

ADME NTP Study S0071 Hexachloro-1,3-butadiene

The contractor abbreviated the test article as HCBd.
Sex/Species: adult male F344 rats and B6C3F1 mice.

Vehicles

Intravenous: propylene glycol in approximately 0.5 g of rat serum, Carbowax 200 (polyethylene glycol 200) in approximately 1.0 g of rat serum, or 10% Carbowax 200 in B6C3F1 mouse serum (v/v).

Oral: corn oil.

CASRN 87-68-3

Radiolabeled with carbon-14 in all four carbons; [14C]Hexachloro-1,3-butadiene

Studies Performed:

Rat Intravenous:

- Single 0.58 mg/kg intravenous dose to rats with sacrifice 240 hours postdose (vehicle, propylene glycol in rat serum).
- Single 1.80 mg/kg intravenous dose to rats with sacrifice 72 hours postdose (vehicle, propylene glycol in rat serum).
- Pretreatment with 200 mg/kg ampicillin by intraperitoneal injection once daily for 4 days immediately preceding the day of a single 1.86 mg/kg intravenous HCBd dose to rats with sacrifice 72 hours following the HCBd dose (vehicle, Carbowax 200 in rat serum).
- Single 27.2 mg/kg intravenous dose to rats with sacrifice 240 hours postdose (vehicle, Carbowax 200 in rat serum).

Rat Oral:

- Single 0.70 mg/kg oral gavage dose to rats with sacrifice 240 hours postdose.
- Single 2.13 mg/kg oral gavage dose to rats with sacrifice 72 hours postdose.
- Single 5.82 mg/kg oral gavage dose to rats with sacrifice 72 hours postdose.
- Single 33.9 mg/kg oral gavage dose to rats with sacrifice 240 hours postdose.
- Single 166 mg/kg oral gavage dose to rats with sacrifice 72 hours postdose.

- Pretreatment with 100 mg/rat lincomycin sulfate and 100 mg/rat neomycin sulfate once daily for 4 days immediately preceding the day of a single 166 mg/kg oral gavage HCBd dose to rats with sacrifice 72 hours following the HCBd dose.

Mouse Intravenous:

- Single 19 mg/kg intravenous dose to mice (3-mouse unit*) with sacrifice 240 hours postdose (vehicle, 10% Carbowax 200 in mouse serum (v/v)).

Mouse Oral:

- Single 2.0 mg/kg oral gavage dose to mice (3-mouse unit*) with sacrifice 240 hours postdose.
- Single 24 mg/kg oral gavage dose to mice (3-mouse unit*) with sacrifice 240 hours postdose.
- Single 50 mg/kg oral gavage dose to mice (3-mouse unit*) with sacrifice 240 hours postdose.

*For the disposition studies, mice were dosed as 3-mouse unit body weight in a volume of 0.3 ml per 3-mouse unit. Individual mice in each 3-mouse unit received one-third of the total dose volume. Mortality was observed in mice at the two higher oral doses (half at the 24 and $\frac{3}{4}$ at the 50 mg/kg dose) as well as for the intravenous dose (1 out of 12 at the 19 mg/kg dose). A higher dose concentration of 110 mg/kg was lethal to all mice.

Recoveries of ^{14}C in rats shown in Tables 1-4 are based on the calculated dose of [^{14}C]HCBd. The values in Tables 2 and 4 have been normalized to 100% total recovery of ^{14}C for each animal.

The purpose of pretreating with antibiotics was to decrease gut flora to determine if gut flora affects disposition or plays a major role in the toxicity of HCBd.

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Table 1
Average Cumulative Excretion of Total ^{14}C After Intravenous Administration of ^{14}C -HCBD;
Based on Total Calculated Dose (% Dose + S.D.)^a

