.091  | 8.755 | 4.251  | 3.573  | 1.147  | 2.621  | 0.945  | 1.085  | 0.524  |
| Blood:plasma ratio | 0.48     | 1.15   | 0.49  | 0.54   | 0.46  | 0.64   | 0.42  | 0.60   | 0.56   | 0.55   | 0.49   | 0.57   | 0.50   | 0.58   |

°=Mean includes results calculated from data less than 30 cpm above background

**Table 3 Mean Recovery of Total Radioactivity in Tissues Following Single Intramuscular Administration of [<sup>3</sup>H]-08-A01-C01 to Wistar Han Rats**

**Target Dose Level: 50 µg mRNA/Animal; 1.29 mg Total Lipid/Animal**

**Results expressed as % administered dose**

| Sample            | 0.25 min |        | 1 h    |        | 2 h    |        | 4 h    |        | 8 h    |        | 24 h   |        | 48 h   |        |
|-------------------|----------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|
|                   | Male     | Female | Male   | Female | Male   | Female | Male   | Female | Male   | Female | Male   | Female | Male   | Female |
| Adrenal glands    | 0.001    | °0.001 | 0.002  | 0.012  | 0.005  | 0.015  | 0.012  | 0.018  | 0.026  | 0.043  | 0.083  | 0.049  | 0.104  | 0.108  |
| Bladder           | 0.000    | °0.000 | 0.001  | 0.001  | 0.001  | 0.001  | 0.001  | 0.001  | 0.002  | 0.000  | 0.002  | 0.001  | 0.002  | 0.002  |
| Brain             | 0.011    | °0.002 | 0.010  | 0.016  | 0.021  | 0.019  | 0.021  | 0.011  | 0.014  | 0.007  | 0.012  | 0.007  | 0.011  | 0.007  |
| Eyes              | 0.000    | °0.000 | 0.000  | 0.001  | 0.001  | 0.001  | 0.002  | 0.001  | 0.002  | 0.001  | 0.002  | 0.001  | 0.003  | 0.002  |
| Heart             | 0.028    | °0.008 | 0.032  | 0.079  | 0.065  | 0.102  | 0.067  | 0.052  | 0.061  | 0.022  | 0.035  | 0.018  | 0.039  | 0.020  |
| Injection site    | 32.887   | 6.815  | 68.829 | 36.411 | 39.053 | 24.094 | 47.710 | 9.056  | 18.731 | 24.993 | 31.957 | 26.295 | 32.823 | 16.426 |
| Kidneys           | 0.069    | 0.030  | 0.077  | 0.171  | 0.149  | 0.272  | 0.136  | 0.082  | 0.109  | 0.040  | 0.068  | 0.039  | 0.071  | 0.042  |
| Large intestine   | 0.011    | °0.004 | 0.018  | 0.032  | 0.054  | 0.075  | 0.236  | 0.148  | 0.463  | 0.346  | 1.091  | 0.293  | 0.810  | 0.714  |
| Liver             | 0.995    | 0.209  | 2.834  | 2.907  | 7.629  | 7.030  | 15.027 | 8.699  | 21.519 | 14.580 | 19.901 | 10.977 | 13.953 | 18.357 |
| Lung              | 0.082    | 0.022  | 0.085  | 0.117  | 0.189  | 0.167  | 0.226  | 0.112  | 0.180  | 0.064  | 0.136  | 0.065  | 0.131  | 0.070  |
| Ovaries (females) | -        | °0.001 | -      | 0.009  | -      | 0.008  | -      | 0.016  | -      | 0.025  | -      | 0.037  | -      | 0.095  |
| Pancreas          | 0.005    | 0.001  | 0.006  | 0.008  | 0.015  | 0.012  | 0.013  | 0.017  | 0.014  | 0.016  | 0.013  | 0.009  | 0.015  | 0.023  |
| Pituitary gland   | 0.000    | °0.000 | 0.000  | 0.001  | 0.000  | 0.001  | 0.001  | 0.000  | 0.000  | 0.000  | 0.000  | 0.000  | 0.000  | 0.001  |
| Prostate (males)  | 0.001    | -      | 0.001  | -      | 0.002  | -      | 0.003  | -      | 0.003  | -      | 0.004  | -      | 0.003  | -      |
| Salivary glands   | 0.004    | °0.002 | 0.005  | 0.008  | 0.007  | 0.009  | 0.009  | 0.006  | 0.007  | 0.003  | 0.008  | 0.003  | 0.010  | 0.007  |
| Small intestine   | 0.032    | °0.015 | 0.124  | 0.135  | 0.353  | 0.285  | 0.623  | 0.462  | 0.972  | 0.580  | 1.275  | 0.536  | 0.971  | 0.698  |
| Spinal cord       | 0.001    | °0.000 | 0.001  | 0.002  | 0.001  | 0.002  | 0.003  | 0.002  | 0.001  | 0.001  | 0.001  | 0.001  | 0.001  | 0.001  |
| Spleen            | 0.014    | °0.011 | 0.087  | 0.098  | 0.232  | 0.418  | 0.351  | 0.419  | 1.118  | 0.845  | 0.957  | 0.685  | 0.914  | 1.146  |
| Stomach           | 0.008    | °0.003 | 0.016  | 0.022  | 0.033  | 0.035  | 0.037  | 0.022  | 0.055  | 0.024  | 0.054  | 0.020  | 0.049  | 0.029  |
| Testes (males)    | 0.007    | -      | 0.010  | -      | 0.017  | -      | 0.030  | -      | 0.034  | -      | 0.074  | -      | 0.074  | -      |
| Thymus            | 0.005    | °0.002 | 0.006  | 0.008  | 0.008  | 0.012  | 0.018  | 0.006  | 0.012  | 0.003  | 0.009  | 0.004  | 0.008  | 0.007  |
| Thyroid           | 0.000    | °0.000 | 0.000  | 0.001  | 0.001  | 0.001  | 0.001  | 0.001  | 0.001  | 0.000  | 0.001  | 0.000  | 0.001  | 0.001  |
| Uterus (females)  | -        | °0.002 | -      | 0.011  | -      | 0.015  | -      | 0.008  | -      | 0.016  | -      | 0.018  | -      | 0.022  |

°=Mean includes results calculated from data less than 30 cpm above background

## 10 APPENDICES

### Appendix 1 Certificates of Analysis for [<sup>3</sup>H]-08-A01-C01 and [<sup>3</sup>H]-CHE

Confidential



#### R&D Formulation Characterization Report

| Batch ID  | LNP ID     | Specific Activity | [Lipid] | Encaps | Encapsulated mRNA | Yield | mRNA/Lipid Ratio | Particle Diameter | Poly-dispersity |
|-----------|------------|-------------------|---------|--------|-------------------|-------|------------------|-------------------|-----------------|
|           |            | dpm/uL            | mg/mL   | %      | mg/mL             | mg    | mg/mg            | nm                |                 |
| NC-0552-1 | 08-A01-C01 | 1,900,000         | 25.7    | 94     | 1.0               | 6.05  | 0.039            | 89                | 0.062           |

#### Notes

Formulated July 6, 2020 for NC-0552 using BioNTech mRNA (AnSo luc 1041 CorVac) and trace labeled with 3H-CHE. Endotoxin below detection limit (<0.5 EU/mL). Sterile filtered using 0.2 µm pore-size filters.  
Stored at -70°C. Thaw at room temperature and dilute on the day of use.

(b) (6)

(b) (6)

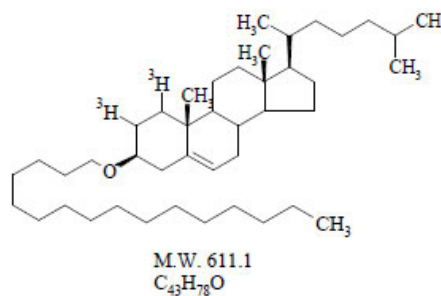
08-July-20  
Date

**Appendix 1      Certificates of Analysis for [ $^3\text{H}$ ]-08-A01-C01 and [ $^3\text{H}$ ]-CHE  
(continued)**

|                                                                                          |                                                         |
|------------------------------------------------------------------------------------------|---------------------------------------------------------|
| <b>TECHNICAL<br/>DATA<br/>SHEET</b>                                                      | $^3\text{H}$                                            |
|                                                                                          | Research Use Only. Not for use in diagnostic procedures |
| <b>CHOLESTERYL HEXADECYL ETHER, [CHOLESTERYL-1,2-<math>^3\text{H}(\text{N})</math>]-</b> |                                                         |
| <b>Product Number: NET859</b>                                                            |                                                         |

**LOT SPECIFIC INFORMATION**

|                    |               |
|--------------------|---------------|
| Lot Number:        | 2656317       |
| Specific Activity: | 51.9 Ci/mmol  |
|                    | 1920 GBq/mmol |
| Production Date:   | 16-Dec-2019   |



**PACKAGING:** 1.0 mCi/ml (37 MBq/ml) in toluene, under argon in an ampoule. Shipped on dry ice.

**STABILITY AND STORAGE RECOMMENDATIONS:** When cholesteryl hexadecyl ether, [cholesteryl-1,2- $^3\text{H}(\text{N})$ ]- is stored at -20°C in its original solvent and at its original concentration, the rate of decomposition is initially 2% for 6 months from date of purification. Stability is nonlinear and not correlated to isotope half-life. Lot to lot variation may occur.

**SPECIFIC ACTIVITY RANGE:** 40-60 Ci/mmol (1480-2220 GBq/mmol)

**RADIOCHEMICAL PURITY:** This product was initially found to be greater than 97% when determined by the following methods. The rate of decomposition can accelerate. It is advisable to check purity prior to use:

High pressure liquid chromatography on a Zorbax C-8 column using the following mobile phase:  
acetonitrile : isopropanol, (35:65).

Thin layer chromatography on silica gel using the following solvent system:  
toluene : hexane, (1:9).

**QUALITY CONTROL:** The radiochemical purity of cholesteryl hexadecyl ether, [cholesteryl-1,2- $^3\text{H}(\text{N})$ ]- is checked at appropriate intervals using the first listed chromatography method.

The precursor used in the synthesis of NET-859 is synthetic.

**HAZARD INFORMATION:** WARNING: This product contains a chemical known to the state of California to cause cancer.

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NET859-REV-02



**Appendix 2 Individual Animal Dosing Summary****Males****Target Dose Level: 50 µg mRNA/Animal; 1.29 mg Total Lipid/Animal**

| Animal ID | Body weight (g) | Dose Received |          |      |
|-----------|-----------------|---------------|----------|------|
|           |                 | mg mRNA       | mg lipid | MBq  |
| 043M      | 270             | 0.0514        | 1.32     | 1.63 |
| 044M      | 264             | 0.0518        | 1.33     | 1.65 |
| 045M      | 244             | 0.0521        | 1.34     | 1.66 |
| 046M      | 263             | 0.0525        | 1.35     | 1.68 |
| 047M      | 232             | 0.0514        | 1.32     | 1.64 |
| 048M      | 228             | 0.0525        | 1.35     | 1.67 |
| 049M      | 259             | 0.0514        | 1.32     | 1.64 |
| 050M      | 249             | 0.0518        | 1.33     | 1.66 |
| 051M      | 257             | 0.0533        | 1.37     | 1.70 |
| 052M      | 258             | 0.0521        | 1.34     | 1.66 |
| 053M      | 249             | 0.0529        | 1.36     | 1.69 |
| 054M      | 235             | 0.0525        | 1.35     | 1.68 |
| 055M      | 247             | 0.0502        | 1.29     | 1.60 |
| 056M      | 256             | 0.0514        | 1.32     | 1.64 |
| 057M      | 266             | 0.0521        | 1.34     | 1.66 |
| 058M      | 263             | 0.0521        | 1.34     | 1.66 |
| 059M      | 243             | 0.0525        | 1.35     | 1.67 |
| 060M      | 248             | 0.0518        | 1.33     | 1.65 |
| 061M      | 240             | 0.0521        | 1.34     | 1.66 |
| 062M      | 259             | 0.0521        | 1.34     | 1.66 |
| 063M      | 238             | 0.0521        | 1.34     | 1.66 |

**Appendix 2 Individual Animal Dosing Summary**  
**(continued)****Females****Target Dose Level: 50 µg mRNA/Animal; 1.29 mg Total Lipid/Animal**

| Animal ID | Body weight (g) | Dose Received |          |      |
|-----------|-----------------|---------------|----------|------|
|           |                 | mg mRNA       | mg lipid | MBq  |
| 022F      | 215             | 0.0521        | 1.34     | 1.66 |
| 023F      | 206             | 0.0529        | 1.36     | 1.68 |
| 024F      | 206             | 0.0514        | 1.32     | 1.64 |
| 025F      | 212             | 0.0533        | 1.37     | 1.70 |
| 026F      | 213             | 0.0525        | 1.35     | 1.68 |
| 027F      | 207             | 0.0529        | 1.36     | 1.69 |
| 028F      | 198             | 0.0529        | 1.36     | 1.68 |
| 029F      | 208             | 0.0529        | 1.36     | 1.69 |
| 030F      | 214             | 0.0518        | 1.33     | 1.64 |
| 031F      | 204             | 0.0537        | 1.38     | 1.71 |
| 032F      | 207             | 0.0533        | 1.37     | 1.70 |
| 033F      | 209             | 0.0521        | 1.34     | 1.66 |
| 034F      | 224             | 0.0510        | 1.31     | 1.62 |
| 035F      | 179             | 0.0482        | 1.24     | 1.53 |
| 036F      | 211             | 0.0467        | 1.20     | 1.49 |
| 037F      | 205             | 0.0506        | 1.30     | 1.61 |
| 038F      | 225             | 0.0502        | 1.29     | 1.60 |
| 039F      | 213             | 0.0525        | 1.35     | 1.67 |
| 040F      | 199             | 0.0533        | 1.37     | 1.69 |
| 041F      | 218             | 0.0529        | 1.36     | 1.69 |
| 042F      | 193             | 0.0533        | 1.37     | 1.70 |

**Appendix 2      Individual Animal Dosing Summary**  
**(continued)****Males****Target Dose Level: 100 µg mRNA/Animal; 2.57 mg Total Lipid/Animal**

| Animal ID | Body weight (g) | Dose Received |          |      |
|-----------|-----------------|---------------|----------|------|
|           |                 | mg mRNA       | mg lipid | MBq  |
| 001M      | 240             | 0.104         | 2.66     | 3.30 |
| 002M      | 243             | 0.106         | 2.73     | 3.38 |
| 003M      | 277             | 0.107         | 2.74     | 3.40 |
| 004M      | 247             | 0.106         | 2.72     | 3.37 |
| 005M      | 243             | 0.107         | 2.76     | 3.42 |
| 006M      | 237             | 0.107         | 2.74     | 3.39 |
| 007M      | 245             | 0.107         | 2.75     | 3.41 |
| 008M      | 237             | 0.106         | 2.73     | 3.39 |
| 009M      | 248             | 0.106         | 2.73     | 3.39 |
| 010M      | 227             | 0.101         | 2.60     | 3.22 |
| 011M      | 267             | 0.105         | 2.71     | 3.36 |
| 012M      | 237             | 0.106         | 2.72     | 3.37 |
| 013M      | 241             | 0.105         | 2.69     | 3.34 |
| 014M      | 264             | 0.107         | 2.76     | 3.42 |
| 015M      | 264             | 0.105         | 2.71     | 3.36 |
| 043M      | 241             | 0.106         | 2.73     | 3.39 |
| 017M      | 252             | 0.106         | 2.73     | 3.39 |
| 018M      | 263             | 0.105         | 2.70     | 3.35 |
| 019M      | 248             | 0.106         | 2.72     | 3.37 |
| 020M      | 246             | 0.106         | 2.73     | 3.39 |
| 021M      | 217             | 0.107         | 2.75     | 3.41 |

**Appendix 3      Urine and Faeces Sample Weights****Males****Target Dose Level: 50 µg mRNA/Animal; 1.29 mg Total Lipid/Animal****Results expressed in g**

| Sample | Timepoint | 061M   | 062M   | 063M   |
|--------|-----------|--------|--------|--------|
| Urine  | Pre-dose  | 6.860  | 18.617 | 14.228 |
|        | 6 h       | 6.139  | 8.101  | 8.153  |
|        | 24 h      | 21.208 | 29.766 | 40.276 |
|        | 48 h      | 28.317 | 28.566 | 36.902 |
| Faeces | Pre-dose  | 11.324 | 7.893  | 6.070  |
|        | 24 h      | 4.716  | 14.327 | 8.659  |
|        | 48 h      | 6.968  | 8.398  | 7.007  |

**Appendix 3      Urine and Faeces Sample Weights**  
**(continued)****Females****Target Dose Level: 50 µg mRNA/Animal; 1.29 mg Total Lipid/Animal****Results expressed in g**

| Sample | Timepoint | 040F   | 041F   | 042F   |
|--------|-----------|--------|--------|--------|
| Urine  | Pre-dose  | 3.963  | 9.453  | 7.513  |
|        | 6 h       | 4.844  | 5.664  | 9.719  |
|        | 24 h      | 20.736 | 29.176 | 21.294 |
|        | 48 h      | 30.371 | 33.928 | 23.141 |
| Faeces | Pre-dose  | 6.110  | 2.679  | 6.010  |
|        | 24 h      | 8.887  | 9.193  | 5.619  |
|        | 48 h      | 4.565  | 6.139  | 4.834  |

**Appendix 3      Urine and Faeces Sample Weights**  
**(continued)****Males****Target Dose Level: 100 µg mRNA/Animal; 2.57 mg Total Lipid/Animal****Results expressed in g**

| Sample | Timepoint | 019M   | 020M   | 021M   |
|--------|-----------|--------|--------|--------|
| Urine  | Pre-dose  | 7.519  | 4.094  | 13.159 |
|        | 6 h       | 8.883  | 8.835  | 10.517 |
|        | 24 h      | 29.916 | 22.983 | 12.664 |
|        | 48 h      | 37.860 | 35.653 | *6.931 |
| Faeces | Pre-dose  | 9.491  | 9.292  | 4.882  |
|        | 24 h      | 11.197 | 14.005 | 8.769  |
|        | 48 h      | 6.950  | 8.229  | *2.449 |

Note that for animal 021M the collection period was approximately 24-31 h.

