

**Disposition of Radioactivity 72 Hours Following Dermal Application of 10 mg/kg [<sup>14</sup>C]HMB,  
Formulated in Ethanol, to Male Harlan Sprague Dawley Rats (Group D-2)<sup>a</sup>**

**Dose Recovered in Excreta (%)**

| End of Collection Period (h) | Urine CPDE <sup>b</sup> | Cage Rinse CPDE | Feces CPDE  | GI Content  | Total |
|------------------------------|-------------------------|-----------------|-------------|-------------|-------|
| 4                            | 0.913 ± 0.866           | 0.527 ± 0.539   | —           | —           | 1.44  |
| 8                            | 3.54 ± 1.23             | 1.64 ± 0.95     | —           | —           | 5.18  |
| 12                           | 6.55 ± 1.37             | 2.96 ± 0.97     | —           | —           | 9.51  |
| 24                           | 13.0 ± 2.8              | 4.92 ± 1.60     | 9.05 ± 3.36 | —           | 26.9  |
| 48                           | 20.6 ± 3.7              | 6.82 ± 2.39     | 17.2 ± 2.7  | —           | 44.7  |
| 72 <sup>c</sup>              | 24.5 ± 3.9              | 9.51 ± 3.18     | 21.8 ± 2.8  | 1.24 ± 0.32 | 57.8  |

**Disposition in Tissues**

| Tissue               | nmol-eq HMB per g Tissue | Tissue/Blood Ratio | Recovery (%)      |
|----------------------|--------------------------|--------------------|-------------------|
| Blood <sup>d</sup>   | 0.345 ± 0.167            | unity              | 0.0493 ± 0.0241   |
| Adipose <sup>d</sup> | 1.06 ± 0.21              | 3.39 ± 0.87        | 0.143 ± 0.029     |
| Muscle <sup>d</sup>  | 0.166 ± 0.059            | 0.502 ± 0.104      | 0.129 ± 0.047     |
| Skin <sup>d</sup>    | 17.8 ± 6.5               | 62.5 ± 34.1        | 6.44 ± 2.14       |
| Brain                | 0.0707 ± 0.0618          | 0.231 ± 0.264      | 0.00069 ± 0.00050 |
| Heart                | 0.254 ± 0.277            | 0.904 ± 1.231      | 0.00144 ± 0.00140 |
| Kidneys              | 1.51 ± 0.28              | 5.08 ± 2.26        | 0.0196 ± 0.0038   |
| Liver                | 1.17 ± 0.36              | 3.78 ± 1.44        | 0.0854 ± 0.0252   |
| Lung                 | 0.277 ± 0.114            | 0.935 ± 0.632      | 0.00249 ± 0.00122 |
| Spleen               | 0.168 ± 0.099            | 0.551 ± 0.385      | 0.00070 ± 0.00037 |
| Adrenals             | 0.538 ± 0.309            | 1.64 ± 1.17        | 0.00016 ± 0.00010 |
| Thymus               | 0.109 ± 0.062            | 0.320 ± 0.151      | 0.00041 ± 0.00024 |
| Thyroid              | 3.07 ± 3.64              | 9.07 ± 10.01       | 0.00004 ± 0.00003 |
| Urinary Bladder      | 10.9 ± 9.3               | 39.2 ± 34.8        | 0.00429 ± 0.00259 |
| Pancreas             | 0.310 ± 0.152            | 1.06 ± 0.77        | 0.00135 ± 0.00044 |
| Testes               | 0.140 ± 0.048            | 0.439 ± 0.156      | 0.00326 ± 0.00096 |
| Cecum                | 7.23 ± 3.35              | 24.3 ± 13.8        | 0.0347 ± 0.0153   |
| Large Intestine      | 1.20 ± 0.43              | 4.12 ± 2.15        | 0.0117 ± 0.0053   |
| Small Intestine      | 5.31 ± 1.10              | 18.3 ± 8.6         | 0.172 ± 0.015     |
| Stomach              | 1.79 ± 0.84              | 5.51 ± 2.39        | 0.0174 ± 0.0085   |

**Disposition Summary**

| Sample                                 | % Dose Recovered     |
|--|----------------------|
| <b>Total Unabsorbed Dose</b>           | <b>16.2 ± 4.5</b>    |
| Applicator                             | 4.20 ± 1.54          |
| Tape/Glue                              | 5.10 ± 2.12          |
| Dose Site Swipes                       | 6.86 ± 1.30          |
| <b>Total Dose Site Skin</b>            | <b>0.275 ± 0.148</b> |
| <b>Total Absorbed Dose<sup>e</sup></b> | <b>67.8 ± 3.2</b>    |
| Urine + Cage Rinse                     | 34.4 ± 3.4           |
| Urine                                  | 24.5 ± 3.9           |
| Cage Rinse                             | 9.51 ± 3.18          |
| Feces                                  | 21.8 ± 2.8           |
| GI Content                             | 1.24 ± 0.32          |
| Carcass                                | 1.35 ± 1.75          |
| Tissues                                | 7.39 ± 2.09          |
| <b>Total Recovered</b>                 | <b>82.7 ± 5.5</b>    |

<sup>a</sup>All values expressed as mean ± standard deviation (SD) (N = 5). The actual dose delivered was 11.7 ± 0.4 mg/kg (49.2 ± 1.8 µCi).

<sup>b</sup>CPDE = Cumulative percent dose excreted.

<sup>c</sup>72 hour (h) urine collection includes urine present in the urinary bladder at study termination.

<sup>d</sup>Tissue weights for the dispersed tissues were calculated using the following percentages of body weight: adipose 7.0%, blood 7.4%, muscle 40.4%, and skin 19% (International Life Sciences Institute, 1994).

<sup>e</sup>Up to 36 h post application, the metal appliances were observed attached to each animal. At the 48 h observation and collection period, the metal appliances were found in the animals' cages. All appliances were removed from the cages, rinsed, bagged, and set aside for processing at necropsy. It is possible because the metal devices no longer covered the dermal dose site from ~36 to 48 h post application through 72 h post application that animals may have received an oral dose due to grooming of the dermal site.