| Dose (mg/kg) | 0.58 | | | | 1.80 | | | | 1.86 ^b | | | | 27.2 | | | | |
|----------------|-------------|------------|--------------------|-------------|-------------|------------|---------------------------|--------------------|-------------------|-------------|------------|--------------------|-------------|-------------|------------|--------------------------|-------------|
| | Urine | Feces | Breath Organics | Total | Urine | Feces | Breath CO ₂ | Breath Organics | Total | Urine | Feces | Breath Organics | Total | Urine | Feces | Breath Organics | Total |
| Time hr day | | | | | | | | | | | | | | | | | |
| 6 | 4.00 ± 1.68 | | | 4.00 ± 1.68 | 4.90 ± 1.17 | | | | 4.90 ± 1.17 | 36.7 ± 2.87 | | | 3.67 ± 2.87 | 2.15 ± 1.47 | | | 2.15 ± 1.90 |
| 12 | 8.62 ± 1.10 | | 1.97 ± 0.16 | 10.6 ± 1.2 | 9.37 ± 2.00 | | 0.68 ± 0.32 | 2.28 ± 0.52 | 12.3 ± 2.3 | 9.94 ± 1.20 | | 3.60 ± 0.29 | 13.5 ± 1.4 | 5.16 ± 1.70 | | | 6.56 ± 1.70 |
| 24 | 12.3 ± 1.2 | 20.0 ± 2.7 | 3.06 ± 0.25 | 35.4 ± 2.1 | 13.9 ± 2.5 | 21.0 ± 5.1 | 1.10 ± 0.33 | 3.30 ± 0.68 | 39.3 ± 7.9 | 16.1 ± 1.7 | 24.3 ± 2.8 | 5.61 ± 0.39 | 46.0 ± 2.5 | 9.57 ± 1.99 | 20.2 ± 4.7 | 2.57 ± 0.30 ^c | 31.2 ± 4.8 |
| 30 | 14.0 ± 1.1 | | 3.26 ± 0.23 | 37.4 ± 2.4 | 15.1 ± 2.9 | | 1.28 ± 0.34 | 3.72 ± 0.76 | 41.1 ± 8.3 | 19.0 ± 1.0 | | 6.28 ± 0.38 | 49.6 ± 2.8 | 9.69 ± 1.94 | | | 32.4 ± 4.8 |
| 48 | 17.1 ± 0.86 | 32.3 ± 2.6 | 3.91 ± 0.28 | 53.3 ± 3.1 | 18.8 ± 3.1 | 33.4 ± 6.2 | | 4.38 ± 0.82 | 58.0 ± 9.7 | 22.9 ± 1.1 | 43.4 ± 3.1 | 7.59 ± 0.16 | 74.8 ± 4.0 | 13.3 ± 2.0 | 36.1 ± 3.4 | 3.59 ± 0.42 | 53.1 ± 5.2 |
| 54 | 17.6 ± 0.9 | | | 46.8 ± 14.3 | 19.7 ± 3.0 | | | | 58.8 ± 9.6 | 23.7 ± 1.0 | | | 75.6 ± 3.7 | 14.1 ± 1.8 | | | 53.8 ± 4.8 |
| 72 | 19.0 ± 0.8 | 36.8 ± 2.9 | | 59.6 ± 3.5 | 21.2 ± 3.2 | 39.0 ± 5.4 | | | 66.0 ± 8.7 | 25.5 ± 1.0 | 51.1 ± 1.9 | | 85.5 ± 1.2 | 15.7 ± 1.7 | 45.7 ± 3.5 | | 65.0 ± 4.7 |
| 96 | 20.2 ± 0.8 | 39.8 ± 3.2 | | 63.1 ± 5.0 | | | | | | | | | 17.0 ± 1.5 | 49.5 ± 2.9 | | | 70.1 ± 4.0 |
| 120 | 21.5 ± 1.5 | 41.2 ± 3.3 | | 66.6 ± 4.0 | | | | | | | | | 17.7 ± 1.4 | 50.9 ± 2.6 | | | 72.2 ± 3.6 |
| 144 | 22.2 ± 1.7 | 42.2 ± 3.4 | | 68.3 ± 4.3 | | | | | | | | | 18.1 ± 1.3 | 51.6 ± 2.7 | | | 73.3 ± 3.6 |
| 168 | 22.5 ± 1.8 | 43.0 ± 3.5 | | 69.4 ± 4.4 | | | | | | | | | 18.4 ± 1.3 | 52.0 ± 2.7 | | | 74.0 ± 3.6 |
| 192 | 22.8 ± 1.8 | 43.4 ± 3.6 | | 70.2 ± 4.5 | | | | | | | | | 18.6 ± 1.3 | 52.3 ± 2.7 | | | 74.5 ± 3.6 |
| 216 | 23.2 ± 1.9 | 43.7 ± 3.6 | | 70.8 ± 4.6 | | | | | | | | | 18.7 ± 1.3 | 52.5 ± 2.6 | | | 74.8 ± 3.5 |
| 240 | 23.4 ± 1.9 | 44.0 ± 3.6 | | 71.3 ± 4.5 | | | | | | | | | 18.8 ± 1.3 | 52.6 ± 2.6 | | | 75.0 ± 3.5 |

^a See Appendix Tables A1-A4 for data from individual rats.

^b Pretreated with antibiotics (200 mg of ampicillin/kg orally daily for 4 days).

^c Time period was 26 hr.

Table 2

Average Cumulative Excretion and Recovery of Total ^{14}C After Intravenous Administration of [^{14}C]HCBD to Rats; Normalized to 100% Total Recovery (% Dose \pm SD)^a