**Appendix 4 Individual Male Concentration Data****Concentration of Total Radioactivity in Whole Blood, Plasma and Tissues 0.25 min Following Single Intramuscular Administration of [<sup>3</sup>H]-08-A01-C01 to Male Wistar Han Rats****Target Dose Level: 50 µg mRNA/Animal; 1.29 mg Total Lipid/Animal****Results expressed as µg lipid equiv/g (mL)**

| Sample              | 043M    | 044M    | 045M   | Mean    | SD      |
|---------------------|---------|---------|--------|---------|---------|
| Adipose tissue      | 0.056   | 0.045   | 0.019  | 0.040   | 0.019   |
| Adrenal glands      | 0.380   | 0.480   | 0.046  | 0.302   | 0.227   |
| Bladder             | 0.096   | 0.045   | 0.007  | 0.049   | 0.045   |
| Bone (femur)        | 0.172   | 0.085   | 0.119  | 0.126   | 0.044   |
| Bone marrow (femur) | 0.775   | 0.326   | 1.182  | 0.761   | 0.428   |
| Brain               | 0.093   | 0.092   | 0.033  | 0.073   | 0.034   |
| Eyes                | 0.025   | 0.013   | 0.005  | 0.014   | 0.010   |
| Heart               | 0.710   | 0.474   | 0.074  | 0.419   | 0.322   |
| Injection site      | 436.090 | 159.310 | 64.429 | 219.940 | 193.100 |
| Kidneys             | 0.808   | 0.600   | 0.123  | 0.511   | 0.351   |
| Large intestine     | 0.020   | 0.027   | 0.003  | 0.017   | 0.012   |
| Liver               | 2.035   | 1.226   | 0.193  | 1.151   | 0.923   |
| Lung                | 1.050   | 0.826   | 0.334  | 0.737   | 0.366   |
| Lymph node (Man)    | 0.152   | 0.069   | 0.049  | 0.090   | 0.055   |
| Lymph node (Mes)    | 0.087   | 0.054   | 0.016  | 0.052   | 0.036   |
| Muscle              | 0.049   | 0.035   | *0.003 | °0.029  | °0.024  |
| Pancreas            | 0.156   | 0.201   | 0.019  | 0.125   | 0.095   |
| Pituitary gland     | 0.962   | 0.535   | 0.115  | 0.537   | 0.424   |
| Prostate            | 0.098   | 0.074   | 0.012  | 0.061   | 0.044   |
| Salivary glands     | 0.169   | 0.145   | 0.028  | 0.114   | 0.076   |
| Skin                | 0.030   | 0.015   | *0.002 | °0.016  | °0.014  |
| Small intestine     | 0.064   | 0.043   | 0.008  | 0.038   | 0.028   |
| Spinal cord         | 0.108   | 0.063   | 0.013  | 0.061   | 0.047   |
| Spleen              | 0.519   | 0.450   | 0.094  | 0.354   | 0.228   |
| Stomach             | 0.022   | 0.027   | 0.005  | 0.018   | 0.012   |
| Testes              | 0.053   | 0.036   | 0.006  | 0.031   | 0.024   |
| Thymus              | 0.119   | 0.169   | 0.030  | 0.106   | 0.071   |
| Thyroid             | 0.292   | 0.307   | 0.053  | 0.217   | 0.142   |
| Whole Blood         | 5.631   | 2.526   | 0.852  | 3.003   | 2.425   |
| Plasma              | 9.854   | 6.519   | 1.732  | 6.035   | 4.083   |
| Blood:plasma ratio  | 0.57    | 0.39    | 0.49   | 0.48    | 0.09    |

\* = Results calculated from data less than 30 cpm above background

° = Mean includes results calculated from data less than 30 cpm above background

**Appendix 4 Individual Male Concentration Data**  
**(continued)****Concentration of Total Radioactivity in Whole Blood, Plasma and Tissues 1 hour Following Single Intramuscular Administration of [<sup>3</sup>H]-08-A01-C01 to Male Wistar Han Rats****Target Dose Level: 50 µg mRNA/Animal; 1.29 mg Total Lipid/Animal****Results expressed as µg lipid equiv/g (mL)**

| Sample              | 046M    | 047M    | 048M    | Mean    | SD     |
|---------------------|---------|---------|---------|---------|--------|
| Adipose tissue      | 0.037   | 0.073   | 0.040   | 0.050   | 0.020  |
| Adrenal glands      | 0.293   | 0.647   | 0.800   | 0.580   | 0.260  |
| Bladder             | 0.111   | 0.087   | 0.088   | 0.095   | 0.013  |
| Bone (femur)        | 0.115   | 0.085   | 0.246   | 0.148   | 0.085  |
| Bone marrow (femur) | 0.561   | 1.150   | 1.021   | 0.910   | 0.310  |
| Brain               | 0.033   | 0.108   | 0.107   | 0.083   | 0.043  |
| Eyes                | 0.014   | 0.019   | 0.049   | 0.027   | 0.019  |
| Heart               | 0.266   | 0.780   | 0.847   | 0.631   | 0.318  |
| Injection site      | 503.490 | 593.230 | 666.280 | 587.670 | 81.536 |
| Kidneys             | 0.322   | 0.710   | 0.857   | 0.630   | 0.276  |
| Large intestine     | 0.026   | 0.032   | 0.037   | 0.031   | 0.005  |
| Liver               | 2.667   | 3.571   | 5.780   | 4.006   | 1.602  |
| Lung                | 0.428   | 1.203   | 0.903   | 0.845   | 0.391  |
| Lymph node (Man)    | 0.151   | 0.166   | 0.145   | 0.154   | 0.011  |
| Lymph node (Mes)    | 0.076   | 0.100   | 0.109   | 0.095   | 0.017  |
| Muscle              | 0.030   | 0.036   | 0.050   | 0.039   | 0.010  |
| Pancreas            | 0.076   | 0.189   | 0.193   | 0.153   | 0.067  |
| Pituitary gland     | 0.202   | 0.502   | 0.634   | 0.446   | 0.221  |
| Prostate            | 0.063   | 0.105   | 0.105   | 0.091   | 0.024  |
| Salivary glands     | 0.084   | 0.151   | 0.208   | 0.148   | 0.062  |
| Skin                | 0.020   | 0.027   | 0.039   | 0.028   | 0.010  |
| Small intestine     | 0.144   | 0.214   | 0.223   | 0.194   | 0.043  |
| Spinal cord         | 0.062   | 0.070   | 0.084   | 0.072   | 0.011  |
| Spleen              | 3.314   | 1.388   | 1.720   | 2.140   | 1.029  |
| Stomach             | 0.024   | 0.043   | 0.049   | 0.039   | 0.013  |
| Testes              | 0.026   | 0.041   | 0.057   | 0.042   | 0.015  |
| Thymus              | 0.201   | 0.133   | 0.226   | 0.187   | 0.048  |
| Thyroid             | 0.126   | 0.599   | 0.448   | 0.391   | 0.241  |
| Whole Blood         | 0.873   | 4.534   | 3.018   | 2.809   | 1.840  |
| Plasma              | 2.937   | 6.047   | 7.153   | 5.379   | 2.186  |
| Blood:plasma ratio  | 0.30    | 0.75    | 0.42    | 0.49    | 0.23   |

**Appendix 4 Individual Male Concentration Data**  
**(continued)****Concentration of Total Radioactivity in Whole Blood, Plasma and Tissues 2 hours Following Single Intramuscular Administration of [3H]-08-A01-C01 to Male Wistar Han Rats****Target Dose Level: 50 µg mRNA/Animal; 1.29 mg Total Lipid/Animal****Results expressed as µg lipid equiv/g (mL)**

| Sample              | 049M    | 050M     | 051M   | Mean    | SD      |
|---------------------|---------|----------|--------|---------|---------|
| Adipose tissue      | 0.084   | 0.034    | 0.090  | 0.070   | 0.031   |
| Adrenal glands      | 1.809   | 0.584    | 1.226  | 1.206   | 0.613   |
| Bladder             | 0.152   | 0.080    | 0.179  | 0.137   | 0.051   |
| Bone (femur)        | 0.250   | 0.180    | 0.273  | 0.235   | 0.048   |
| Bone marrow (femur) | 1.526   | 0.559    | 1.323  | 1.136   | 0.510   |
| Brain               | 0.220   | 0.088    | 0.121  | 0.143   | 0.069   |
| Eyes                | 0.036   | 0.023    | 0.077  | 0.046   | 0.028   |
| Heart               | 1.782   | 0.682    | 0.901  | 1.122   | 0.582   |
| Injection site      | 445.930 | 1052.800 | 88.843 | 529.210 | 487.370 |
| Kidneys             | 1.467   | 0.785    | 1.120  | 1.124   | 0.341   |
| Large intestine     | 0.074   | 0.056    | 0.109  | 0.080   | 0.027   |
| Liver               | 12.023  | 5.816    | 10.885 | 9.574   | 3.304   |
| Lung                | 2.397   | 0.968    | 1.419  | 1.594   | 0.730   |
| Lymph node (Man)    | 0.328   | 0.112    | 0.210  | 0.217   | 0.108   |
| Lymph node (Mes)    | 0.312   | 0.180    | 0.194  | 0.229   | 0.073   |
| Muscle              | 0.083   | 0.060    | 0.057  | 0.067   | 0.014   |
| Pancreas            | 0.296   | 0.179    | 0.792  | 0.423   | 0.325   |
| Pituitary gland     | 1.175   | 0.405    | 0.764  | 0.781   | 0.385   |
| Prostate            | 0.150   | 0.095    | 0.139  | 0.128   | 0.029   |
| Salivary glands     | 0.279   | 0.113    | 0.251  | 0.214   | 0.089   |
| Skin                | 0.083   | 0.032    | 0.048  | 0.054   | 0.026   |
| Small intestine     | 0.455   | 0.458    | 0.500  | 0.471   | 0.025   |
| Spinal cord         | 0.184   | 0.150    | 0.163  | 0.166   | 0.017   |
| Spleen              | 6.771   | 2.590    | 6.403  | 5.255   | 2.315   |
| Stomach             | 0.121   | 0.059    | 0.133  | 0.104   | 0.040   |
| Testes              | 0.120   | 0.039    | 0.077  | 0.079   | 0.040   |
| Thymus              | 0.248   | 0.146    | 0.265  | 0.220   | 0.065   |
| Thyroid             | 0.749   | 0.361    | 0.615  | 0.575   | 0.197   |
| Whole Blood         | 4.913   | 2.788    | 4.384  | 4.028   | 1.106   |
| Plasma              | 10.623  | 6.177    | 9.341  | 8.714   | 2.288   |
| Blood:plasma ratio  | 0.46    | 0.45     | 0.47   | 0.46    | 0.01    |

#### Appendix 4 Individual Male Concentration Data (continued)

##### Concentration of Total Radioactivity in Whole Blood, Plasma and Tissues 4 hours Following Single Intramuscular Administration of [<sup>3</sup>H]-08-A01-C01 to Male Wistar Han Rats

**Target Dose Level: 50 µg mRNA/Animal; 1.29 mg Total Lipid/Animal**

**Results expressed as µg lipid equiv/g (mL)**

| Sample              | 052M    | 053M     | 054M    | Mean    | SD      |
|---------------------|---------|----------|---------|---------|---------|
| Adipose tissue      | 0.062   | 0.092    | 0.124   | 0.093   | 0.031   |
| Adrenal glands      | 2.252   | 1.999    | 3.456   | 2.569   | 0.779   |
| Bladder             | 0.207   | 0.239    | 0.234   | 0.227   | 0.017   |
| Bone (femur)        | 0.264   | 0.234    | 0.506   | 0.335   | 0.149   |
| Bone marrow (femur) | 1.318   | 1.364    | 1.987   | 1.557   | 0.374   |
| Brain               | 0.136   | 0.112    | 0.217   | 0.155   | 0.055   |
| Eyes                | 0.084   | 0.133    | 0.067   | 0.095   | 0.034   |
| Heart               | 0.993   | 0.669    | 1.484   | 1.049   | 0.411   |
| Injection site      | 445.970 | 1001.000 | 412.620 | 619.850 | 330.480 |
| Kidneys             | 0.967   | 0.737    | 1.395   | 1.033   | 0.334   |
| Large intestine     | 0.413   | 0.311    | 0.327   | 0.350   | 0.055   |
| Liver               | 14.739  | 16.391   | 24.445  | 18.525  | 5.193   |
| Lung                | 2.047   | 1.003    | 2.265   | 1.772   | 0.675   |
| Lymph node (Man)    | 0.283   | 0.564    | 0.426   | 0.424   | 0.140   |
| Lymph node (Mes)    | 0.287   | 0.258    | 0.780   | 0.441   | 0.293   |
| Muscle              | 0.064   | 0.057    | 0.104   | 0.075   | 0.025   |
| Pancreas            | 0.277   | 0.413    | 0.393   | 0.361   | 0.073   |
| Pituitary gland     | 0.933   | 2.418    | 0.397   | 1.249   | 1.047   |
| Prostate            | 0.161   | 0.121    | 0.190   | 0.157   | 0.035   |
| Salivary glands     | 0.232   | 0.197    | 0.380   | 0.270   | 0.097   |
| Skin                | 0.073   | 0.052    | 0.131   | 0.085   | 0.041   |
| Small intestine     | 0.822   | 0.698    | 1.235   | 0.919   | 0.281   |
| Spinal cord         | 0.193   | 0.745    | 0.188   | 0.375   | 0.320   |
| Spleen              | 6.146   | 11.159   | 9.529   | 8.945   | 2.557   |
| Stomach             | 0.324   | 0.058    | 0.176   | 0.186   | 0.134   |
| Testes              | 0.105   | 0.098    | 0.185   | 0.129   | 0.049   |
| Thymus              | 0.210   | 0.371    | 0.800   | 0.461   | 0.305   |
| Thyroid             | 1.055   | 1.301    | 0.936   | 1.097   | 0.186   |
| Whole Blood         | 3.547   | 2.519    | 4.133   | 3.400   | 0.817   |
| Plasma              | 8.820   | 4.802    | 12.644  | 8.755   | 3.922   |
| Blood:plasma ratio  | 0.40    | 0.52     | 0.33    | 0.42    | 0.10    |

#### Appendix 4 Individual Male Concentration Data (continued)

##### Concentration of Total Radioactivity in Whole Blood, Plasma and Tissues 8 hours Following Single Intramuscular Administration of [<sup>3</sup>H]-08-A01-C01 to Male Wistar Han Rats

**Target Dose Level: 50 µg mRNA/Animal; 1.29 mg Total Lipid/Animal**

**Results expressed as µg lipid equiv/g (mL)**

| Sample              | 055M    | 056M    | 057M    | Mean    | SD      |
|---------------------|---------|---------|---------|---------|---------|
| Adipose tissue      | 0.076   | 0.163   | 0.109   | 0.116   | 0.044   |
| Adrenal glands      | 4.440   | 4.886   | 9.835   | 6.387   | 2.995   |
| Bladder             | N.S.    | 0.198   | 0.224   | 0.211   | N.A.    |
| Bone (femur)        | 0.510   | 0.355   | 0.639   | 0.502   | 0.142   |
| Bone marrow (femur) | 3.050   | 1.943   | 2.199   | 2.397   | 0.579   |
| Brain               | 0.105   | 0.096   | 0.103   | 0.101   | 0.005   |
| Eyes                | N.S.    | 0.071   | 0.104   | 0.088   | N.A.    |
| Heart               | 1.418   | 1.008   | 1.142   | 1.189   | 0.209   |
| Injection site      | 181.620 | 497.270 | 219.870 | 299.590 | 172.260 |
| Kidneys             | 0.934   | 0.795   | 0.783   | 0.837   | 0.084   |
| Large intestine     | 0.735   | 0.665   | 0.672   | 0.690   | 0.039   |
| Liver               | 23.158  | 22.178  | 38.412  | 27.916  | 9.103   |
| Lung                | 1.679   | 1.643   | 1.701   | 1.674   | 0.029   |
| Lymph node (Man)    | 0.432   | 1.053   | 0.601   | 0.695   | 0.321   |
| Lymph node (Mes)    | 0.444   | 0.609   | 0.892   | 0.649   | 0.226   |
| Muscle              | 0.082   | 0.096   | 0.127   | 0.101   | 0.023   |
| Pancreas            | 0.352   | 0.418   | 0.276   | 0.349   | 0.071   |
| Pituitary gland     | 0.635   | 0.477   | 0.894   | 0.669   | 0.211   |
| Prostate            | 0.184   | 0.127   | 0.139   | 0.150   | 0.030   |
| Salivary glands     | 0.170   | 0.157   | 0.202   | 0.176   | 0.023   |
| Skin                | 0.138   | 0.111   | 0.117   | 0.122   | 0.014   |
| Small intestine     | 1.423   | 1.518   | 1.634   | 1.525   | 0.106   |
| Spinal cord         | 0.146   | 0.119   | 0.239   | 0.168   | 0.063   |
| Spleen              | 21.122  | 24.073  | 28.107  | 24.434  | 3.507   |
| Stomach             | 0.345   | 0.107   | 0.777   | 0.410   | 0.340   |
| Testes              | 0.153   | 0.107   | 0.179   | 0.146   | 0.037   |
| Thymus              | 0.317   | 0.278   | 0.282   | 0.292   | 0.021   |
| Thyroid             | 0.940   | 0.611   | 0.792   | 0.781   | 0.165   |
| Whole Blood         | 2.215   | 1.968   | 1.817   | 2.000   | 0.201   |
| Plasma              | 3.978   | 3.465   | 3.275   | 3.573   | 0.364   |
| Blood:plasma ratio  | 0.56    | 0.57    | 0.55    | 0.56    | 0.01    |