| Sample | Urine | Feces | Breath CO ₂ | Breath Organics | Tissues | Total |
|------------------|----------------|----------------|---------------------------|--------------------|----------------|----------------|
| Dose (mg/kg) | | | 0.58 | | | |
| Time hour day | | | | | | |
| 6 | 6.81 +/- 3.033 | | | | | 6.81 +/- 3.033 |
| 12 | 11.7 +/- 1.424 | | | 2.70 +/- 0.370 | | 14.4 +/- 1.848 |
| 24 1 | 16.8 +/- 2.158 | 27.3 +/- 3.749 | | 4.20 +/- 0.581 | | 48.3 +/- 5.257 |
| 48 2 | 23.3 +/- 1.144 | 43.9 +/- 1.300 | | 5.35 +/- 0.601 | | 72.8 +/- 1.188 |
| 72 3 | 25.8 +/- 1.353 | 50.0 +/- 1.198 | | | | 81.2 +/- 1.303 |
| 96 4 | 27.5 +/- 1.038 | 54.1 +/- 1.555 | | | | 87.0 +/- 0.894 |
| 120 5 | 29.3 +/- 2.103 | 56.1 +/- 2.308 | | | | 90.8 +/- 1.807 |
| 240 10 | 31.9 +/- 2.254 | 59.9 +/- 2.574 | | | 2.80 +/- 0.225 | 100 +/- 0 |
| Dose (mg/kg) | | | 1.8 | | | |
| Time hour day | | | | | | |
| 6 | 5.97 +/- 1.515 | | | | | 5.97 +/- 1.815 |
| 12 | 11.3 +/- 2.149 | | 0.80 +/- 0.339 | 2.73 +/- 0.394 | | 14.8 +/- 1.937 |
| 24 1 | 18.7 +/- 2.284 | 25.1 +/- 4.085 | 1.31 +/- 0.310 | 3.98 +/- 0.483 | | 47.1 +/- 5.119 |
| 48 2 | 22.7 +/- 2.064 | 40.2 +/- 4.174 | 1.63 +/- 0.302 | 5.27 +/- 0.886 | | 69.7 +/- 8.587 |
| 72 3 | 25.6 +/- 2.784 | 47.0 +/- 2.734 | | 0 +/- 0 | 30.4 +/- 4.212 | 100 +/- 0 |
| Dose (mg/kg) | | | 1.86 ^b | | | |
| Time hour day | | | | | | |
| 6 | 3.79 +/- 2.987 | | | | | 3.79 +/- 2.987 |
| 12 | 10.1 +/- 1.050 | | | 3.67 +/- 0.184 | | 13.8 +/- 1.034 |
| 24 1 | 16.3 +/- 1.111 | 24.9 +/- 3.782 | | 6.69 +/- 0.178 | | 48.9 +/- 2.877 |
| 48 2 | 23.3 +/- 0.413 | 44.3 +/- 2.873 | | 7.28 +/- 0.889 | | 74.9 +/- 2.578 |
| 72 3 | 28.1 +/- 0.235 | 52.2 +/- 0.787 | | | 14.3 +/- 0.773 | 100 +/- 0 |
| Dose (mg/kg) | | | 27.2 | | | |
| Time hour day | | | | | | |
| 6 | 2.74 +/- 2.428 | | | | | 2.74 +/- 2.427 |
| 12 | 6.66 +/- 2.001 | | | 1.83 +/- 0.101 | | 8.50 +/- 1.862 |
| 24 1 | 12.4 +/- 2.207 | 26.3 +/- 5.844 | | | | 40.5 +/- 4.343 |
| 48 2 | 17.3 +/- 2.079 | 47.0 +/- 2.372 | | 4.70 +/- 0.653 | | 69.1 +/- 3.240 |
| 72 3 | 20.4 +/- 1.500 | 59.5 +/- 2.462 | | | | 84.7 +/- 2.521 |
| 96 4 | 22.2 +/- 1.161 | 64.5 +/- 1.710 | | | | 91.4 +/- 1.609 |
| 120 5 | 23.1 +/- 1.109 | 68.3 +/- 1.019 | | | | 94.1 +/- 0.886 |
| 240 10 | 24.5 +/- 0.998 | 68.6 +/- 0.677 | | | 2.18 +/- 0.199 | 100 +/- 0 |

^aOriginal report Appendix has data from individual rats.

^bPretreated with antibiotics (200 mg of ampicillin/kg orally daily for 4 days).

Table 3
Average Cumulative Excretion of Total ¹⁴C After Oral Administration of ¹⁴C-HCBD;
Based on Total Calculated Dose (% Dose ± S.D.)

| Dose (mg/kg) | | 0.70 | | | | 2.13 | | | | 5.82 ^b | | | | |
|--------------|-----|-------------|--------------|-----------------|-------------|-------------|------------|-----------------|-------------|-------------------|------------|------------------------|-----------------|--------------|
| Excreta | | Urine | Feces | Breath Organics | Total | Urine | Feces | Breath Organics | Total | Urine | Feces | Breath CO ₂ | Breath Organics | Total |
| Time hr | day | | | | | | | | | | | | | |
| 6 | | 0.89 ± 0.99 | | | 0.89 ± 0.99 | 1.05 ± 0.74 | | | 1.05 ± 0.74 | 0.70 ± 0.95 | | | | 0.702 ± 0.95 |
| 12 | | 6.22 ± 2.78 | | 1.36 ± 0.28 | 7.59 ± 2.60 | 5.33 ± 0.92 | | 1.32 ± 0.42 | 6.65 ± 1.29 | 4.27 ± 1.33 | | 0.39 ± 0.03 | 1.35 ± 0.15 | 6.002 ± 1.46 |
| 24 | 1 | 13.2 ± 2.69 | 25.4 ± 4.89 | 2.47 ± 0.47 | 41.0 ± 2.9 | 10.2 ± 1.2 | 34.6 ± 5.8 | 2.632 ± 0.52 | 47.4 ± 4.5 | 6.56 ± 2.04 | 32.5 ± 5.2 | 0.57 ± 0.13 | 2.72 ± 0.48 | 42.32 ± 3.2 |
| 30 | | 13.8 ± 2.6 | | 2.86 ± 0.33 | 41.6 ± 3.0 | 11.5 ± 1.32 | | 3.082 ± 0.63 | 49.2 ± 4.4 | 7.86 ± 2.18 | | | | 43.6 ± 3.8 |
| 48 | 2 | 17.8 ± 4.0 | 39.3 ± 2.5 | 3.59 ± 0.26 | 60.2 ± 2.5 | 14.3 ± 2.0 | 45.2 ± 5.8 | 3.692 ± 0.56 | 63.2 ± 4.5 | 9.68 ± 2.72 | 45.4 ± 3.9 | | | 58.42 ± 2.7 |
| 54 | | 18.4 ± 3.9 | | | 60.8 ± 2.4 | 14.8 ± 2.02 | | | 63.6 ± 4.5 | 10.5 ± 2.70 | | | | 59.32 ± 2.6 |
| 72 | 3 | 20.1 ± 4.3 | 45.8 ± 1.6 | | 69.2 ± 3.2 | 16.3 ± 2.42 | 51.3 ± 4.9 | | 71.4 ± 3.1 | 12.4 ± 2.62 | 51.2 ± 2.8 | | | 66.92 ± 1.6 |
| 96 | 4 | 21.4 ± 4.7 | 49.1 ± 1.5 | | 73.1 ± 5.02 | | | | | | | | | |
| 120 | 5 | 22.3 ± 4.6 | 50.7 ± 1.8 | | 76.2 ± 4.72 | | | | | | | | | |
| 144 | 6 | 22.9 ± 4.6 | 51.72 ± 1.8 | | 77.8 ± 4.82 | | | | | | | | | |
| 168 | 7 | 23.2 ± 4.5 | 52.42 ± 1.9 | | 78.8 ± 4.82 | | | | | | | | | |
| 192 | 8 | 23.5 ± 4.5 | 52.8 ± 1.8 | | 79.6 ± 4.82 | | | | | | | | | |
| 216 | 9 | 23.7 ± 4.5 | 53.0 ± 1.92 | | 80.0 ± 4.8 | | | | | | | | | |
| 240 | 10 | 23.9 ± 4.4 | 53.32 ± 1.82 | | 80.4 ± 4.72 | | | | | | | | | |