N.S. = No sample due to oxidiser failure

N.A. = Not applicable

#### Appendix 4 Individual Male Concentration Data (continued)

##### Concentration of Total Radioactivity in Whole Blood, Plasma and Tissues 24 hours Following Single Intramuscular Administration of [<sup>3</sup>H]-08-A01-C01 to Male Wistar Han Rats

**Target Dose Level: 50 µg mRNA/Animal; 1.29 mg Total Lipid/Animal**

**Results expressed as µg lipid equiv/g (mL)**

| Sample              | 058M    | 059M    | 060M    | Mean    | SD     |
|---------------------|---------|---------|---------|---------|--------|
| Adipose tissue      | 0.079   | 0.116   | 0.182   | 0.126   | 0.053  |
| Adrenal glands      | 10.795  | 21.060  | 27.988  | 19.948  | 8.650  |
| Bladder             | 0.211   | 0.394   | 0.365   | 0.323   | 0.099  |
| Bone (femur)        | 0.456   | 0.408   | 0.649   | 0.504   | 0.127  |
| Bone marrow (femur) | 2.286   | 3.625   | 4.824   | 3.579   | 1.270  |
| Brain               | 0.049   | 0.099   | 0.124   | 0.090   | 0.038  |
| Eyes                | 0.098   | 0.113   | 0.178   | 0.129   | 0.042  |
| Heart               | 0.640   | 0.590   | 0.520   | 0.583   | 0.060  |
| Injection site      | 178.010 | 330.550 | 292.960 | 267.170 | 79.471 |
| Kidneys             | 0.522   | 0.407   | 0.584   | 0.504   | 0.090  |
| Large intestine     | 0.592   | 1.611   | 3.019   | 1.741   | 1.219  |
| Liver               | 17.750  | 21.966  | 30.365  | 23.360  | 6.422  |
| Lung                | 0.942   | 1.334   | 1.672   | 1.316   | 0.365  |
| Lymph node (Man)    | 0.577   | 0.689   | 0.965   | 0.744   | 0.200  |
| Lymph node (Mes)    | 0.905   | 1.040   | 1.373   | 1.106   | 0.241  |
| Muscle              | 0.092   | 0.068   | 0.133   | 0.098   | 0.033  |
| Pancreas            | 0.294   | 0.382   | 0.513   | 0.396   | 0.110  |
| Pituitary gland     | 0.489   | 0.768   | 0.711   | 0.656   | 0.147  |
| Prostate            | 0.150   | 0.183   | 0.215   | 0.183   | 0.032  |
| Salivary glands     | 0.168   | 0.243   | 0.317   | 0.243   | 0.075  |
| Skin                | 0.134   | 0.166   | 0.287   | 0.195   | 0.081  |
| Small intestine     | 0.971   | 1.994   | 2.670   | 1.878   | 0.855  |
| Spinal cord         | 0.091   | 0.144   | 0.127   | 0.121   | 0.027  |
| Spleen              | 19.140  | 15.796  | 33.523  | 22.819  | 9.419  |
| Stomach             | 0.110   | 0.168   | 0.386   | 0.222   | 0.145  |
| Testes              | 0.234   | 0.286   | 0.392   | 0.304   | 0.080  |
| Thymus              | 0.163   | 0.235   | 0.368   | 0.255   | 0.104  |
| Thyroid             | 0.721   | 0.660   | 1.081   | 0.820   | 0.228  |
| Whole Blood         | 1.473   | 1.237   | 1.112   | 1.274   | 0.183  |
| Plasma              | 2.584   | 2.935   | 2.345   | 2.621   | 0.297  |
| Blood:plasma ratio  | 0.57    | 0.42    | 0.47    | 0.49    | 0.08   |

**Appendix 4 Individual Male Concentration Data**  
**(continued)****Concentration of Total Radioactivity in Whole Blood, Plasma and Tissues 48 hours Following Single Intramuscular Administration of [3H]-08-A01-C01 to Male Wistar Han Rats****Target Dose Level: 50 µg mRNA/Animal; 1.29 mg Total Lipid/Animal****Results expressed as µg lipid equiv/g (mL)**

| Sample              | 061M    | 062M    | 063M    | Mean    | SD     |
|---------------------|---------|---------|---------|---------|--------|
| Adipose tissue      | 0.104   | 0.162   | 0.121   | 0.129   | 0.030  |
| Adrenal glands      | 13.913  | 35.091  | 15.424  | 21.476  | 11.815 |
| Bladder             | 0.274   | 0.447   | 0.298   | 0.340   | 0.094  |
| Bone (femur)        | 0.344   | 0.577   | 0.639   | 0.520   | 0.155  |
| Bone marrow (femur) | 2.566   | 5.049   | 3.455   | 3.690   | 1.258  |
| Brain               | 0.051   | 0.112   | 0.087   | 0.083   | 0.031  |
| Eyes                | 0.100   | 0.121   | 0.160   | 0.127   | 0.031  |
| Heart               | 0.418   | 0.955   | 0.642   | 0.672   | 0.270  |
| Injection site      | 292.370 | 196.910 | 317.030 | 268.770 | 63.446 |
| Kidneys             | 0.309   | 0.673   | 0.463   | 0.482   | 0.182  |
| Large intestine     | 0.998   | 1.235   | 2.045   | 1.426   | 0.549  |
| Liver               | 17.734  | 20.580  | 16.177  | 18.164  | 2.233  |
| Lung                | 0.809   | 1.885   | 1.170   | 1.288   | 0.548  |
| Lymph node (Man)    | 0.728   | 1.078   | 0.656   | 0.820   | 0.226  |
| Lymph node (Mes)    | 0.924   | 1.620   | 0.626   | 1.057   | 0.510  |
| Muscle              | 0.078   | 0.115   | 0.647   | 0.280   | 0.318  |
| Pancreas            | 0.291   | 0.506   | 0.964   | 0.587   | 0.344  |
| Pituitary gland     | 0.431   | 0.610   | 0.588   | 0.543   | 0.098  |
| Prostate            | 0.110   | 0.265   | 0.135   | 0.170   | 0.083  |
| Salivary glands     | 0.286   | 0.370   | 0.234   | 0.297   | 0.069  |
| Skin                | 0.177   | 0.267   | 0.183   | 0.209   | 0.051  |
| Small intestine     | 1.178   | 2.030   | 1.681   | 1.630   | 0.428  |
| Spinal cord         | 0.089   | 0.129   | 0.267   | 0.162   | 0.093  |
| Spleen              | 12.073  | 25.689  | 20.887  | 19.550  | 6.906  |
| Stomach             | 0.122   | 0.315   | 0.268   | 0.235   | 0.101  |
| Testes              | 0.214   | 0.471   | 0.275   | 0.320   | 0.134  |
| Thymus              | 0.226   | 0.362   | 0.299   | 0.296   | 0.068  |
| Thyroid             | 0.830   | 1.797   | 1.406   | 1.344   | 0.486  |
| Whole Blood         | 0.594   | 0.473   | 0.536   | 0.535   | 0.060  |
| Plasma              | 1.021   | 1.003   | 1.230   | 1.085   | 0.126  |
| Blood:plasma ratio  | 0.58    | 0.47    | 0.44    | 0.50    | 0.08   |

**Appendix 5 Individual Female Concentration Data****Concentration of Total Radioactivity in Whole Blood, Plasma and Tissues 0.25 min Following Single Intramuscular Administration of [<sup>3</sup>H]-08-A01-C01 to Female Wistar Han Rats****Target Dose Level: 50 µg mRNA/Animal; 1.29 mg Total Lipid/Animal****Results expressed as µg lipid equiv/g (mL)**

| Sample              | 022F   | 023F <sup>A</sup> | 024F   | Mean   | SD     |
|---------------------|--------|-------------------|--------|--------|--------|
| Adipose tissue      | 0.203  | *0.002            | 0.015  | °0.073 | °0.113 |
| Adrenal glands      | 0.578  | *0.000            | 0.143  | °0.240 | °0.301 |
| Bladder             | 0.050  | *0.000            | 0.048  | °0.033 | °0.029 |
| Bone (femur)        | 0.146  | 0.003             | 0.019  | 0.056  | 0.079  |
| Bone marrow (femur) | N.S.   | 0.264             | *0.128 | °0.196 | N.A.   |
| Brain               | 0.036  | *0.002            | 0.011  | °0.016 | °0.018 |
| Eyes                | 0.015  | *0.000            | 0.004  | °0.006 | °0.008 |
| Injection site      | 27.519 | 77.480            | 4.697  | 36.566 | 37.225 |
| Heart               | 0.310  | *0.001            | 0.121  | °0.144 | °0.156 |
| Kidneys             | 0.544  | 0.126             | 0.143  | 0.271  | 0.236  |
| Large intestine     | 0.019  | *0.001            | 0.004  | °0.008 | °0.010 |
| Liver               | 0.635  | 0.018             | 0.316  | 0.323  | 0.309  |
| Lung                | 0.550  | 0.012             | 0.177  | 0.247  | 0.275  |
| Lymph node (Man)    | 0.088  | *0.000            | 0.025  | °0.038 | °0.045 |
| Lymph node (Mes)    | 0.127  | *0.000            | 0.018  | °0.048 | °0.069 |
| Muscle              | 0.024  | 0.006             | 0.007  | 0.012  | 0.010  |
| Ovaries             | 0.206  | *0.000            | 0.106  | °0.104 | °0.103 |
| Pancreas            | 0.072  | 0.008             | 0.030  | 0.037  | 0.033  |
| Pituitary gland     | 0.310  | *0.000            | 0.113  | °0.141 | °0.157 |
| Salivary glands     | 0.133  | *0.000            | 0.028  | °0.054 | °0.070 |
| Skin                | 0.018  | 0.004             | 0.009  | 0.010  | 0.007  |
| Small intestine     | 0.051  | *0.001            | 0.010  | °0.021 | °0.026 |
| Spinal cord         | 0.057  | *0.000            | 0.016  | °0.024 | °0.029 |
| Spleen              | 0.366  | *0.004            | 0.570  | °0.313 | °0.287 |
| Stomach             | 0.032  | *0.001            | 0.013  | °0.015 | °0.016 |
| Thymus              | 0.159  | *0.003            | 0.047  | °0.069 | °0.080 |
| Thyroid             | 0.181  | *0.000            | 0.097  | °0.093 | °0.091 |
| Uterus              | 0.090  | *0.000            | 0.037  | °0.043 | °0.045 |
| Whole Blood         | 2.016  | 0.013             | 0.778  | 0.936  | 1.011  |
| Plasma              | 4.189  | 0.005             | 1.487  | 1.894  | 2.121  |
| Blood:plasma ratio  | 0.48   | 2.43              | 0.52   | 1.15   | 1.12   |

N.S. = No sample due to analysis error (the bone marrow was not able to be removed from the bone since the bone was initially crushed for analysis)

A = Animal 023F appeared to have a slow distribution compared with the other animals

\* = Results calculated from data less than 30 cpm above background

° = Mean includes results calculated from data less than 30 cpm above background

## Appendix 5 Individual Female Concentration Data (continued)

### Concentration of Total Radioactivity in Whole Blood, Plasma and Tissues 1 hour Following Single Intramuscular Administration of [<sup>3</sup>H]-08-A01-C01 to Female Wistar Han Rats

**Target Dose Level: 50 µg mRNA/Animal; 1.29 mg Total Lipid/Animal**

**Results expressed as µg lipid equiv/g (mL)**

| Sample              | 025F   | 026F    | 027F    | Mean    | SD      |
|---------------------|--------|---------|---------|---------|---------|
| Adipose tissue      | 0.145  | 0.234   | 0.069   | 0.149   | 0.083   |
| Adrenal glands      | 1.779  | 2.131   | 3.254   | 2.388   | 0.770   |
| Bladder             | 0.123  | 0.206   | 0.166   | 0.165   | 0.042   |
| Bone (femur)        | 0.216  | 0.285   | 0.223   | 0.241   | 0.038   |
| Bone marrow (femur) | 0.886  | 1.219   | 0.926   | 1.010   | 0.182   |
| Brain               | 0.096  | 0.139   | 0.115   | 0.117   | 0.022   |
| Eyes                | 0.052  | 0.052   | 0.027   | 0.043   | 0.015   |
| Heart               | 1.273  | 1.884   | 1.120   | 1.426   | 0.404   |
| Injection site      | 31.021 | 202.720 | 366.100 | 199.950 | 167.560 |
| Kidneys             | 1.568  | 2.396   | 1.112   | 1.692   | 0.651   |
| Large intestine     | 0.060  | 0.065   | 0.070   | 0.065   | 0.005   |
| Liver               | 6.342  | 4.717   | 4.674   | 5.244   | 0.951   |
| Lung                | 1.455  | 1.954   | 1.313   | 1.574   | 0.336   |
| Lymph node (Man)    | 0.226  | 0.266   | 0.176   | 0.223   | 0.045   |
| Lymph node (Mes)    | 0.207  | 0.226   | 0.155   | 0.196   | 0.037   |
| Muscle              | 0.080  | 0.093   | 0.072   | 0.082   | 0.011   |
| Ovaries             | 1.630  | 1.650   | 0.736   | 1.339   | 0.522   |
| Pancreas            | 0.208  | 0.343   | 0.234   | 0.261   | 0.072   |
| Pituitary gland     | 0.607  | 1.114   | 0.810   | 0.844   | 0.255   |
| Salivary glands     | 0.245  | 0.327   | 0.140   | 0.237   | 0.094   |
| Skin                | 0.056  | 0.956   | 0.148   | 0.387   | 0.495   |
| Small intestine     | 0.281  | 0.223   | 0.235   | 0.247   | 0.031   |
| Spinal cord         | 0.111  | 0.119   | 0.137   | 0.122   | 0.013   |
| Spleen              | 2.423  | 2.626   | 3.355   | 2.801   | 0.490   |
| Stomach             | 0.085  | 0.118   | 0.070   | 0.091   | 0.025   |
| Thymus              | 0.248  | 0.483   | 0.164   | 0.298   | 0.165   |
| Thyroid             | 0.510  | 0.997   | 0.533   | 0.680   | 0.275   |
| Uterus              | 0.194  | 0.251   | 0.164   | 0.203   | 0.044   |
| Whole Blood         | 5.057  | 8.484   | 4.243   | 5.928   | 2.251   |
| Plasma              | 9.655  | 14.318  | 8.680   | 10.884  | 3.014   |
| Blood:plasma ratio  | 0.52   | 0.59    | 0.49    | 0.54    | 0.05    |

**Appendix 5 Individual Female Concentration Data**  
**(continued)****Concentration of Total Radioactivity in Whole Blood, Plasma and Tissues 2 hours Following Single Intramuscular Administration of [<sup>3</sup>H]-08-A01-C01 to Female Wistar Han Rats****Target Dose Level: 50 µg mRNA/Animal; 1.29 mg Total Lipid/Animal****Results expressed as µg lipid equiv/g (mL)**

| Sample              | 028F  | 029F   | 030F    | Mean   | SD      |
|---------------------|-------|--------|---------|--------|---------|
| Adipose tissue      | 0.110 | 0.274  | 0.162   | 0.182  | 0.084   |
| Adrenal glands      | 1.429 | 8.981  | 2.285   | 4.232  | 4.135   |
| Bladder             | 0.062 | 0.289  | 0.114   | 0.155  | 0.119   |
| Bone (femur)        | 0.132 | 0.566  | 0.189   | 0.296  | 0.236   |
| Bone marrow (femur) | 0.575 | 1.722  | 1.714   | 1.337  | 0.660   |
| Brain               | 0.063 | 0.241  | 0.095   | 0.133  | 0.095   |
| Eyes                | 0.034 | 0.117  | 0.023   | 0.058  | 0.051   |
| Heart               | 0.554 | 3.221  | 1.272   | 1.682  | 1.380   |
| Injection site      | 0.092 | 1.744  | 277.600 | 93.144 | 159.740 |
| Kidneys             | 0.623 | 2.870  | 5.408   | 2.967  | 2.394   |
| Large intestine     | 0.027 | 0.198  | 0.092   | 0.106  | 0.086   |
| Liver               | 5.209 | 21.794 | 10.108  | 12.370 | 8.521   |
| Lung                | 0.908 | 4.000  | 1.313   | 2.074  | 1.681   |
| Lymph node (Man)    | 0.198 | 0.701  | 0.188   | 0.362  | 0.293   |
| Lymph node (Mes)    | 1.473 | 0.640  | 0.381   | 0.831  | 0.571   |
| Muscle              | 0.045 | 0.140  | 0.114   | 0.100  | 0.049   |
| Ovaries             | 0.474 | 2.683  | 1.756   | 1.638  | 1.109   |
| Pancreas            | 0.116 | 0.825  | 0.270   | 0.404  | 0.373   |
| Pituitary gland     | 0.414 | 1.853  | 0.599   | 0.955  | 0.783   |
| Salivary glands     | 0.141 | 0.562  | 0.182   | 0.295  | 0.232   |
| Skin                | 0.040 | 0.263  | 0.486   | 0.263  | 0.223   |
| Small intestine     | 0.305 | 0.664  | 0.473   | 0.481  | 0.180   |
| Spinal cord         | 0.109 | 0.289  | 0.118   | 0.172  | 0.102   |
| Spleen              | 2.066 | 23.785 | 4.788   | 10.213 | 11.832  |
| Stomach             | 0.088 | 0.211  | 0.077   | 0.126  | 0.074   |
| Thymus              | 0.109 | 1.108  | 0.160   | 0.459  | 0.562   |
| Thyroid             | 0.371 | 1.791  | 1.163   | 1.109  | 0.711   |
| Uterus              | 0.169 | 0.568  | 0.178   | 0.305  | 0.228   |
| Whole Blood         | 2.194 | 14.470 | 3.655   | 6.773  | 6.706   |
| Plasma              | 4.442 | 15.480 | 7.350   | 9.091  | 5.721   |
| Blood:plasma ratio  | 0.49  | 0.93   | 0.50    | 0.64   | 0.25    |

**Appendix 5 Individual Female Concentration Data**  
**(continued)****Concentration of Total Radioactivity in Whole Blood, Plasma and Tissues 4 hours Following Single Intramuscular Administration of [<sup>3</sup>H]-08-A01-C01 to Female Wistar Han Rats****Target Dose Level: 50 µg mRNA/Animal; 1.29 mg Total Lipid/Animal****Results expressed as µg lipid equiv/g (mL)**

| Sample              | 031F  | 032F    | 033F   | Mean   | SD     |
|---------------------|-------|---------|--------|--------|--------|
| Adipose tissue      | 0.134 | 0.061   | 0.296  | 0.163  | 0.121  |
| Adrenal glands      | 1.879 | 3.483   | 4.255  | 3.206  | 1.212  |
| Bladder             | 0.043 | 0.101   | 0.175  | 0.106  | 0.066  |
| Bone (femur)        | 0.136 | 0.194   | 0.321  | 0.217  | 0.095  |
| Bone marrow (femur) | 0.448 | 0.818   | 1.480  | 0.915  | 0.522  |
| Brain               | 0.033 | 0.058   | 0.133  | 0.075  | 0.052  |
| Eyes                | 0.022 | 0.046   | 0.048  | 0.038  | 0.015  |
| Heart               | 0.296 | 0.746   | 1.734  | 0.925  | 0.735  |
| Injection site      | 8.920 | 103.630 | 56.133 | 56.227 | 47.355 |
| Kidneys             | 0.328 | 0.627   | 1.486  | 0.814  | 0.601  |
| Large intestine     | 0.165 | 0.222   | 0.283  | 0.224  | 0.059  |
| Liver               | 8.503 | 14.685  | 20.519 | 14.569 | 6.009  |
| Lung                | 0.610 | 1.159   | 1.898  | 1.222  | 0.646  |
| Lymph node (Man)    | 0.173 | 0.454   | 0.546  | 0.391  | 0.194  |
| Lymph node (Mes)    | 0.316 | 0.598   | 0.695  | 0.536  | 0.197  |
| Muscle              | 0.033 | 0.057   | 0.301  | 0.130  | 0.148  |
| Ovaries             | 0.555 | 2.916   | 3.552  | 2.341  | 1.579  |
| Pancreas            | 0.358 | 0.270   | 0.568  | 0.398  | 0.153  |
| Pituitary gland     | 0.251 | 0.317   | 0.805  | 0.458  | 0.303  |
| Salivary glands     | 0.087 | 0.156   | 0.262  | 0.169  | 0.088  |
| Skin                | 0.043 | 0.371   | 0.197  | 0.204  | 0.164  |
| Small intestine     | 0.684 | 0.739   | 1.089  | 0.838  | 0.220  |
| Spinal cord         | 0.073 | 0.061   | 0.236  | 0.124  | 0.098  |
| Spleen              | 9.910 | 11.442  | 13.587 | 11.646 | 1.847  |
| Stomach             | 0.050 | 0.113   | 0.141  | 0.101  | 0.047  |
| Thymus              | 0.130 | 0.267   | 0.231  | 0.209  | 0.071  |
| Thyroid             | 0.225 | 0.718   | 0.867  | 0.604  | 0.336  |
| Uterus              | 0.080 | 0.096   | 0.246  | 0.140  | 0.091  |
| Whole Blood         | 1.090 | 1.981   | 5.022  | 2.698  | 2.062  |
| Plasma              | 2.037 | 3.442   | 7.274  | 4.251  | 2.711  |
| Blood:plasma ratio  | 0.53  | 0.58    | 0.69   | 0.60   | 0.08   |

**Appendix 5 Individual Female Concentration Data**  
**(continued)****Concentration of Total Radioactivity in Whole Blood, Plasma and Tissues 8 hours Following Single Intramuscular Administration of [<sup>3</sup>H]-08-A01-C01 to Female Wistar Han Rats****Target Dose Level: 50 µg mRNA/Animal; 1.29 mg Total Lipid/Animal****Results expressed as µg lipid equiv/g (mL)**

| Sample              | 034F   | 035F    | 036F    | Mean    | SD     |
|---------------------|--------|---------|---------|---------|--------|
| Adipose tissue      | 0.095  | 0.041   | 0.072   | 0.069   | 0.027  |
| Adrenal glands      | 7.562  | 6.554   | 7.538   | 7.218   | 0.575  |
| Bladder             | 0.047  | 0.080   | 0.127   | 0.085   | 0.040  |
| Bone (femur)        | 0.243  | 0.143   | 0.144   | 0.177   | 0.057  |
| Bone marrow (femur) | 1.262  | 1.350   | 1.210   | 1.274   | 0.071  |
| Brain               | 0.047  | 0.030   | 0.058   | 0.045   | 0.014  |
| Eyes                | 0.046  | 0.013   | 0.032   | 0.030   | 0.016  |
| Heart               | 0.532  | 0.193   | 0.448   | 0.391   | 0.177  |
| Injection site      | 30.227 | 174.950 | 172.620 | 125.930 | 82.890 |
| Kidneys             | 0.416  | 0.239   | 0.372   | 0.342   | 0.092  |
| Large intestine     | 0.679  | 0.381   | 0.764   | 0.608   | 0.201  |
| Liver               | 22.242 | 25.442  | 27.834  | 25.172  | 2.806  |
| Lung                | 0.661  | 0.378   | 0.846   | 0.628   | 0.236  |
| Lymph node (Man)    | 0.315  | 0.251   | 0.551   | 0.372   | 0.158  |
| Lymph node (Mes)    | 0.790  | 0.481   | 0.915   | 0.729   | 0.223  |
| Muscle              | 0.040  | 0.160   | 0.075   | 0.091   | 0.062  |
| Ovaries             | 2.960  | 1.276   | 5.029   | 3.088   | 1.880  |
| Pancreas            | 0.390  | 0.087   | 0.241   | 0.239   | 0.151  |
| Pituitary gland     | 0.169  | 0.099   | 0.157   | 0.141   | 0.037  |
| Salivary glands     | 0.124  | 0.074   | 0.082   | 0.094   | 0.027  |
| Skin                | 0.137  | 0.057   | 0.155   | 0.116   | 0.052  |
| Small intestine     | 1.162  | 0.839   | 1.098   | 1.033   | 0.171  |
| Spinal cord         | 0.051  | 0.021   | 0.060   | 0.044   | 0.020  |
| Spleen              | 19.387 | 16.090  | 23.763  | 19.747  | 3.849  |
| Stomach             | 0.243  | 0.040   | 0.094   | 0.126   | 0.105  |
| Thymus              | 0.111  | 0.086   | 0.102   | 0.100   | 0.013  |
| Thyroid             | 0.395  | 0.131   | 0.395   | 0.307   | 0.152  |
| Uterus              | 0.584  | 0.055   | 0.223   | 0.287   | 0.270  |
| Whole Blood         | 0.731  | 0.319   | 0.833   | 0.628   | 0.272  |
| Plasma              | 1.421  | 0.574   | 1.447   | 1.147   | 0.496  |
| Blood:plasma ratio  | 0.51   | 0.56    | 0.58    | 0.55    | 0.03   |

## Appendix 5 Individual Female Concentration Data (continued)

### Concentration of Total Radioactivity in Whole Blood, Plasma and Tissues 24 hours Following Single Intramuscular Administration of [<sup>3</sup>H]-08-A01-C01 to Female Wistar Han Rats

**Target Dose Level: 50 µg mRNA/Animal; 1.29 mg Total Lipid/Animal**

**Results expressed as µg lipid equiv/g (mL)**

| Sample              | 037F   | 038F    | 039F    | Mean    | SD      |
|---------------------|--------|---------|---------|---------|---------|
| Adipose tissue      | 0.031  | 0.042   | 0.053   | 0.042   | 0.011   |
| Adrenal glands      | 9.718  | 3.981   | 9.084   | 7.595   | 3.145   |
| Bladder             | 0.141  | 0.135   | 0.235   | 0.171   | 0.056   |
| Bone (femur)        | 0.158  | 0.105   | 0.278   | 0.180   | 0.089   |
| Bone marrow (femur) | 1.180  | 1.058   | 1.978   | 1.405   | 0.500   |
| Brain               | 0.040  | 0.039   | 0.063   | 0.047   | 0.014   |
| Eyes                | 0.063  | 0.037   | 0.057   | 0.052   | 0.014   |
| Heart               | 0.342  | 0.259   | 0.355   | 0.318   | 0.052   |
| Injection site      | 2.568  | 202.540 | 162.510 | 122.540 | 105.810 |
| Kidneys             | 0.270  | 0.412   | 0.361   | 0.348   | 0.072   |
| Large intestine     | 0.561  | 0.370   | 0.465   | 0.466   | 0.095   |
| Liver               | 13.368 | 10.520  | 21.469  | 15.119  | 5.681   |
| Lung                | 0.519  | 0.822   | 0.945   | 0.762   | 0.219   |
| Lymph node (Man)    | 0.259  | 0.242   | 0.589   | 0.363   | 0.195   |
| Lymph node (Mes)    | 0.944  | 0.550   | 1.095   | 0.863   | 0.281   |
| Muscle              | 0.028  | 0.114   | 0.133   | 0.092   | 0.056   |
| Ovaries             | 4.091  | 5.266   | 6.363   | 5.240   | 1.136   |
| Pancreas            | 0.176  | 0.362   | 0.422   | 0.320   | 0.128   |
| Pituitary gland     | 0.309  | 0.213   | 0.379   | 0.300   | 0.083   |
| Salivary glands     | 0.084  | 0.083   | 0.119   | 0.096   | 0.021   |
| Skin                | 0.047  | 0.156   | 0.151   | 0.118   | 0.062   |
| Small intestine     | 0.748  | 0.661   | 0.769   | 0.726   | 0.057   |
| Spinal cord         | 0.047  | 0.034   | 0.064   | 0.048   | 0.015   |
| Spleen              | 15.606 | 12.977  | 23.440  | 17.341  | 5.443   |
| Stomach             | 0.094  | 0.054   | 0.096   | 0.081   | 0.024   |
| Thymus              | 0.154  | 0.190   | 0.135   | 0.159   | 0.028   |
| Thyroid             | 0.302  | 0.294   | 0.410   | 0.335   | 0.065   |
| Uterus              | 0.307  | 0.207   | 0.354   | 0.289   | 0.075   |
| Whole Blood         | 0.475  | 0.380   | 0.779   | 0.544   | 0.208   |
| Plasma              | 0.930  | 0.681   | 1.223   | 0.945   | 0.271   |
| Blood:plasma ratio  | 0.51   | 0.56    | 0.64    | 0.57    | 0.06    |

**Appendix 5 Individual Female Concentration Data**  
**(continued)****Concentration of Total Radioactivity in Whole Blood, Plasma and Tissues 48 hours Following Single Intramuscular Administration of [<sup>3</sup>H]-08-A01-C01 to Female Wistar Han Rats****Target Dose Level: 50 µg mRNA/Animal; 1.29 mg Total Lipid/Animal****Results expressed as µg lipid equiv/g (mL)**

| Sample              | 040F   | 041F   | 042F   | Mean   | SD     |
|---------------------|--------|--------|--------|--------|--------|
| Adipose tissue      | 0.081  | 0.201  | 0.414  | 0.232  | 0.168  |
| Adrenal glands      | 12.979 | 15.142 | 16.707 | 14.942 | 1.872  |
| Bladder             | 0.234  | 0.640  | 0.293  | 0.389  | 0.219  |
| Bone (femur)        | 0.299  | 1.911  | 0.351  | 0.854  | 0.916  |
| Bone marrow (femur) | 2.096  | 1.993  | 7.463  | 3.851  | 3.129  |
| Brain               | 0.038  | 0.046  | 0.072  | 0.052  | 0.018  |
| Eyes                | 0.064  | 0.105  | 0.121  | 0.097  | 0.029  |
| Heart               | 0.352  | 0.369  | 0.539  | 0.420  | 0.103  |
| Injection site      | 93.643 | 27.547 | 62.073 | 61.088 | 33.059 |
| Kidneys             | 0.314  | 0.378  | 0.412  | 0.368  | 0.050  |
| Large intestine     | 1.210  | 1.507  | 1.031  | 1.249  | 0.241  |
| Liver               | 24.416 | 20.707 | 46.111 | 30.411 | 13.722 |
| Lung                | 0.921  | 0.719  | 1.053  | 0.898  | 0.168  |
| Lymph node (Man)    | 0.600  | 0.516  | 0.784  | 0.633  | 0.137  |
| Lymph node (Mes)    | 1.557  | 1.669  | 1.800  | 1.675  | 0.122  |
| Muscle              | 0.126  | 0.068  | 0.119  | 0.104  | 0.032  |
| Ovaries             | 9.305  | 13.544 | 13.933 | 12.261 | 2.567  |
| Pancreas            | 0.364  | 0.298  | 1.170  | 0.611  | 0.485  |
| Pituitary gland     | 0.910  | 0.816  | 0.810  | 0.845  | 0.056  |
| Salivary glands     | 0.200  | 0.204  | 0.288  | 0.231  | 0.049  |
| Skin                | 0.303  | 0.173  | 0.416  | 0.297  | 0.122  |
| Small intestine     | 1.142  | 1.461  | 1.339  | 1.314  | 0.161  |
| Spinal cord         | 0.043  | 0.075  | 0.069  | 0.062  | 0.017  |
| Spleen              | 19.456 | 16.775 | 45.234 | 27.155 | 15.714 |
| Stomach             | 0.154  | 0.197  | 0.233  | 0.195  | 0.040  |
| Thymus              | 0.314  | 0.248  | 0.536  | 0.366  | 0.151  |
| Thyroid             | 0.584  | 0.870  | 0.512  | 0.655  | 0.190  |
| Uterus              | 0.267  | 0.521  | 0.581  | 0.456  | 0.167  |
| Whole Blood         | 0.258  | 0.338  | 0.320  | 0.305  | 0.042  |
| Plasma              | 0.429  | 0.598  | 0.546  | 0.524  | 0.087  |
| Blood:plasma ratio  | 0.60   | 0.57   | 0.59   | 0.58   | 0.02   |

**Appendix 6 Individual Male Recovery Data****Recovery of Total Radioactivity in Tissues 0.25 min Following Single Intramuscular Administration of [<sup>3</sup>H]-08-A01-C01 to Male Wistar Han Rats****Target Dose Level: 50 µg mRNA/Animal; 1.29 mg Total Lipid/Animal****Results expressed as % administered dose**

| Sample          | 043M   | 044M  | 045M   | Mean   | SD     |
|-----------------|--------|-------|--------|--------|--------|
| Adrenal glands  | 0.002  | 0.002 | 0.000  | 0.001  | 0.001  |
| Bladder         | 0.001  | 0.000 | 0.000  | 0.000  | 0.000  |
| Brain           | 0.013  | 0.014 | 0.005  | 0.011  | 0.005  |
| Eyes            | 0.001  | 0.000 | 0.000  | 0.000  | 0.000  |
| Heart           | 0.056  | 0.024 | 0.004  | 0.028  | 0.026  |
| Injection site  | 82.460 | 6.097 | 10.103 | 32.887 | 42.978 |
| Kidneys         | 0.103  | 0.087 | 0.016  | 0.069  | 0.046  |
| Large intestine | 0.012  | 0.018 | 0.002  | 0.011  | 0.008  |
| Liver           | 1.735  | 1.083 | 0.167  | 0.995  | 0.787  |
| Lung            | 0.133  | 0.082 | 0.031  | 0.082  | 0.051  |
| Pancreas        | 0.004  | 0.010 | 0.001  | 0.005  | 0.005  |
| Pituitary gland | 0.001  | 0.000 | 0.000  | 0.000  | 0.000  |
| Prostate        | 0.002  | 0.002 | 0.000  | 0.001  | 0.001  |
| Salivary glands | 0.007  | 0.005 | 0.001  | 0.004  | 0.003  |
| Small intestine | 0.051  | 0.040 | 0.005  | 0.032  | 0.024  |
| Spinal cord     | 0.002  | 0.001 | 0.000  | 0.001  | 0.001  |
| Spleen          | 0.020  | 0.019 | 0.003  | 0.014  | 0.009  |
| Stomach         | 0.008  | 0.013 | 0.002  | 0.008  | 0.006  |
| Testes          | 0.012  | 0.008 | 0.001  | 0.007  | 0.005  |
| Thymus          | 0.005  | 0.010 | 0.001  | 0.005  | 0.005  |
| Thyroid         | 0.000  | 0.000 | 0.000  | 0.000  | 0.000  |