| Dose (mg/kg) | | 33.9 | | | | 166 | | | | 166 ^c | | | | |
|--------------|-----|-------------|-------------|-----------------|-------------|---------------|-------------|------------------------|-----------------|------------------|---------------|-------------|--------------|-------------|
| Excreta | | Urine | Feces | Breath Organics | Total | Urine | Feces | Breath CO ₂ | Breath Organics | Total | Urine | Feces | Breath | Total |
| Time hr | day | | | | | | | | | | | | | |
| 6 | | 1.18 ± 0.65 | | | 1.18 ± 0.65 | 1.05 ± 0.23 | | | | 1.05 ± 0.23 | 0.92 ± 0.39 | | | 0.94 ± 0.34 |
| 12 | | 3.46 ± 1.32 | | 1.98 ± 1.91 | 5.44 ± 0.64 | 1.85 ± 0.38 | | 0.21 ± 0.06 | 0.96 ± 0.36 | 3.00 ± 0.35 | 1.95 ± 0.42 | | 0.86 ± 0.15 | 2.60 ± 0.38 |
| 24 | 1 | 7.57 ± 1.10 | 29.5 ± 15.9 | 3.99 ± 2.75 | 41.1 ± 15.7 | 3.102 ± 0.782 | 2.37 ± 1.94 | 0.37 ± 0.04 | 2.42 ± 0.27 | 11.3 ± 3.9 | 3.33 ± 1.01 | 2.69 ± 3.49 | 1.792 ± 0.20 | 7.80 ± 3.9 |
| 30 | | 7.79 ± 0.81 | | 4.95 ± 2.25 | 42.2 ± 16.0 | 3.562 ± 0.972 | | | | 11.92 ± 4.0 | 3.72 ± 1.212 | | 2.072 ± 0.26 | 8.48 ± 4.0 |
| 48 | 2 | 11.5 ± 2.0 | 43.2 ± 15.2 | 5.88 ± 1.73 | 60.8 ± 13.7 | 4.222 ± 1.202 | 5.94 ± 2.87 | | | 17.32 ± 6.3 | 5.362 ± 1.762 | 3.42 ± 3.23 | 2.882 ± 0.41 | 11.72 ± 4.2 |
| 54 | | 12.0 ± 2.3 | | | 61.3 ± 13.4 | 4.382 ± 1.062 | | | | 17.52 ± 6.3 | 5.482 ± 1.792 | | | 11.8 ± 4.2 |
| 72 | 3 | 13.5 ± 2.8 | 52.6 ± 10.8 | | 72.2 ± 8.2 | 5.122 ± 0.582 | 18.3 ± 5.6 | | | 33.02 ± 10.6 | 6.25 ± 1.842 | 3.84 ± 3.08 | | 13.4 ± 4.2 |
| 96 | 4 | 14.6 ± 3.2 | 56.0 ± 9.6 | | 76.6 ± 6.6 | | | | | | | | | |
| 120 | 5 | 15.1 ± 3.3 | 57.4 ± 9.0 | | 78.6 ± 5.8 | | | | | | | | | |
| 144 | 6 | 15.4 ± 3.4 | 58.4 ± 8.6 | | 80.0 ± 5.3 | | | | | | | | | |
| 168 | 7 | 15.7 ± 3.5 | 58.8 ± 8.6 | | 80.6 ± 5.3 | | | | | | | | | |
| 192 | 8 | 15.9 ± 3.6 | 59.2 ± 8.5 | | 81.4 ± 6.3 | | | | | | | | | |
| 216 | 9 | 16.0 ± 3.6 | 59.3 ± 8.5 | | 81.5 ± 5.1 | | | | | | | | | |
| 240 | 10 | 16.1 ± 3.7 | 59.5 ± 8.5 | | 81.6 ± 5.1 | | | | | | | | | |

^a Original report Appendix 2 has data from individual rats.

^b One animal was found dead at 24 h. Values after this time are the average for 3 animals.

^c Pretreated with antibiotics (100 mg each of lincomycin sulfate and neomycin sulfate per kg of body weight daily for 4 days).

Table 4

Average Cumulative Excretion and Recovery of Total ^{14}C After Oral Administration of [^{14}C]HCBd to Rats; Normalized to 100% Total Recovery (% Dose)^a

| Sample | Urine | Feces | Breath CO ₂ | Breath Organics | Tissues | Total |
|--------------|----------------|-----------------|------------------------|-----------------|-----------------|----------------|
| Dose (mg/kg) | | | 0.7 | | | |
| Time | | | | | | |
| hour day | | | | | | |
| 6 | 1.11 +/- 1.442 | | | | | 1.11 +/- 1.442 |
| 12 | 7.41 +/- 3.281 | | | 1.67 +/- 0.469 | | 9.09 +/- 2.572 |
| 24 1 | 15.9 +/- 2.800 | 31.2 +/- 8.329 | | 3.02 +/- 0.776 | | 50.1 +/- 5.804 |
| 48 2 | 21.4 +/- 4.514 | 48.0 +/- 5.962 | | 3.25 +/- 2.232 | | 73.3 +/- 3.566 |
| 72 3 | 24.2 +/- 4.703 | 55.9 +/- 4.807 | | | | 84.1 +/- 1.338 |
| 96 4 | 25.8 +/- 5.078 | 59.8 +/- 3.908 | | | | 89.6 +/- 0.524 |
| 120 5 | 28.9 +/- 4.892 | 61.7 +/- 3.809 | | | | 92.6 +/- 0.408 |
| 240 10 | 28.9 +/- 4.492 | 64.9 +/- 3.834 | | | 2.22 +/- 0.134 | 100 +/- 0 |
| Dose (mg/kg) | | | 2.13 | | | |
| Time | | | | | | |
| hour day | | | | | | |
| 6 | 1.21 +/- 0.846 | | | | | 1.21 +/- 0.845 |
| 12 | 6.05 +/- 1.165 | | | 1.49 +/- 0.499 | | 7.55 +/- 1.385 |
| 24 1 | 11.3 +/- 1.322 | 39.0 +/- 6.835 | | 2.98 +/- 0.831 | | 53.4 +/- 4.941 |
| 48 2 | 16.2 +/- 2.592 | 51.1 +/- 7.129 | | 4.18 +/- 0.685 | | 71.5 +/- 5.884 |
| 72 3 | 18.5 +/- 3.142 | 58.0 +/- 5.906 | | | 19.2 +/- 5.878 | 100 +/- 0 |
| Dose (mg/kg) | | | 5.82 ^b | | | |
| Time | | | | | | |
| hour day | | | | | | |
| 6 | 0.85 +/- 1.432 | | | | | 0.85 +/- 1.432 |
| 12 | 5.14 +/- 1.954 | | 0.46 +/- 0.033 | 1.82 +/- 0.209 | | 7.23 +/- 5.727 |
| 24 1 | 7.88 +/- 2.881 | 39.4 +/- 9.119 | 0.68 +/- 0.130 | 3.27 +/- 0.473 | | 51.3 +/- 24.94 |
| 48 2 | 11.6 +/- 3.221 | 55.1 +/- 7.743 | | | | 70.7 +/- 15.56 |
| 72 3 | 14.9 +/- 2.945 | 61.9 +/- 6.397 | | | 14.3 +/- 4.999 | 100 +/- 0 |
| Dose (mg/kg) | | | 33.9 | | | |
| Time | | | | | | |
| hour day | | | | | | |
| 6 | 1.42 +/- 0.788 | | | | | 1.42 +/- 0.787 |
| 12 | 4.14 +/- 1.568 | | | 2.44 +/- 2.470 | | 6.59 +/- 0.914 |
| 24 1 | 9.19 +/- 1.703 | 34.9 +/- 16.744 | | | | 46.5 +/- 13.21 |
| 48 2 | 13.9 +/- 2.988 | 51.5 +/- 15.154 | | 7.40 +/- 2.561 | | 72.8 +/- 11.12 |
| 72 3 | 16.4 +/- 3.959 | 63.0 +/- 9.154 | | | | 88.8 +/- 4.583 |
| 96 4 | 17.7 +/- 4.485 | 67.1 +/- 7.402 | | | | 92.3 +/- 2.409 |
| 120 5 | 18.3 +/- 4.687 | 68.9 +/- 8.832 | | | | 94.6 +/- 1.886 |
| 240 10 | 19.5 +/- 5.145 | 71.4 +/- 5.623 | | | 1.55 +/- 0.5807 | 100 +/- 0 |
| Dose (mg/kg) | | | 166 ^c | | | |
| Time | | | | | | |
| hour day | | | | | | |
| 6 | 1.11 +/- 0.478 | | | | | 1.11 +/- 0.477 |
| 12 | 2.27 +/- 0.470 | | | 1.00 +/- 0.220 | | 3.27 +/- 0.437 |
| 24 1 | 3.85 +/- 1.032 | 3.29 +/- 5.091 | 0.22 +/- 0.080 | 2.09 +/- 0.316 | | 9.24 +/- 5.115 |
| 48 2 | 6.21 +/- 1.890 | 4.13 +/- 4.786 | 0.39 +/- 0.017 | 2.88 +/- 0.167 | | 13.7 +/- 5.527 |
| 72 3 | 7.27 +/- 2.136 | 4.83 +/- 4.872 | | | 64.7 +/- 6.500 | 100 +/- 0 |

^a See Appendix Tables in original report for data from individual rats.2

^b One animal was found dead at 24 h. Values after this time are the average for 3 animals.