**Appendix 6 Individual Male Recovery Data  
(continued)****Recovery of Total Radioactivity in Tissues 1 hour Following Single Intramuscular Administration of [<sup>3</sup>H]-08-A01-C01 to Male Wistar Han Rats****Target Dose Level: 50 µg mRNA/Animal; 1.29 mg Total Lipid/Animal****Results expressed as % administered dose**

| Sample          | 046M   | 047M   | 048M   | Mean   | SD     |
|-----------------|--------|--------|--------|--------|--------|
| Adrenal glands  | 0.001  | 0.003  | 0.002  | 0.002  | 0.001  |
| Bladder         | 0.001  | 0.001  | 0.000  | 0.001  | 0.000  |
| Brain           | 0.005  | 0.014  | 0.013  | 0.010  | 0.005  |
| Eyes            | 0.000  | 0.000  | 0.001  | 0.000  | 0.000  |
| Heart           | 0.015  | 0.036  | 0.045  | 0.032  | 0.015  |
| Injection site  | 74.148 | 46.614 | 85.725 | 68.829 | 20.090 |
| Kidneys         | 0.047  | 0.086  | 0.098  | 0.077  | 0.027  |
| Large intestine | 0.016  | 0.017  | 0.021  | 0.018  | 0.002  |
| Liver           | 2.218  | 2.607  | 3.676  | 2.834  | 0.755  |
| Lung            | 0.043  | 0.131  | 0.081  | 0.085  | 0.044  |
| Pancreas        | 0.004  | 0.009  | 0.006  | 0.006  | 0.003  |
| Pituitary gland | 0.000  | 0.000  | 0.000  | 0.000  | 0.000  |
| Prostate        | 0.001  | 0.002  | 0.001  | 0.001  | 0.001  |
| Salivary glands | 0.003  | 0.005  | 0.006  | 0.005  | 0.002  |
| Small intestine | 0.102  | 0.133  | 0.136  | 0.124  | 0.019  |
| Spinal cord     | 0.001  | 0.000  | 0.001  | 0.001  | 0.000  |
| Spleen          | 0.115  | 0.063  | 0.082  | 0.087  | 0.026  |
| Stomach         | 0.007  | 0.019  | 0.023  | 0.016  | 0.008  |
| Testes          | 0.007  | 0.009  | 0.013  | 0.010  | 0.003  |
| Thymus          | 0.008  | 0.004  | 0.007  | 0.006  | 0.002  |
| Thyroid         | 0.000  | 0.001  | 0.000  | 0.000  | 0.000  |

**Appendix 6 Individual Male Recovery Data  
(continued)****Recovery of Total Radioactivity in Tissues 2 hours Following Single Intramuscular Administration of [<sup>3</sup>H]-08-A01-C01 to Male Wistar Han Rats****Target Dose Level: 50 µg mRNA/Animal; 1.29 mg Total Lipid/Animal****Results expressed as % administered dose**

| Sample          | 049M   | 050M   | 051M   | Mean   | SD     |
|-----------------|--------|--------|--------|--------|--------|
| Adrenal glands  | 0.006  | 0.003  | 0.005  | 0.005  | 0.001  |
| Bladder         | 0.001  | 0.001  | 0.001  | 0.001  | 0.000  |
| Brain           | 0.033  | 0.013  | 0.016  | 0.021  | 0.011  |
| Eyes            | 0.001  | 0.000  | 0.002  | 0.001  | 0.001  |
| Heart           | 0.109  | 0.036  | 0.051  | 0.065  | 0.039  |
| Injection site  | 53.157 | 53.477 | 10.525 | 39.053 | 24.707 |
| Kidneys         | 0.203  | 0.096  | 0.148  | 0.149  | 0.054  |
| Large intestine | 0.063  | 0.035  | 0.063  | 0.054  | 0.016  |
| Liver           | 10.166 | 4.262  | 8.460  | 7.629  | 3.038  |
| Lung            | 0.313  | 0.094  | 0.160  | 0.189  | 0.113  |
| Pancreas        | 0.011  | 0.006  | 0.028  | 0.015  | 0.012  |
| Pituitary gland | 0.000  | 0.000  | 0.000  | 0.000  | 0.000  |
| Prostate        | 0.002  | 0.002  | 0.003  | 0.002  | 0.000  |
| Salivary glands | 0.010  | 0.004  | 0.008  | 0.007  | 0.003  |
| Small intestine | 0.418  | 0.305  | 0.336  | 0.353  | 0.058  |
| Spinal cord     | 0.001  | 0.001  | 0.002  | 0.001  | 0.001  |
| Spleen          | 0.296  | 0.101  | 0.299  | 0.232  | 0.114  |
| Stomach         | 0.034  | 0.017  | 0.047  | 0.033  | 0.015  |
| Testes          | 0.027  | 0.008  | 0.017  | 0.017  | 0.009  |
| Thymus          | 0.010  | 0.005  | 0.008  | 0.008  | 0.002  |
| Thyroid         | 0.001  | 0.001  | 0.000  | 0.001  | 0.000  |

**Appendix 6 Individual Male Recovery Data**  
**(continued)****Recovery of Total Radioactivity in Tissues 4 hours Following Single Intramuscular Administration of [<sup>3</sup>H]-08-A01-C01 to Male Wistar Han Rats****Target Dose Level: 50 µg mRNA/Animal; 1.29 mg Total Lipid/Animal****Results expressed as % administered dose**

| Sample          | 052M   | 053M   | 054M   | Mean   | SD     |
|-----------------|--------|--------|--------|--------|--------|
| Adrenal glands  | 0.013  | 0.009  | 0.014  | 0.012  | 0.002  |
| Bladder         | 0.001  | 0.002  | 0.001  | 0.001  | 0.000  |
| Brain           | 0.019  | 0.015  | 0.029  | 0.021  | 0.007  |
| Eyes            | 0.002  | 0.002  | 0.001  | 0.002  | 0.001  |
| Heart           | 0.071  | 0.033  | 0.096  | 0.067  | 0.032  |
| Injection site  | 61.619 | 36.450 | 45.061 | 47.710 | 12.792 |
| Kidneys         | 0.151  | 0.088  | 0.169  | 0.136  | 0.042  |
| Large intestine | 0.271  | 0.219  | 0.216  | 0.236  | 0.031  |
| Liver           | 12.655 | 13.898 | 18.528 | 15.027 | 3.095  |
| Lung            | 0.356  | 0.080  | 0.241  | 0.226  | 0.139  |
| Pancreas        | 0.007  | 0.020  | 0.011  | 0.013  | 0.007  |
| Pituitary gland | 0.001  | 0.001  | 0.000  | 0.001  | 0.000  |
| Prostate        | 0.003  | 0.002  | 0.003  | 0.003  | 0.001  |
| Salivary glands | 0.009  | 0.007  | 0.012  | 0.009  | 0.002  |
| Small intestine | 0.632  | 0.499  | 0.737  | 0.623  | 0.120  |
| Spinal cord     | 0.002  | 0.004  | 0.002  | 0.003  | 0.001  |
| Spleen          | 0.309  | 0.410  | 0.334  | 0.351  | 0.052  |
| Stomach         | 0.053  | 0.027  | 0.033  | 0.037  | 0.013  |
| Testes          | 0.028  | 0.021  | 0.039  | 0.030  | 0.009  |
| Thymus          | 0.010  | 0.011  | 0.033  | 0.018  | 0.013  |
| Thyroid         | 0.001  | 0.001  | 0.001  | 0.001  | 0.000  |

**Appendix 6 Individual Male Recovery Data  
(continued)****Recovery of Total Radioactivity in Tissues 8 hours Following Single Intramuscular Administration of [<sup>3</sup>H]-08-A01-C01 to Male Wistar Han Rats****Target Dose Level: 50 µg mRNA/Animal; 1.29 mg Total Lipid/Animal****Results expressed as % administered dose**

| Sample          | 055M   | 056M   | 057M   | Mean   | SD    |
|-----------------|--------|--------|--------|--------|-------|
| Adrenal glands  | 0.013  | 0.023  | 0.042  | 0.026  | 0.015 |
| Bladder         | N.S.   | 0.001  | 0.002  | 0.002  | N.A.  |
| Brain           | 0.014  | 0.013  | 0.014  | 0.014  | 0.001 |
| Eyes            | N.S.   | 0.001  | 0.002  | 0.002  | N.A.  |
| Heart           | 0.071  | 0.051  | 0.061  | 0.061  | 0.010 |
| Injection site  | 18.863 | 19.984 | 17.346 | 18.731 | 1.324 |
| Kidneys         | 0.114  | 0.107  | 0.108  | 0.109  | 0.004 |
| Large intestine | 0.536  | 0.424  | 0.430  | 0.463  | 0.063 |
| Liver           | 17.280 | 17.862 | 29.414 | 21.519 | 6.844 |
| Lung            | 0.226  | 0.146  | 0.169  | 0.180  | 0.042 |
| Pancreas        | 0.010  | 0.021  | 0.012  | 0.014  | 0.006 |
| Pituitary gland | 0.000  | 0.000  | 0.001  | 0.000  | 0.000 |
| Prostate        | 0.004  | 0.002  | 0.001  | 0.003  | 0.001 |
| Salivary glands | 0.008  | 0.006  | 0.007  | 0.007  | 0.001 |
| Small intestine | 0.850  | 1.034  | 1.031  | 0.972  | 0.106 |
| Spinal cord     | 0.001  | 0.001  | 0.001  | 0.001  | 0.000 |
| Spleen          | 1.037  | 1.022  | 1.293  | 1.118  | 0.152 |
| Stomach         | 0.043  | 0.026  | 0.097  | 0.055  | 0.037 |
| Testes          | 0.034  | 0.022  | 0.045  | 0.034  | 0.012 |
| Thymus          | 0.013  | 0.010  | 0.012  | 0.012  | 0.001 |
| Thyroid         | 0.001  | 0.001  | 0.001  | 0.001  | 0.000 |

N.S. = No sample due to oxidiser failure

N.A. = Not applicable

**Appendix 6 Individual Male Recovery Data  
(continued)****Recovery of Total Radioactivity in Tissues 24 hours Following Single Intramuscular Administration of [<sup>3</sup>H]-08-A01-C01 to Male Wistar Han Rats****Target Dose Level: 50 µg mRNA/Animal; 1.29 mg Total Lipid/Animal****Results expressed as % administered dose**

| Sample          | 058M   | 059M   | 060M   | Mean   | SD    |
|-----------------|--------|--------|--------|--------|-------|
| Adrenal glands  | 0.052  | 0.059  | 0.137  | 0.083  | 0.047 |
| Bladder         | 0.002  | 0.002  | 0.002  | 0.002  | 0.000 |
| Brain           | 0.006  | 0.013  | 0.017  | 0.012  | 0.006 |
| Eyes            | 0.002  | 0.002  | 0.004  | 0.002  | 0.001 |
| Heart           | 0.051  | 0.026  | 0.026  | 0.035  | 0.014 |
| Injection site  | 39.854 | 26.623 | 29.394 | 31.957 | 6.978 |
| Kidneys         | 0.075  | 0.053  | 0.075  | 0.068  | 0.012 |
| Large intestine | 0.332  | 0.895  | 2.045  | 1.091  | 0.873 |
| Liver           | 14.444 | 16.303 | 28.957 | 19.901 | 7.897 |
| Lung            | 0.109  | 0.118  | 0.179  | 0.136  | 0.038 |
| Pancreas        | 0.007  | 0.017  | 0.015  | 0.013  | 0.005 |
| Pituitary gland | 0.000  | 0.000  | 0.000  | 0.000  | 0.000 |
| Prostate        | 0.003  | 0.004  | 0.005  | 0.004  | 0.001 |
| Salivary glands | 0.005  | 0.008  | 0.012  | 0.008  | 0.004 |
| Small intestine | 0.693  | 1.198  | 1.934  | 1.275  | 0.624 |
| Spinal cord     | 0.001  | 0.002  | 0.002  | 0.001  | 0.001 |
| Spleen          | 0.977  | 0.660  | 1.234  | 0.957  | 0.287 |
| Stomach         | 0.021  | 0.033  | 0.107  | 0.054  | 0.046 |
| Testes          | 0.057  | 0.058  | 0.105  | 0.074  | 0.028 |
| Thymus          | 0.007  | 0.010  | 0.009  | 0.009  | 0.002 |
| Thyroid         | 0.001  | 0.001  | 0.001  | 0.001  | 0.000 |

**Appendix 6 Individual Male Recovery Data**  
**(continued)****Recovery of Total Radioactivity in Tissues 48 hours Following Single Intramuscular Administration of [<sup>3</sup>H]-08-A01-C01 to Male Wistar Han Rats****Target Dose Level: 50 µg mRNA/Animal; 1.29 mg Total Lipid/Animal****Results expressed as % administered dose**

| Sample          | 061M   | 062M   | 063M   | Mean   | SD     |
|-----------------|--------|--------|--------|--------|--------|
| Adrenal glands  | 0.078  | 0.157  | 0.078  | 0.104  | 0.046  |
| Bladder         | 0.001  | 0.002  | 0.002  | 0.002  | 0.000  |
| Brain           | 0.006  | 0.016  | 0.012  | 0.011  | 0.005  |
| Eyes            | 0.002  | 0.003  | 0.003  | 0.003  | 0.000  |
| Heart           | 0.024  | 0.055  | 0.037  | 0.039  | 0.016  |
| Injection site  | 49.053 | 18.355 | 31.059 | 32.823 | 15.425 |
| Kidneys         | 0.045  | 0.104  | 0.063  | 0.071  | 0.031  |
| Large intestine | 0.541  | 0.624  | 1.264  | 0.810  | 0.395  |
| Liver           | 12.962 | 17.164 | 11.734 | 13.953 | 2.848  |
| Lung            | 0.088  | 0.173  | 0.133  | 0.131  | 0.043  |
| Pancreas        | 0.010  | 0.013  | 0.023  | 0.015  | 0.007  |
| Pituitary gland | 0.000  | 0.000  | 0.000  | 0.000  | 0.000  |
| Prostate        | 0.002  | 0.004  | 0.004  | 0.003  | 0.001  |
| Salivary glands | 0.010  | 0.012  | 0.008  | 0.010  | 0.002  |
| Small intestine | 0.635  | 1.258  | 1.020  | 0.971  | 0.314  |
| Spinal cord     | 0.001  | 0.001  | 0.002  | 0.001  | 0.001  |
| Spleen          | 0.544  | 1.271  | 0.926  | 0.914  | 0.364  |
| Stomach         | 0.027  | 0.065  | 0.056  | 0.049  | 0.019  |
| Testes          | 0.053  | 0.109  | 0.060  | 0.074  | 0.030  |
| Thymus          | 0.004  | 0.012  | 0.009  | 0.008  | 0.004  |
| Thyroid         | 0.001  | 0.002  | 0.001  | 0.001  | 0.001  |

**Appendix 7 Individual Female Recovery Data****Recovery of Total Radioactivity in Tissues 0.25 min Following Single Intramuscular Administration of [<sup>3</sup>H]-08-A01-C01 to Female Wistar Han Rats****Target Dose Level: 50 µg mRNA/Animal; 1.29 mg Total Lipid/Animal****Results expressed as % administered dose**

| Sample          | 022F  | 023F   | 024F  | Mean   | SD     |
|-----------------|-------|--------|-------|--------|--------|
| Adrenal glands  | 0.003 | *0.000 | 0.001 | °0.001 | °0.002 |
| Bladder         | 0.000 | *0.000 | 0.000 | °0.000 | °0.000 |
| Brain           | 0.005 | *0.000 | 0.002 | °0.002 | °0.002 |
| Eyes            | 0.000 | *0.000 | 0.000 | °0.000 | °0.000 |
| Heart           | 0.017 | *0.000 | 0.006 | °0.008 | °0.008 |
| Injection site  | 8.145 | 11.578 | 0.723 | 6.815  | 5.549  |
| Kidneys         | 0.063 | 0.012  | 0.014 | 0.030  | 0.028  |
| Large intestine | 0.010 | *0.000 | 0.002 | °0.004 | °0.005 |
| Liver           | 0.435 | 0.010  | 0.180 | 0.209  | 0.214  |
| Lung            | 0.051 | 0.001  | 0.013 | 0.022  | 0.026  |
| Ovaries         | 0.002 | *0.000 | 0.001 | °0.001 | °0.001 |
| Pancreas        | 0.002 | 0.000  | 0.001 | 0.001  | 0.001  |
| Pituitary gland | 0.000 | *0.000 | 0.000 | °0.000 | °0.000 |
| Salivary glands | 0.004 | *0.000 | 0.001 | °0.002 | °0.002 |
| Small intestine | 0.038 | *0.001 | 0.005 | °0.015 | °0.020 |
| Spinal cord     | 0.000 | *0.000 | 0.000 | °0.000 | °0.000 |
| Spleen          | 0.014 | *0.000 | 0.017 | °0.011 | °0.009 |
| Stomach         | 0.007 | *0.000 | 0.002 | °0.003 | °0.003 |
| Thymus          | 0.005 | *0.000 | 0.002 | °0.002 | °0.002 |
| Thyroid         | 0.000 | *0.000 | 0.000 | °0.000 | °0.000 |
| Uterus          | 0.004 | *0.000 | 0.002 | °0.002 | °0.002 |

\*=Results calculated from data less than 30 cpm above background

°=Mean includes results calculated from data less than 30 cpm above background

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**Appendix 7 Individual Female Recovery Data**  
**(continued)****Recovery of Total Radioactivity in Tissues 1 hour Following Single Intramuscular Administration of [<sup>3</sup>H]-08-A01-C01 to Female Wistar Han Rats****Target Dose Level: 50 µg mRNA/Animal; 1.29 mg Total Lipid/Animal****Results expressed as % administered dose**

| Sample          | 025F   | 026F   | 027F   | Mean   | SD     |
|-----------------|--------|--------|--------|--------|--------|
| Adrenal glands  | 0.010  | 0.011  | 0.015  | 0.012  | 0.003  |
| Bladder         | 0.001  | 0.001  | 0.001  | 0.001  | 0.000  |
| Brain           | 0.013  | 0.019  | 0.015  | 0.016  | 0.003  |
| Eyes            | 0.001  | 0.001  | 0.001  | 0.001  | 0.000  |
| Heart           | 0.066  | 0.109  | 0.062  | 0.079  | 0.026  |
| Injection site  | 10.609 | 47.776 | 50.847 | 36.411 | 22.398 |
| Kidneys         | 0.162  | 0.250  | 0.102  | 0.171  | 0.074  |
| Large intestine | 0.030  | 0.035  | 0.029  | 0.032  | 0.003  |
| Liver           | 3.586  | 2.713  | 2.421  | 2.907  | 0.606  |
| Lung            | 0.112  | 0.131  | 0.106  | 0.117  | 0.013  |
| Ovaries         | 0.012  | 0.010  | 0.004  | 0.009  | 0.004  |
| Pancreas        | 0.009  | 0.009  | 0.007  | 0.008  | 0.001  |
| Pituitary gland | 0.000  | 0.001  | 0.001  | 0.001  | 0.000  |
| Salivary glands | 0.008  | 0.009  | 0.006  | 0.008  | 0.002  |
| Small intestine | 0.153  | 0.130  | 0.121  | 0.135  | 0.017  |
| Spinal cord     | 0.002  | 0.002  | 0.001  | 0.002  | 0.001  |
| Spleen          | 0.082  | 0.099  | 0.112  | 0.098  | 0.015  |
| Stomach         | 0.024  | 0.021  | 0.023  | 0.022  | 0.002  |
| Thymus          | 0.007  | 0.013  | 0.004  | 0.008  | 0.005  |
| Thyroid         | 0.001  | 0.001  | 0.001  | 0.001  | 0.000  |
| Uterus          | 0.008  | 0.010  | 0.015  | 0.011  | 0.004  |