^c Pretreated with antibiotics (100 mg each of lincomycin sulfate and neomycin sulfate per kg of body weight daily for 4 days).

Table 5

Average % Dose Excreted as [¹⁴C]HCBD in Urine of F344 Male Rats
After Administration of 14C-HCBD

| Route | Dose | Time (hours) | %[¹⁴ C]HCBD in Urine Composite | Avg % Dose Excreted | Avg % Dose Excreted as [¹⁴ C]HCBC |
|-------|--------------------------|--------------|--|---------------------|---|
| IV | 27 mg/kg | 0-6 | 0.17 | 2.15 ± 1.9 | 0.00365 |
| | | 6-12 | 2.75 | 3.00 ± 0.75 | 0.0826 |
| | | 12-24 | 3.94 | 4.42 ± 1.4 | 0.174 |
| | | 24-48 | 5.45 | 3.77 ± 0.23 | 0.205 |
| IV | 1.8 mg/kg | 0-6 | 13.7 | 4.90 ± 1.2 | 0.671 |
| | | 6-12 | 12.4 | 4.48 ± 1.2 | 0.554 |
| IV | 1.9 mg/kg Antibiotics | 0-6 | 7.80 | 3.67 ± 2.9 | 0.287 |
| | | 6-12 | 3.79 | 6.26 ± 2.8 | 0.237 |
| Oral | 34 mg/kg | 0-6 | 2.92 | 1.18 ± 0.65 | 0.0344 |
| | | 6-12 | 0.23 | 2.32 ± 1.6 | 0.00534 |
| | | 12-24 | 2.73 | 4.11 ± 1.6 | 0.112 |
| | | 24-48 | 5.45 | 3.92 ± 2.0 | 0.214 |
| Oral | 166 mg/kg | 0-6 | 1.54 | 1.05 ± 0.24 | 0.0162 |
| | | 6-12 | 0.65 | 0.804 ± 0.14 | 0.0523 |

Table 6
 Concentration of Total ^{14}C in Blood and Plasma after Administration of ^{14}C -HCBD

| Time (hr) | Dose (mg/kg) | Route | ng-eq/g | | % dose/g | | Blood-Plasma Ratio |
|-----------|--------------|-------------------|---|----------------------|--|------------------------------|--------------------|
| | | | Plasma | Blood | Plasma | Blood | |
| 72 | 1.80 | IV | 96.4 ± 6.6 | 89.4 ± 6.0 | 0.019 ± 0.001 | 0.0178 ± 0.0012 | 0.93 |
| 72 | 2.13 | Oral | 44.3 ± 7.8 | 52.9 ± 7.7 | 0.0078 ± 0.0011 | 0.0092 ± 0.0012 | 1.2 |
| 72 | 5.82 | Oral | 103 ± 6 ^a | 138 ± 6 ^a | 0.0065 ± 0.0005 ^a | 0.0090 ± 0.0004 ^a | 1.3 |
| 72 | 166 | Oral ^d | 23,300 ± 5,900 | 18,300 ± 4,400 | 0.058 ± 0.014 | 0.046 ± 0.011 | 0.78 |
| 72 | 166 | Oral | 20,200 ± 2,300 | 17,200 ± 2,100 | 0.046 ± 0.007 | 0.039 ± 0.006 | 0.85 |
| 240 | 0.58 | IV | 4.40 ± 0.29 | 8.25 ± 1.05 | 0.0034 ± 0.0002 | 0.0064 ± 0.0008 | 1.9 |
| 240 | 27 | IV | 332 ± 63 | 771 ± 41 | 0.0049 ± 0.0009 | 0.012 ± 0.001 | 2.3 |
| 240 | 0.70 | Oral | 2.22 ± 0.41 | 8.52 ± 0.91 | 0.0014 ± 0.0002 | 0.0060 ± 0.0014 | 3.9 |
| 240 | 34 | Oral | 111 ± 16 ^{a,b} 85.6 ± 48 ^c | 288 ± 71 | 0.0013 ± 0.0002 ^{a,b} 0.0010 ± 0.0005 ^c | 0.0033 ± 0.0008 | 2.6 |

^a Average for three animals only.

^b One animal was omitted as values were >90% different from the other three.

^c Average for all four animals.

^d Pretreated with antibiotics (100 mg/kg of lincomycin and neomycin each day for 4 days).