**Appendix 7      Individual Female Recovery Data**  
**(continued)****Recovery of Total Radioactivity in Tissues 2 hours Following Single Intramuscular Administration of [<sup>3</sup>H]-08-A01-C01 to Female Wistar Han Rats****Target Dose Level: 50 µg mRNA/Animal; 1.29 mg Total Lipid/Animal****Results expressed as % administered dose**

| Sample          | 028F  | 029F   | 030F   | Mean   | SD     |
|-----------------|-------|--------|--------|--------|--------|
| Adrenal glands  | 0.010 | 0.022  | 0.012  | 0.015  | 0.006  |
| Bladder         | 0.000 | 0.001  | 0.001  | 0.001  | 0.001  |
| Brain           | 0.008 | 0.034  | 0.014  | 0.019  | 0.014  |
| Eyes            | 0.001 | 0.003  | 0.000  | 0.001  | 0.001  |
| Heart           | 0.028 | 0.201  | 0.077  | 0.102  | 0.089  |
| Injection site  | 0.018 | 0.236  | 72.027 | 24.094 | 41.511 |
| Kidneys         | 0.056 | 0.264  | 0.497  | 0.272  | 0.221  |
| Large intestine | 0.018 | 0.142  | 0.065  | 0.075  | 0.063  |
| Liver           | 3.203 | 12.436 | 5.452  | 7.030  | 4.815  |
| Lung            | 0.080 | 0.311  | 0.110  | 0.167  | 0.125  |
| Ovaries         | 0.003 | 0.012  | 0.009  | 0.008  | 0.004  |
| Pancreas        | 0.003 | 0.022  | 0.010  | 0.012  | 0.010  |
| Pituitary gland | 0.000 | 0.002  | 0.000  | 0.001  | 0.001  |
| Salivary glands | 0.005 | 0.015  | 0.007  | 0.009  | 0.006  |
| Small intestine | 0.205 | 0.367  | 0.283  | 0.285  | 0.081  |
| Spinal cord     | 0.002 | 0.004  | 0.001  | 0.002  | 0.002  |
| Spleen          | 0.063 | 1.010  | 0.180  | 0.418  | 0.516  |
| Stomach         | 0.027 | 0.057  | 0.022  | 0.035  | 0.019  |
| Thymus          | 0.003 | 0.028  | 0.004  | 0.012  | 0.014  |
| Thyroid         | 0.000 | 0.002  | 0.001  | 0.001  | 0.001  |
| Uterus          | 0.008 | 0.025  | 0.011  | 0.015  | 0.009  |

**Appendix 7 Individual Female Recovery Data**  
**(continued)****Recovery of Total Radioactivity in Tissues 4 hours Following Single Intramuscular Administration of [<sup>3</sup>H]-08-A01-C01 to Female Wistar Han Rats****Target Dose Level: 50 µg mRNA/Animal; 1.29 mg Total Lipid/Animal****Results expressed as % administered dose**

| Sample          | 031F  | 032F   | 033F   | Mean  | SD    |
|-----------------|-------|--------|--------|-------|-------|
| Adrenal glands  | 0.011 | 0.019  | 0.023  | 0.018 | 0.006 |
| Bladder         | 0.000 | 0.001  | 0.001  | 0.001 | 0.000 |
| Brain           | 0.005 | 0.007  | 0.020  | 0.011 | 0.008 |
| Eyes            | 0.001 | 0.001  | 0.001  | 0.001 | 0.000 |
| Heart           | 0.013 | 0.046  | 0.097  | 0.052 | 0.042 |
| Injection site  | 2.619 | 19.042 | 5.508  | 9.056 | 8.768 |
| Kidneys         | 0.031 | 0.062  | 0.154  | 0.082 | 0.064 |
| Large intestine | 0.111 | 0.136  | 0.198  | 0.148 | 0.045 |
| Liver           | 5.207 | 8.846  | 12.045 | 8.699 | 3.421 |
| Lung            | 0.054 | 0.093  | 0.188  | 0.112 | 0.069 |
| Ovaries         | 0.003 | 0.022  | 0.022  | 0.016 | 0.011 |
| Pancreas        | 0.016 | 0.009  | 0.027  | 0.017 | 0.009 |
| Pituitary gland | 0.000 | 0.000  | 0.001  | 0.000 | 0.000 |
| Salivary glands | 0.003 | 0.005  | 0.011  | 0.006 | 0.005 |
| Small intestine | 0.354 | 0.435  | 0.596  | 0.462 | 0.123 |
| Spinal cord     | 0.001 | 0.001  | 0.003  | 0.002 | 0.001 |
| Spleen          | 0.390 | 0.421  | 0.447  | 0.419 | 0.028 |
| Stomach         | 0.014 | 0.022  | 0.029  | 0.022 | 0.008 |
| Thymus          | 0.004 | 0.007  | 0.006  | 0.006 | 0.002 |
| Thyroid         | 0.000 | 0.001  | 0.001  | 0.001 | 0.000 |
| Uterus          | 0.005 | 0.004  | 0.016  | 0.008 | 0.007 |

**Appendix 7 Individual Female Recovery Data**  
**(continued)****Recovery of Total Radioactivity in Tissues 8 hours Following Single Intramuscular Administration of [<sup>3</sup>H]-08-A01-C01 to Female Wistar Han Rats****Target Dose Level: 50 µg mRNA/Animal; 1.29 mg Total Lipid/Animal****Results expressed as % administered dose**

| Sample          | 034F   | 035F   | 036F   | Mean   | SD     |
|-----------------|--------|--------|--------|--------|--------|
| Adrenal glands  | 0.048  | 0.031  | 0.051  | 0.043  | 0.011  |
| Bladder         | 0.000  | 0.000  | 0.001  | 0.000  | 0.000  |
| Brain           | 0.007  | 0.004  | 0.009  | 0.007  | 0.002  |
| Eyes            | 0.001  | 0.000  | 0.001  | 0.001  | 0.000  |
| Heart           | 0.029  | 0.010  | 0.027  | 0.022  | 0.011  |
| Injection site  | 10.296 | 26.182 | 38.500 | 24.993 | 14.139 |
| Kidneys         | 0.056  | 0.022  | 0.042  | 0.040  | 0.017  |
| Large intestine | 0.409  | 0.233  | 0.397  | 0.346  | 0.098  |
| Liver           | 13.264 | 12.033 | 18.443 | 14.580 | 3.402  |
| Lung            | 0.089  | 0.028  | 0.074  | 0.064  | 0.031  |
| Ovaries         | 0.022  | 0.010  | 0.042  | 0.025  | 0.016  |
| Pancreas        | 0.034  | 0.002  | 0.011  | 0.016  | 0.016  |
| Pituitary gland | 0.000  | 0.000  | 0.000  | 0.000  | 0.000  |
| Salivary glands | 0.005  | 0.002  | 0.003  | 0.003  | 0.001  |
| Small intestine | 0.718  | 0.308  | 0.714  | 0.580  | 0.235  |
| Spinal cord     | 0.001  | 0.000  | 0.001  | 0.001  | 0.000  |
| Spleen          | 0.853  | 0.601  | 1.082  | 0.845  | 0.241  |
| Stomach         | 0.043  | 0.005  | 0.023  | 0.024  | 0.019  |
| Thymus          | 0.004  | 0.002  | 0.003  | 0.003  | 0.001  |
| Thyroid         | 0.001  | 0.000  | 0.001  | 0.000  | 0.000  |
| Uterus          | 0.030  | 0.004  | 0.014  | 0.016  | 0.013  |

**Appendix 7 Individual Female Recovery Data**  
**(continued)****Recovery of Total Radioactivity in Tissues 24 hours Following Single Intramuscular Administration of [<sup>3</sup>H]-08-A01-C01 to Female Wistar Han Rats****Target Dose Level: 50 µg mRNA/Animal; 1.29 mg Total Lipid/Animal****Results expressed as % administered dose**

| Sample          | 037F  | 038F   | 039F   | Mean   | SD     |
|-----------------|-------|--------|--------|--------|--------|
| Adrenal glands  | 0.064 | 0.032  | 0.050  | 0.049  | 0.016  |
| Bladder         | 0.001 | 0.001  | 0.001  | 0.001  | 0.000  |
| Brain           | 0.005 | 0.006  | 0.009  | 0.007  | 0.002  |
| Eyes            | 0.001 | 0.001  | 0.001  | 0.001  | 0.000  |
| Heart           | 0.019 | 0.014  | 0.020  | 0.018  | 0.003  |
| Injection site  | 0.444 | 39.677 | 38.765 | 26.295 | 22.392 |
| Kidneys         | 0.029 | 0.053  | 0.035  | 0.039  | 0.013  |
| Large intestine | 0.334 | 0.283  | 0.263  | 0.293  | 0.037  |
| Liver           | 9.112 | 9.776  | 14.042 | 10.977 | 2.675  |
| Lung            | 0.053 | 0.071  | 0.072  | 0.065  | 0.010  |
| Ovaries         | 0.031 | 0.038  | 0.043  | 0.037  | 0.006  |
| Pancreas        | 0.005 | 0.007  | 0.014  | 0.009  | 0.004  |
| Pituitary gland | 0.000 | 0.000  | 0.000  | 0.000  | 0.000  |
| Salivary glands | 0.003 | 0.003  | 0.004  | 0.003  | 0.001  |
| Small intestine | 0.575 | 0.601  | 0.432  | 0.536  | 0.091  |
| Spinal cord     | 0.001 | 0.001  | 0.001  | 0.001  | 0.000  |
| Spleen          | 0.591 | 0.508  | 0.955  | 0.685  | 0.237  |
| Stomach         | 0.019 | 0.011  | 0.029  | 0.020  | 0.009  |
| Thymus          | 0.003 | 0.005  | 0.003  | 0.004  | 0.001  |
| Thyroid         | 0.000 | 0.000  | 0.001  | 0.000  | 0.000  |
| Uterus          | 0.027 | 0.009  | 0.017  | 0.018  | 0.009  |

**Appendix 7 Individual Female Recovery Data**  
**(continued)****Recovery of Total Radioactivity in Tissues 48 hours Following Single Intramuscular Administration of [<sup>3</sup>H]-08-A01-C01 to Female Wistar Han Rats****Target Dose Level: 50 µg mRNA/Animal; 1.29 mg Total Lipid/Animal****Results expressed as % administered dose**

| Sample          | 040F   | 041F   | 042F   | Mean   | SD    |
|-----------------|--------|--------|--------|--------|-------|
| Adrenal glands  | 0.085  | 0.126  | 0.114  | 0.108  | 0.021 |
| Bladder         | 0.001  | 0.004  | 0.002  | 0.002  | 0.001 |
| Brain           | 0.005  | 0.006  | 0.010  | 0.007  | 0.002 |
| Eyes            | 0.001  | 0.003  | 0.003  | 0.002  | 0.001 |
| Heart           | 0.018  | 0.017  | 0.024  | 0.020  | 0.004 |
| Injection site  | 20.139 | 5.852  | 23.287 | 16.426 | 9.292 |
| Kidneys         | 0.036  | 0.045  | 0.044  | 0.042  | 0.005 |
| Large intestine | 0.570  | 0.928  | 0.644  | 0.714  | 0.189 |
| Liver           | 15.122 | 13.811 | 26.137 | 18.357 | 6.770 |
| Lung            | 0.066  | 0.066  | 0.076  | 0.070  | 0.006 |
| Ovaries         | 0.075  | 0.113  | 0.097  | 0.095  | 0.019 |
| Pancreas        | 0.011  | 0.007  | 0.050  | 0.023  | 0.024 |
| Pituitary gland | 0.001  | 0.001  | 0.000  | 0.001  | 0.000 |
| Salivary glands | 0.007  | 0.005  | 0.009  | 0.007  | 0.002 |
| Small intestine | 0.540  | 0.825  | 0.729  | 0.698  | 0.145 |
| Spinal cord     | 0.001  | 0.002  | 0.001  | 0.001  | 0.000 |
| Spleen          | 0.772  | 0.848  | 1.818  | 1.146  | 0.583 |
| Stomach         | 0.023  | 0.028  | 0.035  | 0.029  | 0.006 |
| Thymus          | 0.007  | 0.005  | 0.009  | 0.007  | 0.002 |
| Thyroid         | 0.001  | 0.001  | 0.001  | 0.001  | 0.000 |
| Uterus          | 0.010  | 0.031  | 0.025  | 0.022  | 0.010 |

**Appendix 8 Individual Male 100 µg mRNA data****Concentration of Total Radioactivity in Whole Blood, Plasma and Tissues 0.25 min Following Single Intramuscular Administration of [<sup>3</sup>H]-08-A01-C01 to Male Wistar Han Rats****Target Dose Level: 100 µg mRNA/Animal; 2.57 mg Total Lipid/Animal****Results expressed as µg lipid equiv/g (mL)**

| Sample              | 001M   | 002M   | 003M    | Mean   | SD     |
|---------------------|--------|--------|---------|--------|--------|
| Adipose tissue      | 0.075  | 0.108  | 0.018   | 0.067  | 0.046  |
| Adrenal glands      | 0.193  | 0.192  | 0.184   | 0.190  | 0.005  |
| Bladder             | 0.035  | 0.079  | 0.026   | 0.047  | 0.028  |
| Bone (femur)        | 0.195  | 0.054  | 0.044   | 0.098  | 0.085  |
| Bone marrow (femur) | 0.312  | 0.163  | 0.229   | 0.234  | 0.075  |
| Brain               | 0.050  | 0.047  | 0.046   | 0.048  | 0.002  |
| Eyes                | 0.015  | 0.021  | 0.007   | 0.014  | 0.007  |
| Heart               | 0.394  | 0.365  | 0.460   | 0.406  | 0.048  |
| Injection site      | 16.832 | 24.313 | 179.840 | 73.662 | 92.030 |
| Kidneys             | 0.576  | 0.552  | 0.273   | 0.467  | 0.169  |
| Large intestine     | 0.016  | 0.012  | 0.051   | 0.026  | 0.022  |
| Liver               | 0.963  | 0.503  | 0.670   | 0.712  | 0.233  |
| Lung                | 0.689  | 0.497  | 0.410   | 0.532  | 0.143  |
| Lymph node (Man)    | 0.043  | 0.046  | 0.042   | 0.044  | 0.002  |
| Lymph node (Mes)    | 0.045  | 0.020  | 0.018   | 0.028  | 0.015  |
| Muscle              | 0.035  | 0.040  | 0.285   | 0.120  | 0.143  |
| Pancreas            | 0.088  | 0.068  | 0.068   | 0.075  | 0.012  |
| Pituitary gland     | 0.787  | 0.796  | 0.225   | 0.603  | 0.327  |
| Prostate            | 0.035  | 0.045  | 0.047   | 0.042  | 0.006  |
| Salivary glands     | 0.087  | 0.087  | 0.049   | 0.074  | 0.022  |
| Skin                | 2.094  | 3.233  | 12.691  | 6.499  | 6.668  |
| Small intestine     | 0.046  | 0.030  | 0.016   | 0.031  | 0.015  |
| Spinal cord         | 0.091  | 0.064  | 0.068   | 0.074  | 0.015  |
| Spleen              | 0.426  | 1.463  | 0.221   | 0.704  | 0.666  |
| Stomach             | 0.032  | 0.026  | *0.007  | °0.022 | °0.013 |
| Testes              | 0.033  | 0.030  | 0.020   | 0.028  | 0.007  |
| Thymus              | 0.121  | 0.161  | 0.216   | 0.166  | 0.048  |
| Thyroid             | 0.175  | 0.498  | 0.105   | 0.259  | 0.209  |
| Whole Blood         | 2.291  | 2.426  | 1.678   | 2.132  | 0.398  |
| Plasma              | 5.640  | 5.530  | 3.924   | 5.031  | 0.960  |
| Blood:plasma ratio  | 0.41   | 0.44   | 0.43    | 0.42   | 0.02   |

\* = Results calculated from data less than 30 cpm above background

° = Mean includes results calculated from data less than 30 cpm above background

**Appendix 8  
(continued)****Individual Male 100 µg mRNA Data****Concentration of Total Radioactivity in Whole Blood, Plasma and  
Tissues 1 hour Following Single Intramuscular Administration of  
[<sup>3</sup>H]-08-A01-C01 to Male Wistar Han Rats****Target Dose Level: 100 µg mRNA/Animal; 2.57 mg Total Lipid/Animal****Results expressed as µg lipid equiv/g (mL)**

| Sample              | 004M    | 005M   | 006M    | Mean    | SD     |
|---------------------|---------|--------|---------|---------|--------|
| Adipose tissue      | 0.193   | 0.307  | 0.350   | 0.283   | 0.081  |
| Adrenal glands      | 1.775   | 1.877  | 2.208   | 1.953   | 0.227  |
| Bladder             | 0.224   | 0.098  | 0.264   | 0.195   | 0.086  |
| Bone (femur)        | 1.102   | 0.530  | 0.566   | 0.733   | 0.320  |
| Bone marrow (femur) | 2.111   | 4.732  | 2.456   | 3.100   | 1.424  |
| Brain               | 0.253   | 0.297  | 0.296   | 0.282   | 0.025  |
| Eyes                | 0.229   | 0.070  | 0.093   | 0.131   | 0.086  |
| Heart               | 1.948   | 3.461  | 2.496   | 2.635   | 0.766  |
| Injection site      | 152.370 | 78.654 | 150.890 | 127.300 | 42.139 |
| Kidneys             | 3.017   | 3.096  | 3.170   | 3.094   | 0.077  |
| Large intestine     | 0.090   | 0.091  | 0.152   | 0.111   | 0.035  |
| Liver               | 13.805  | 10.906 | 16.323  | 13.678  | 2.711  |
| Lung                | 3.523   | 3.532  | 2.901   | 3.319   | 0.362  |
| Lymph node (Man)    | 0.366   | 0.379  | 0.437   | 0.394   | 0.038  |
| Lymph node (Mes)    | 0.268   | 0.412  | 0.389   | 0.356   | 0.077  |
| Muscle              | 0.184   | 0.213  | 0.195   | 0.198   | 0.015  |
| Pancreas            | 0.335   | 0.375  | 0.469   | 0.393   | 0.069  |
| Pituitary gland     | 1.389   | 1.810  | 1.717   | 1.639   | 0.221  |
| Prostate            | 0.328   | 0.363  | 0.380   | 0.357   | 0.027  |
| Salivary glands     | 0.471   | 0.613  | 0.493   | 0.526   | 0.076  |
| Skin                | 3.043   | 0.407  | 1.179   | 1.543   | 1.355  |
| Small intestine     | 0.393   | 3.191  | 3.563   | 2.382   | 1.733  |
| Spinal cord         | 0.216   | 0.356  | 0.303   | 0.292   | 0.071  |
| Spleen              | 4.066   | 4.402  | 4.868   | 4.445   | 0.402  |
| Stomach             | 0.332   | 2.377  | 8.099   | 3.603   | 4.026  |
| Testes              | 0.185   | 0.196  | 0.486   | 0.289   | 0.171  |
| Thymus              | 0.332   | 0.343  | 0.596   | 0.424   | 0.149  |
| Thyroid             | 1.219   | 1.909  | 1.266   | 1.465   | 0.385  |
| Whole Blood         | 7.985   | 11.835 | 10.357  | 10.059  | 1.942  |
| Plasma              | 23.703  | 26.782 | 26.070  | 25.518  | 1.612  |
| Blood:plasma ratio  | 0.34    | 0.44   | 0.40    | 0.39    | 0.05   |

**Appendix 8  
(continued)****Individual Male 100 µg mRNA Data****Concentration of Total Radioactivity in Whole Blood, Plasma and  
Tissues 2 hours Following Single Intramuscular Administration of  
[<sup>3</sup>H]-08-A01-C01 to Male Wistar Han Rats****Target Dose Level: 100 µg mRNA/Animal; 2.57 mg Total Lipid/Animal****Results expressed as µg lipid equiv/g (mL)**

| Sample              | 007M   | 008M   | 009M   | Mean   | SD     |
|---------------------|--------|--------|--------|--------|--------|
| Adipose tissue      | 0.311  | 0.211  | 0.486  | 0.336  | 0.140  |
| Adrenal glands      | 3.152  | 3.337  | 2.559  | 3.016  | 0.406  |
| Bladder             | 0.310  | 0.241  | 0.479  | 0.343  | 0.122  |
| Bone (femur)        | 0.835  | 0.462  | 0.385  | 0.561  | 0.241  |
| Bone marrow (femur) | 3.322  | 2.694  | 2.057  | 2.691  | 0.632  |
| Brain               | 0.348  | 0.310  | 0.250  | 0.302  | 0.049  |
| Eyes                | 0.126  | 0.104  | 0.064  | 0.098  | 0.031  |
| Heart               | 2.866  | 3.359  | 3.481  | 3.235  | 0.326  |
| Injection site      | 6.971  | 61.485 | 30.751 | 33.069 | 27.331 |
| Kidneys             | 2.887  | 2.858  | 2.679  | 2.808  | 0.113  |
| Large intestine     | 0.283  | 0.125  | 0.148  | 0.185  | 0.085  |
| Liver               | 33.320 | 24.542 | 22.034 | 26.632 | 5.926  |
| Lung                | 3.839  | 2.982  | 3.769  | 3.530  | 0.476  |
| Lymph node (Man)    | 0.784  | 0.413  | 0.474  | 0.557  | 0.199  |
| Lymph node (Mes)    | 0.859  | 0.503  | 0.333  | 0.565  | 0.268  |
| Muscle              | 0.220  | 0.182  | 0.189  | 0.197  | 0.020  |
| Pancreas            | 0.595  | 0.512  | 0.557  | 0.554  | 0.041  |
| Pituitary gland     | 1.998  | 1.921  | 1.729  | 1.883  | 0.139  |
| Prostate            | 0.458  | 0.354  | 0.461  | 0.424  | 0.061  |
| Salivary glands     | 0.740  | 0.597  | 0.539  | 0.625  | 0.104  |
| Skin                | 0.524  | 0.353  | 0.454  | 0.444  | 0.086  |
| Small intestine     | 1.147  | 0.887  | 0.755  | 0.930  | 0.199  |
| Spinal cord         | 0.396  | 0.373  | 0.360  | 0.377  | 0.018  |
| Spleen              | 14.103 | 8.227  | 7.803  | 10.044 | 3.521  |
| Stomach             | 0.234  | 0.142  | 0.143  | 0.173  | 0.053  |
| Testes              | 0.239  | 0.402  | 0.317  | 0.320  | 0.081  |
| Thymus              | 0.447  | 0.424  | 0.371  | 0.414  | 0.039  |
| Thyroid             | 1.906  | 1.397  | 1.481  | 1.595  | 0.273  |
| Whole Blood         | 11.413 | 10.005 | 10.736 | 10.718 | 0.704  |
| Plasma              | 25.479 | 22.927 | 22.340 | 23.582 | 1.669  |
| Blood:plasma ratio  | 0.45   | 0.44   | 0.48   | 0.45   | 0.02   |

**Appendix 8 Individual Male 100 µg mRNA Data  
(continued)****Concentration of Total Radioactivity in Whole Blood, Plasma and  
Tissues 4 hours Following Single Intramuscular Administration of  
[<sup>3</sup>H]-08-A01-C01 to Male Wistar Han Rats****Target Dose Level: 100 µg mRNA/Animal; 2.57 mg Total Lipid/Animal****Results expressed as µg lipid equiv/g (mL)**

| Sample              | 010M   | 011M    | 012M    | Mean    | SD      |
|---------------------|--------|---------|---------|---------|---------|
| Adipose tissue      | 0.222  | 0.262   | 0.105   | 0.196   | 0.082   |
| Adrenal glands      | 5.481  | 2.469   | 2.491   | 3.480   | 1.732   |
| Bladder             | 0.237  | 0.151   | 0.156   | 0.181   | 0.048   |
| Bone (femur)        | 1.452  | 1.249   | 0.348   | 1.016   | 0.588   |
| Bone marrow (femur) | 1.880  | 3.875   | 1.459   | 2.405   | 1.291   |
| Brain               | 0.373  | 0.123   | 0.090   | 0.195   | 0.155   |
| Eyes                | 0.095  | 0.056   | 0.042   | 0.065   | 0.027   |
| Heart               | 1.233  | 1.095   | 1.064   | 1.131   | 0.090   |
| Injection site      | 55.286 | 464.630 | 257.860 | 259.260 | 204.680 |
| Kidneys             | 2.190  | 1.607   | 1.007   | 1.601   | 0.591   |
| Large intestine     | 0.180  | 0.713   | 0.338   | 0.410   | 0.274   |
| Liver               | 38.606 | 14.955  | 19.426  | 24.329  | 12.565  |
| Lung                | 1.255  | 3.060   | 1.398   | 1.904   | 1.003   |
| Lymph node (Man)    | 0.694  | 0.271   | 0.242   | 0.402   | 0.253   |
| Lymph node (Mes)    | 0.970  | 0.427   | 0.502   | 0.633   | 0.294   |
| Muscle              | 0.129  | 0.076   | 0.085   | 0.097   | 0.029   |
| Pancreas            | 0.189  | 0.419   | 0.299   | 0.302   | 0.115   |
| Pituitary gland     | 0.870  | 0.599   | 0.480   | 0.649   | 0.200   |
| Prostate            | 0.244  | 0.133   | 0.133   | 0.170   | 0.064   |
| Salivary glands     | 0.334  | 0.192   | 0.170   | 0.232   | 0.089   |
| Skin                | 0.931  | 0.178   | 2.172   | 1.094   | 1.007   |
| Small intestine     | 0.758  | 1.381   | 1.189   | 1.110   | 0.319   |
| Spinal cord         | 0.154  | 0.094   | 0.111   | 0.120   | 0.031   |
| Spleen              | 9.286  | 27.731  | 9.780   | 15.599  | 10.510  |
| Stomach             | 0.057  | 0.131   | 0.302   | 0.163   | 0.125   |
| Testes              | 0.397  | 0.134   | 0.110   | 0.214   | 0.159   |
| Thymus              | 0.164  | 0.229   | 0.185   | 0.193   | 0.033   |
| Thyroid             | 1.256  | 0.565   | 0.742   | 0.854   | 0.359   |
| Whole Blood         | 4.741  | 2.416   | 2.502   | 3.220   | 1.318   |
| Plasma              | 11.200 | 5.253   | 5.862   | 7.438   | 3.272   |
| Blood:plasma ratio  | 0.42   | 0.46    | 0.43    | 0.44    | 0.02    |

**Appendix 8  
(continued)****Individual Male 100 µg mRNA Data****Concentration of Total Radioactivity in Whole Blood, Plasma and  
Tissues 8 hours Following Single Intramuscular Administration of  
[<sup>3</sup>H]-08-A01-C01 to Male Wistar Han Rats****Target Dose Level: 100 µg mRNA/Animal; 2.57 mg Total Lipid/Animal****Results expressed as µg lipid equiv/g (mL)**

| Sample              | 013M    | 014M    | 015M   | Mean   | SD     |
|---------------------|---------|---------|--------|--------|--------|
| Adipose tissue      | 0.134   | 0.147   | 0.269  | 0.184  | 0.075  |
| Adrenal glands      | 6.445   | 9.564   | 32.615 | 16.208 | 14.294 |
| Bladder             | 0.741   | 0.264   | 0.499  | 0.501  | 0.238  |
| Bone (femur)        | 0.835   | 0.274   | 0.855  | 0.655  | 0.330  |
| Bone marrow (femur) | 1.920   | 1.495   | 2.225  | 1.880  | 0.367  |
| Brain               | 0.165   | 0.120   | 0.214  | 0.166  | 0.047  |
| Eyes                | 0.188   | 0.146   | 0.229  | 0.188  | 0.041  |
| Heart               | 2.084   | 1.104   | 2.398  | 1.862  | 0.675  |
| Injection site      | 126.340 | 106.800 | 2.416  | 78.521 | 66.629 |
| Kidneys             | 2.145   | 1.122   | 1.472  | 1.580  | 0.520  |
| Large intestine     | 1.713   | 1.199   | 1.781  | 1.564  | 0.318  |
| Liver               | 34.463  | 41.789  | 61.002 | 45.751 | 13.706 |
| Lung                | 2.999   | 1.707   | 3.360  | 2.689  | 0.869  |
| Lymph node (Man)    | 1.158   | 0.644   | 1.099  | 0.967  | 0.282  |
| Lymph node (Mes)    | 1.076   | 1.409   | 1.701  | 1.395  | 0.313  |
| Muscle              | 0.158   | 0.096   | 0.196  | 0.150  | 0.051  |
| Pancreas            | 0.433   | 0.326   | 0.579  | 0.446  | 0.127  |
| Pituitary gland     | 0.858   | 0.517   | 0.994  | 0.790  | 0.246  |
| Prostate            | 0.314   | 0.176   | 0.386  | 0.292  | 0.107  |
| Salivary glands     | 0.242   | 0.168   | 0.386  | 0.265  | 0.111  |
| Skin                | 0.295   | 0.285   | 0.547  | 0.376  | 0.148  |
| Small intestine     | 2.012   | 1.963   | 1.865  | 1.946  | 0.075  |
| Spinal cord         | 0.185   | 0.148   | 0.252  | 0.195  | 0.053  |
| Spleen              | 24.956  | 16.693  | 35.344 | 25.664 | 9.345  |
| Stomach             | 0.113   | 0.187   | 2.187  | 0.829  | 1.177  |
| Testes              | 0.269   | 0.328   | 0.361  | 0.319  | 0.047  |
| Thymus              | 0.110   | 0.295   | 0.481  | 0.295  | 0.185  |
| Thyroid             | 1.544   | 0.885   | 2.170  | 1.533  | 0.642  |
| Whole Blood         | 3.450   | 2.106   | 4.202  | 3.253  | 1.062  |
| Plasma              | 7.541   | 4.597   | 8.168  | 6.768  | 1.907  |
| Blood:plasma ratio  | 0.46    | 0.46    | 0.51   | 0.48   | 0.03   |

## Appendix 8 Individual Male 100 µg mRNA Data (continued)

### Concentration of Total Radioactivity in Whole Blood, Plasma and Tissues 24 hours Following Single Intramuscular Administration of [<sup>3</sup>H]-08-A01-C01 to Male Wistar Han Rats

Target Dose Level: 100 µg mRNA/Animal; 2.57 mg Total Lipid/Animal

Results expressed as µg lipid equiv/g (mL)

| Sample              | 016M   | 017M   | 018M    | Mean    | SD      |
|---------------------|--------|--------|---------|---------|---------|
| Adipose tissue      | 0.268  | 0.219  | 0.261   | 0.249   | 0.027   |
| Adrenal glands      | 63.795 | 42.538 | 52.924  | 53.085  | 10.629  |
| Bladder             | 0.609  | 0.643  | 0.373   | 0.542   | 0.147   |
| Bone (femur)        | 1.254  | 2.075  | 0.950   | 1.426   | 0.582   |
| Bone marrow (femur) | 5.002  | 4.711  | 7.513   | 5.742   | 1.541   |
| Brain               | 0.186  | 0.221  | 0.255   | 0.221   | 0.034   |
| Eyes                | 0.342  | 0.247  | 0.360   | 0.316   | 0.061   |
| Heart               | 1.613  | 1.877  | 1.760   | 1.750   | 0.132   |
| Injection site      | 50.606 | 70.405 | 268.240 | 129.750 | 120.340 |
| Kidneys             | 1.971  | 1.774  | 2.460   | 2.068   | 0.353   |
| Large intestine     | 5.083  | 2.282  | 3.210   | 3.525   | 1.427   |
| Liver               | 51.485 | 71.224 | 45.827  | 56.179  | 13.334  |
| Lung                | 3.831  | 3.615  | 3.360   | 3.602   | 0.236   |
| Lymph node (Man)    | 3.227  | 1.555  | 1.570   | 2.117   | 0.961   |
| Lymph node (Mes)    | 5.835  | 3.496  | 3.765   | 4.366   | 1.279   |
| Muscle              | 0.208  | 0.263  | 0.247   | 0.239   | 0.028   |
| Pancreas            | 0.767  | 0.966  | 0.781   | 0.838   | 0.111   |
| Pituitary gland     | 1.320  | 1.362  | 1.603   | 1.428   | 0.152   |
| Prostate            | 0.407  | 0.446  | 0.481   | 0.445   | 0.037   |
| Salivary glands     | 0.617  | 0.561  | 0.701   | 0.626   | 0.071   |
| Skin                | 0.833  | 0.937  | 0.645   | 0.805   | 0.148   |
| Small intestine     | 3.736  | 3.157  | 3.433   | 3.442   | 0.289   |
| Spinal cord         | 0.229  | 0.200  | 0.326   | 0.252   | 0.066   |
| Spleen              | 47.746 | 74.940 | 44.431  | 55.706  | 16.739  |
| Stomach             | 0.572  | 0.802  | 0.489   | 0.621   | 0.162   |
| Testes              | 0.638  | 0.502  | 0.616   | 0.585   | 0.073   |
| Thymus              | 0.473  | 0.568  | 0.506   | 0.516   | 0.048   |
| Thyroid             | 1.845  | 1.890  | 2.651   | 2.129   | 0.453   |
| Whole Blood         | 2.448  | 1.756  | 3.404   | 2.536   | 0.827   |
| Plasma              | 5.639  | 5.297  | 8.191   | 6.376   | 1.581   |
| Blood:plasma ratio  | 0.43   | 0.33   | 0.42    | 0.39    | 0.05    |

**Appendix 8  
(continued)****Individual Male 100 µg mRNA Data****Concentration of Total Radioactivity in Whole Blood, Plasma and  
Tissues 48 hours Following Single Intramuscular Administration of  
[<sup>3</sup>H]-08-A01-C01 to Male Wistar Han Rats****Target Dose Level: 100 µg mRNA/Animal; 2.57 mg Total Lipid/Animal****Results expressed as µg lipid equiv/g (mL)**

| Sample              | 019M   | 020M   | Mean   |
|---------------------|--------|--------|--------|
| Adipose tissue      | 0.276  | 0.234  | 0.255  |
| Adrenal glands      | 52.496 | 45.684 | 49.090 |
| Bladder             | 0.779  | 0.849  | 0.814  |
| Bone (femur)        | 0.639  | 0.867  | 0.753  |
| Bone marrow (femur) | 3.233  | 2.890  | 3.062  |
| Brain               | 0.477  | 0.173  | 0.325  |
| Eyes                | 0.239  | 0.260  | 0.249  |
| Heart               | 1.132  | 1.158  | 1.145  |
| Injection site      | 48.800 | 59.876 | 54.338 |
| Kidneys             | 0.971  | 1.131  | 1.051  |
| Large intestine     | 4.144  | 2.190  | 3.167  |
| Liver               | 48.512 | 36.690 | 42.601 |
| Lung                | 1.853  | 2.477  | 2.165  |
| Lymph node (Man)    | 2.418  | 1.157  | 1.788  |
| Lymph node (Mes)    | 5.067  | 3.297  | 4.182  |
| Muscle              | 0.166  | 0.926  | 0.546  |
| Pancreas            | 0.540  | 0.701  | 0.620  |
| Pituitary gland     | 0.987  | 0.884  | 0.936  |
| Prostate            | 0.308  | 0.285  | 0.296  |
| Salivary glands     | 0.488  | 0.588  | 0.538  |
| Skin                | 0.640  | 0.699  | 0.670  |
| Small intestine     | 3.644  | 3.750  | 3.697  |
| Spinal cord         | 0.212  | 0.237  | 0.224  |
| Spleen              | 35.545 | 33.899 | 34.722 |
| Stomach             | 0.794  | 1.011  | 0.903  |
| Testes              | 0.523  | 0.555  | 0.539  |
| Thymus              | 0.514  | 0.655  | 0.584  |
| Thyroid             | 1.604  | 1.523  | 1.564  |
| Whole Blood         | 0.967  | 1.011  | 0.989  |
| Plasma              | 1.451  | 1.493  | 1.472  |
| Blood:plasma ratio  | 0.67   | 0.68   | 0.67   |