Table 7

Total ^{14}C in Tissues 72 h After Oral Administration of 166 mg/kg
of [^{14}C]HCBD to Rats¹⁻⁴

| TISSUE | No. of Rats Averaged | ng-meq Capd per g Tiss | TEB | | % Dose in Total Tissue | |
|--------------------|----------------------|------------------------|------------------|---|------------------------|--|
| I.. BLOOD. | 4 | 17446 +/- 2149 | 1.000. | 0 | .668 +/- .132. | |
| II.. MAJOR TISSUES | | | | | | |
| SKIN: | | | | | | |
| Ear | 4 | 28075 +/- 4679 | 1.604 +/- .116 | | 2.954 +/- .547 | |
| Neck | 4 | 12625 +/- 1676 | .729 +/- .106 | | 1.147 +/- .206. | |
| Hindlegs | 4 | 9158 +/- 1594 | .524 +/- .044 | | .838 +/- .223. | |
| Skin AVG | 4 | 16619 +/- 2227 | .952 +/- .045 | | 1.513 +/- .302 | |
| MUSCLE: | | | | | | |
| Neck | 4 | 8803 +/- 900 | .508 +/- .061 | | 2.664 +/- .399 | |
| Abdomen | 4 | 11512 +/- 8370 | .633 +/- .383 | | 3.634 +/- 3.027 | |
| Hindleg | 4 | 8927 +/- 1452 | .517 +/- .102 | | 2.695 +/- .473. | |
| Muscle AVG | 4 | 9747 +/- 2898 | .552 +/- .104 | | 2.997 +/- 1.189. | |
| ADIPOSE | | | | | | |
| Kidney | 4 | 179873 +/- 73290 | 10.366 +/- 4.091 | | 10.685 +/- 3.823. | |
| Epididymal | 4 | 214388 +/- 58147 | 12.148 +/- 2.397 | | 13.046 +/- 4.159 | |
| Mesenteric | 4 | 172478 +/- 86840 | 9.689 +/- 3.859 | | 10.742 +/- 6.495. | |
| Adipose AVG | 4 | 188913 +/- 46123 | 10.734 +/- 1.856 | | 11.491 +/- 3.385 | |
| LIVER: | 4 | 78122 +/- 7076 | 4.498 +/- .319 | | 1.344 +/- .219. | |
| III. OTHER TISSUES | | | | | | |
| Kidneys | 4 | 94062 +/- 12671 | 5.531 +/- .679 | | .530 +/- .071. | |
| Bladder | 4 | 54009 +/- 29764 | 3.218 +/- 2.148 | | .013 +/- .005 | |
| Brain | 4 | 10767 +/- 2081 | .614 +/- .074 | | .038 +/- .010 | |

- 1.. All calculations are significant to 3 figures.
- 2.. TEB = Tissue:Blood Ratio.
3. Adipose, Skin and Muscle Averages are the average of the averages for each subject.
4. Original report Appendix has data from individual animals.

| | | | | | | | |
|---------------|--|---------------|----------|-----------|----------------------------|--------------|------------------------|
| STUDY ID: | H-1 | Length (hrs): | 72 | Route: | ORAL | Dose date: | 03-26-84 (MM-DD-YY) |
| SUBJECT ID'S: | R-1, R-2 R-3, & R-4 | # of Rats: | 4 | Species: | RAT | Avg. Wt. (g) | 267 +/- 10 |
| | | Strain: | F344 | Age: | 90 DAYS | | |
| AVG DOSE Amt: | 167 mg/kg +/- 13.2 44.5 mg Capd +/- 2.1 1.06e7 dpm +/- 4.94655e6 | Vehicle: | CORN OIL | Compound: | Hexachlorobutadiene (HCBD) | | |

Spec. Act: .2897 dpm/ng ^{14}C -Capd

Table 8

Total ^{14}C in Tissues 72 h After Oral Administration of 5.8 mg/kg
of [^{14}C]HCBd to Rats¹⁻⁴

| TISSUE | No. of Subjects Averaged | ng-eq Comp per g Tiss | TBR | | | % Dose in Total Tissue |
|--------------------|--------------------------------|-----------------------------|--------|-----|--------|------------------------------|
| I. BLOOD | 3 | 140 +/- 5 | 1.000 | +/- | 0 | .151 +/- .006 |
| II. MAJOR TISSUES | | | | | | |
| SKIN: | | | | | | |
| Ear | 3 | 451 +/- 41 | 3.222 | +/- | .174 | 1.157 +/- .126 |
| Neck | 3 | 189 +/- 55 | 1.348 | +/- | .355 | .485 +/- .146 |
| Hindpaws | 3 | 101 +/- 30 | .724 | +/- | .206 | .260 +/- .078 |
| Skin AVG | 3 | 247 +/- 39 | 1.764 | +/- | .226 | .634 +/- .108 |
| MUSCLE: | | | | | | |
| Neck | 3 | 130 +/- 17 | .927 | +/- | .091 | 1.110 +/- .160 |
| Abdomen | 3 | 104 +/- 23 | .740 | +/- | .162 | .855 +/- .200 |
| Hindleg | 3 | 136 +/- 19 | .978 | +/- | .172 | 1.162 +/- .144 |
| Muscle AVG | 3 | 123 +/- 1 | .882 | +/- | .031 | 1.052 +/- .026 |
| ADIPOSE | | | | | | |
| Kidney | 3 | 5272 +/- 2282 | 37.424 | +/- | 15.035 | 9.030 +/- 4.037 |
| Epididymal | 3 | 7564 +/- 836 | 53.967 | +/- | 3.891 | 12.931 +/- 1.657 |
| Mesenteric | 3 | 2791 +/- 1038 | 19.848 | +/- | 6.853 | 4.776 +/- 1.836 |
| Adipose AVG | 3 | 5209 +/- 1340 | 37.080 | +/- | 8.349 | 8.912 +/- 2.423 |
| LIVER: | 3 | 2083 +/- 171 | 14.872 | +/- | .655 | 1.131 +/- .190 |
| III. OTHER TISSUES | | | | | | |
| Kidneys | 3 | 10372 +/- 2396 | 73.775 | +/- | 14.166 | 1.199 +/- .227 |
| Bladder | 3 | 735 +/- 915 | 5.110 | +/- | 6.231 | .006 +/- .006 |
| Brain | 3 | 229 +/- 16 | 1.633 | +/- | .060 | .024 +/- .002 |