**Appendix 8  
(continued)****Individual Male 100 µg mRNA Data****Recovery of Total Radioactivity in Tissues 0.25 min Following Single Intramuscular Administration of [<sup>3</sup>H]-08-A01-C01 to Male Wistar Han Rats****Target Dose Level: 100 µg mRNA/Animal; 2.57 mg Total Lipid/Animal****Results expressed as % administered dose**

| Sample          | 001M  | 002M  | 003M   | Mean   | SD     |
|-----------------|-------|-------|--------|--------|--------|
| Adrenal glands  | 0.000 | 0.000 | 0.000  | 0.000  | 0.000  |
| Bladder         | 0.000 | 0.000 | 0.000  | 0.000  | 0.000  |
| Brain           | 0.003 | 0.003 | 0.003  | 0.003  | 0.000  |
| Eyes            | 0.000 | 0.000 | 0.000  | 0.000  | 0.000  |
| Heart           | 0.011 | 0.009 | 0.017  | 0.013  | 0.004  |
| Injection site  | 1.865 | 3.345 | 18.252 | 7.821  | 9.064  |
| Kidneys         | 0.037 | 0.033 | 0.019  | 0.030  | 0.010  |
| Large intestine | 0.006 | 0.004 | 0.018  | 0.009  | 0.008  |
| Liver           | 0.368 | 0.185 | 0.278  | 0.277  | 0.091  |
| Lung            | 0.028 | 0.017 | 0.023  | 0.023  | 0.005  |
| Pancreas        | 0.001 | 0.001 | 0.002  | 0.001  | 0.000  |
| Pituitary gland | 0.000 | 0.000 | 0.000  | 0.000  | 0.000  |
| Prostate        | 0.000 | 0.000 | 0.000  | 0.000  | 0.000  |
| Salivary glands | 0.001 | 0.002 | 0.001  | 0.001  | 0.000  |
| Small intestine | 0.016 | 0.009 | 0.006  | 0.010  | 0.005  |
| Spinal cord     | 0.001 | 0.001 | 0.000  | 0.001  | 0.000  |
| Spleen          | 0.010 | 0.026 | 0.006  | 0.014  | 0.011  |
| Stomach         | 0.005 | 0.004 | *0.002 | °0.003 | °0.002 |
| Testes          | 0.004 | 0.003 | 0.003  | 0.003  | 0.001  |
| Thymus          | 0.003 | 0.003 | 0.004  | 0.003  | 0.001  |
| Thyroid         | 0.000 | 0.000 | 0.000  | 0.000  | 0.000  |

\*=Results calculated from data less than 30 cpm above background

°=Mean includes results calculated from data less than 30 cpm above background

**Appendix 8  
(continued)****Individual Male 100 µg mRNA Data****Recovery of Total Radioactivity in Tissues 1 hour Following Single  
Intramuscular Administration of [<sup>3</sup>H]-08-A01-C01 to Male Wistar Han  
Rats****Target Dose Level: 100 µg mRNA/Animal; 2.57 mg Total Lipid/Animal****Results expressed as % administered dose**

| Sample          | 004M   | 005M   | 006M   | Mean   | SD    |
|-----------------|--------|--------|--------|--------|-------|
| Adrenal glands  | 0.005  | 0.003  | 0.004  | 0.004  | 0.001 |
| Bladder         | 0.001  | 0.000  | 0.001  | 0.001  | 0.000 |
| Brain           | 0.019  | 0.020  | 0.020  | 0.019  | 0.001 |
| Eyes            | 0.002  | 0.001  | 0.001  | 0.001  | 0.001 |
| Heart           | 0.049  | 0.103  | 0.074  | 0.075  | 0.027 |
| Injection site  | 15.619 | 13.609 | 16.094 | 15.107 | 1.319 |
| Kidneys         | 0.191  | 0.176  | 0.188  | 0.185  | 0.008 |
| Large intestine | 0.024  | 0.027  | 0.050  | 0.034  | 0.014 |
| Liver           | 5.198  | 3.856  | 5.564  | 4.873  | 0.899 |
| Lung            | 0.148  | 0.159  | 0.103  | 0.137  | 0.030 |
| Pancreas        | 0.004  | 0.006  | 0.007  | 0.006  | 0.002 |
| Pituitary gland | 0.000  | 0.000  | 0.000  | 0.000  | 0.000 |
| Prostate        | 0.003  | 0.003  | 0.003  | 0.003  | 0.000 |
| Salivary glands | 0.007  | 0.009  | 0.011  | 0.009  | 0.002 |
| Small intestine | 0.132  | 1.003  | 1.062  | 0.732  | 0.521 |
| Spinal cord     | 0.001  | 0.003  | 0.001  | 0.002  | 0.001 |
| Spleen          | 0.090  | 0.087  | 0.089  | 0.089  | 0.001 |
| Stomach         | 0.075  | 0.362  | 1.259  | 0.565  | 0.618 |
| Testes          | 0.020  | 0.021  | 0.057  | 0.033  | 0.021 |
| Thymus          | 0.007  | 0.005  | 0.006  | 0.006  | 0.001 |
| Thyroid         | 0.001  | 0.001  | 0.001  | 0.001  | 0.000 |

**Appendix 8 Individual Male Recovery Data**  
**(continued)****Recovery of Total Radioactivity in Tissues 2 hours Following Single Intramuscular Administration of [<sup>3</sup>H]-08-A01-C01 to Male Wistar Han Rats****Target Dose Level: 100 µg mRNA/Animal; 2.57 mg Total Lipid/Animal****Results expressed as % administered dose**

| Sample          | 007M   | 008M  | 009M  | Mean  | SD    |
|-----------------|--------|-------|-------|-------|-------|
| Adrenal glands  | 0.008  | 0.006 | 0.007 | 0.007 | 0.001 |
| Bladder         | 0.001  | 0.001 | 0.001 | 0.001 | 0.000 |
| Brain           | 0.024  | 0.021 | 0.018 | 0.021 | 0.003 |
| Eyes            | 0.001  | 0.001 | 0.001 | 0.001 | 0.000 |
| Heart           | 0.078  | 0.095 | 0.115 | 0.096 | 0.019 |
| Injection site  | 0.598  | 9.070 | 3.532 | 4.400 | 4.302 |
| Kidneys         | 0.180  | 0.148 | 0.160 | 0.163 | 0.016 |
| Large intestine | 0.088  | 0.038 | 0.055 | 0.061 | 0.025 |
| Liver           | 11.802 | 8.114 | 8.654 | 9.523 | 1.992 |
| Lung            | 0.147  | 0.112 | 0.153 | 0.137 | 0.022 |
| Pancreas        | 0.008  | 0.007 | 0.011 | 0.009 | 0.002 |
| Pituitary gland | 0.001  | 0.000 | 0.000 | 0.000 | 0.000 |
| Prostate        | 0.003  | 0.004 | 0.004 | 0.004 | 0.001 |
| Salivary glands | 0.012  | 0.010 | 0.013 | 0.011 | 0.002 |
| Small intestine | 0.434  | 0.294 | 0.281 | 0.336 | 0.085 |
| Spinal cord     | 0.003  | 0.004 | 0.002 | 0.003 | 0.001 |
| Spleen          | 0.271  | 0.155 | 0.192 | 0.206 | 0.059 |
| Stomach         | 0.036  | 0.023 | 0.026 | 0.028 | 0.007 |
| Testes          | 0.025  | 0.045 | 0.036 | 0.035 | 0.010 |
| Thymus          | 0.010  | 0.008 | 0.007 | 0.008 | 0.001 |
| Thyroid         | 0.001  | 0.001 | 0.001 | 0.001 | 0.000 |

**Appendix 8 Individual Male Recovery Data**  
**(continued)****Recovery of Total Radioactivity in Tissues 4 hours Following Single Intramuscular Administration of [<sup>3</sup>H]-08-A01-C01 to Male Wistar Han Rats****Target Dose Level: 100 µg mRNA/Animal; 2.57 mg Total Lipid/Animal****Results expressed as % administered dose**

| Sample          | 010M   | 011M   | 012M   | Mean   | SD     |
|-----------------|--------|--------|--------|--------|--------|
| Adrenal glands  | 0.010  | 0.005  | 0.005  | 0.007  | 0.003  |
| Bladder         | 0.001  | 0.000  | 0.000  | 0.001  | 0.000  |
| Brain           | 0.027  | 0.009  | 0.006  | 0.014  | 0.011  |
| Eyes            | 0.001  | 0.001  | 0.000  | 0.001  | 0.000  |
| Heart           | 0.031  | 0.043  | 0.033  | 0.036  | 0.007  |
| Injection site  | 5.231  | 59.191 | 24.168 | 29.530 | 27.377 |
| Kidneys         | 0.141  | 0.101  | 0.058  | 0.100  | 0.041  |
| Large intestine | 0.062  | 0.258  | 0.123  | 0.147  | 0.100  |
| Liver           | 13.675 | 6.428  | 7.436  | 9.180  | 3.926  |
| Lung            | 0.079  | 0.141  | 0.069  | 0.096  | 0.039  |
| Pancreas        | 0.003  | 0.008  | 0.006  | 0.006  | 0.003  |
| Pituitary gland | 0.000  | 0.000  | 0.000  | 0.000  | 0.000  |
| Prostate        | 0.002  | 0.001  | 0.001  | 0.001  | 0.001  |
| Salivary glands | 0.005  | 0.003  | 0.003  | 0.004  | 0.001  |
| Small intestine | 0.234  | 0.614  | 0.356  | 0.401  | 0.194  |
| Spinal cord     | 0.001  | 0.001  | 0.001  | 0.001  | 0.000  |
| Spleen          | 0.177  | 0.530  | 0.167  | 0.291  | 0.207  |
| Stomach         | 0.007  | 0.035  | 0.043  | 0.028  | 0.019  |
| Testes          | 0.048  | 0.017  | 0.012  | 0.026  | 0.019  |
| Thymus          | 0.003  | 0.005  | 0.003  | 0.003  | 0.001  |
| Thyroid         | 0.001  | 0.000  | 0.001  | 0.001  | 0.000  |

**Appendix 8 Individual Male Recovery Data**  
**(continued)****Recovery of Total Radioactivity in Tissues 8 hours Following Single Intramuscular Administration of [<sup>3</sup>H]-08-A01-C01 to Male Wistar Han Rats****Target Dose Level: 100 µg mRNA/Animal; 2.57 mg Total Lipid/Animal****Results expressed as % administered dose**

| Sample          | 013M   | 014M   | 015M   | Mean   | SD    |
|-----------------|--------|--------|--------|--------|-------|
| Adrenal glands  | 0.025  | 0.021  | 0.080  | 0.042  | 0.033 |
| Bladder         | 0.002  | 0.001  | 0.001  | 0.001  | 0.001 |
| Brain           | 0.012  | 0.009  | 0.014  | 0.012  | 0.003 |
| Eyes            | 0.002  | 0.001  | 0.002  | 0.002  | 0.001 |
| Heart           | 0.058  | 0.035  | 0.081  | 0.058  | 0.023 |
| Injection site  | 8.806  | 17.803 | 0.313  | 8.974  | 8.746 |
| Kidneys         | 0.134  | 0.073  | 0.091  | 0.099  | 0.031 |
| Large intestine | 0.511  | 0.398  | 0.634  | 0.514  | 0.118 |
| Liver           | 11.864 | 16.293 | 24.504 | 17.553 | 6.414 |
| Lung            | 0.192  | 0.129  | 0.197  | 0.172  | 0.038 |
| Pancreas        | 0.005  | 0.006  | 0.012  | 0.007  | 0.004 |
| Pituitary gland | 0.000  | 0.000  | 0.000  | 0.000  | 0.000 |
| Prostate        | 0.002  | 0.001  | 0.003  | 0.002  | 0.001 |
| Salivary glands | 0.004  | 0.003  | 0.008  | 0.005  | 0.003 |
| Small intestine | 0.585  | 0.529  | 0.633  | 0.582  | 0.052 |
| Spinal cord     | 0.002  | 0.001  | 0.002  | 0.002  | 0.000 |
| Spleen          | 0.560  | 0.369  | 0.848  | 0.592  | 0.241 |
| Stomach         | 0.021  | 0.019  | 0.288  | 0.109  | 0.155 |
| Testes          | 0.031  | 0.036  | 0.038  | 0.035  | 0.004 |
| Thymus          | 0.002  | 0.004  | 0.007  | 0.004  | 0.002 |
| Thyroid         | 0.001  | 0.001  | 0.001  | 0.001  | 0.000 |

**Appendix 8 Individual Male Recovery Data**  
**(continued)****Recovery of Total Radioactivity in Tissues 24 hours Following Single Intramuscular Administration of [<sup>3</sup>H]-08-A01-C01 to Male Wistar Han Rats****Target Dose Level: 100 µg mRNA/Animal; 2.57 mg Total Lipid/Animal****Results expressed as % administered dose**

| Sample          | 016M   | 017M   | 018M   | Mean   | SD     |
|-----------------|--------|--------|--------|--------|--------|
| Adrenal glands  | 0.137  | 0.095  | 0.106  | 0.113  | 0.022  |
| Bladder         | 0.003  | 0.002  | 0.001  | 0.002  | 0.001  |
| Brain           | 0.012  | 0.015  | 0.019  | 0.015  | 0.003  |
| Eyes            | 0.004  | 0.002  | 0.004  | 0.003  | 0.001  |
| Heart           | 0.038  | 0.052  | 0.051  | 0.047  | 0.008  |
| Injection site  | 3.590  | 15.406 | 29.435 | 16.144 | 12.938 |
| Kidneys         | 0.107  | 0.104  | 0.165  | 0.125  | 0.034  |
| Large intestine | 1.668  | 0.752  | 0.996  | 1.139  | 0.475  |
| Liver           | 22.736 | 26.544 | 20.865 | 23.382 | 2.894  |
| Lung            | 0.170  | 0.160  | 0.226  | 0.185  | 0.036  |
| Pancreas        | 0.010  | 0.016  | 0.012  | 0.013  | 0.003  |
| Pituitary gland | 0.000  | 0.000  | 0.000  | 0.000  | 0.000  |
| Prostate        | 0.003  | 0.004  | 0.004  | 0.004  | 0.000  |
| Salivary glands | 0.011  | 0.010  | 0.011  | 0.010  | 0.001  |
| Small intestine | 1.194  | 0.896  | 1.321  | 1.137  | 0.218  |
| Spinal cord     | 0.002  | 0.001  | 0.002  | 0.002  | 0.001  |
| Spleen          | 1.003  | 1.590  | 1.111  | 1.234  | 0.312  |
| Stomach         | 0.066  | 0.099  | 0.065  | 0.077  | 0.019  |
| Testes          | 0.070  | 0.056  | 0.075  | 0.067  | 0.010  |
| Thymus          | 0.007  | 0.009  | 0.007  | 0.008  | 0.002  |
| Thyroid         | 0.001  | 0.001  | 0.001  | 0.001  | 0.000  |

**Appendix 8 Individual Male Recovery Data**  
**(continued)****Recovery of Total Radioactivity in Tissues 48 hours Following Single Intramuscular Administration of [<sup>3</sup>H]-08-A01-C01 to Male Wistar Han Rats****Target Dose Level: 100 µg mRNA/Animal; 2.57 mg Total Lipid/Animal****Results expressed as % administered dose**

| Sample          | 019M   | 020M   | Mean   |
|-----------------|--------|--------|--------|
| Adrenal glands  | 0.155  | 0.112  | 0.134  |
| Bladder         | 0.002  | 0.002  | 0.002  |
| Brain           | 0.034  | 0.012  | 0.023  |
| Eyes            | 0.002  | 0.003  | 0.002  |
| Heart           | 0.030  | 0.031  | 0.030  |
| Injection site  | 2.978  | 10.414 | 6.696  |
| Kidneys         | 0.063  | 0.076  | 0.070  |
| Large intestine | 1.070  | 0.719  | 0.894  |
| Liver           | 17.436 | 16.159 | 16.797 |
| Lung            | 0.071  | 0.132  | 0.102  |
| Pancreas        | 0.007  | 0.006  | 0.006  |
| Pituitary gland | 0.000  | 0.000  | 0.000  |
| Prostate        | 0.003  | 0.002  | 0.003  |
| Salivary glands | 0.008  | 0.009  | 0.008  |
| Small intestine | 0.790  | 1.021  | 0.905  |
| Spinal cord     | 0.002  | 0.002  | 0.002  |
| Spleen          | 0.886  | 0.649  | 0.768  |
| Stomach         | 0.044  | 0.047  | 0.046  |
| Testes          | 0.064  | 0.054  | 0.059  |
| Thymus          | 0.006  | 0.005  | 0.006  |
| Thyroid         | 0.001  | 0.001  | 0.001  |