- All calculations are significant to 3 figures.
- TBR = Tissue:Blood Ratio
- Adipose, Skin and Muscle Averages are the average of the averages for each subject.
- Original report Appendix has data from individual animals.

| | | | | | | | |
|---------------|-------------------------------------|---------------|----------|-----------|----------------------------|--------------|-----------------------|
| STUDY ID: | H-2 | Length (hrs): | 72 | Route: | oral | Dose date: | 3-26-84 (MM-DD-YY) |
| SUBJECT ID'S: | R-6,R-7,R-8 | # of Subj: | 3 | Species: | RAT | Avg. Wt. (g) | 262 +/- 6 |
| | | Strain: | F344 | Age: | 96 DAYS | | |
| AVG DOSE Amt: | 5.81 mg/kg +/- .1 | Vehicle: | CORN OIL | Compound: | Hexachlorobutadiene (HCBd) | | |
| | 1.5 mg Compd +/- 0 | | | | | | |
| | 1.1033e7 dpm +/- 2.081666e5 | | | | | | |
| Spec. Act: | 7.199 dpm/ng ^{14}C -Compd | | | | | | |

Table 9

Total ^{14}C in Tissues 72 h After Oral Administration of 2.1 mg/kg
of [^{14}C]HCBd to Rats¹⁻⁴

| TISSUE | No. of Subjects Averaged | ng-mg Capd per g Tiss | TBR | % Dose1 in Total1 Tissue1 |
|--------------------|--------------------------|-----------------------|-------------------|---------------------------|
| I. BLOOD | 4 | 53 +/- 8 | 1.0001 +/- 0 | .156 +/- .021 |
| II. MAJOR TISSUES | | | | |
| SKIN: | | | | |
| Ear | 4 | 192 +/- 32 | 3.619 +/- .113 | 1.349 +/- .212 |
| Neck | 4 | 111 +/- 33 | 2.0671 +/- .436 | .776 +/- .226 |
| Hindpaws | 4 | 84 +/- 19 | 1.579 +/- .177 | .589 +/- .1251 |
| Skin AVG | 4 | 129 +/- 26 | 2.422 +/- .158 | .906 +/- .1721 |
| MUSCLE: | | | | |
| Neck | 4 | 54 +/- 8 | 1.031 +/- .150 | 1.271 +/- .197 |
| Abdomen | 4 | 73 +/- 31 | 1.358 +/- .409 | 1.712 +/- .689 |
| Hindleg | 4 | 36 +/- 10 | .669 +/- .115 | .835 +/- .2171 |
| Muscle AVG | 4 | 54 +/- 14 | 1.019 +/- .144 | 1.273 +/- .307 |
| ADIPOSE | | | | |
| Kidney | 4 | 3420 +/- 2865 | 65.640 +/- 58.903 | 15.993 +/- 13.3581 |
| Epididymal | 4 | 2256 +/- 889 | 41.565 +/- 11.409 | 10.556 +/- 4.0561 |
| Mesenteric | 4 | 1039 +/- 514 | 19.588 +/- 10.162 | 4.863 +/- 2.363 |
| Adipose AVG | 4 | 2238 +/- 1171 | 42.264 +/- 23.318 | 10.471 +/- 5.422 |
| LIVER: | 4 | 793 +/- 120 | 14.989 +/- .394 | 1.190 +/- .2141 |
| III. OTHER TISSUES | | | | |
| Kidneys | 4 | 3550 +/- 809 | 66.785 +/- 7.622 | 1.202 +/- .1881 |
| Bladder | 4 | 177 +/- 48 | 3.390 +/- 1.0071 | .004 +/- .002 |
| Brain | 4 | 102 +/- 18 | 1.926 +/- .134 | .029 +/- .006 |

1.1 All calculations are significant to 3 figures.1

2.1 TBR = Tissue:Blood Ratio1

3. Adipose, Skin and Muscle Averages are the average of the averages for each subject.1

4. Original report Appendix has data from individual animals.

| | | | |
|---|-------------------|--------------------------------------|---|
| STUDY ID: H-3 | Length (hrs): 72 | Route: ORAL | Dose date: 4-3-84 (MM-DD-YY) |
| SUBJECT ID'S: R-9, R-10 R-11, R-12 | # of Subj: 4 | Species: RAT Strain: F344 | Avg. Wt. (g) 268 +/- 3 Age: 103 DAYS |
| AVG DOSE Amt: 2 mg/kg +/- 0 .6 mg Capd +/- 0 1.0675e7 dwt1 +/- 2.21735e51 | Vehicle: CORN OIL | Compound: Hexachlorobutadiene (HCBd) | |
| Spec. Act: 18.7 dwt/ng ^{14}C -Capd1 | | | |

Table 10

Total ^{14}C in Tissues 72 h After Intravenous Administration of 1.8 mg/kg
of [^{14}C]HCBD to Rats¹⁻⁴

| TISSUE | No. of Subjects Averaged | ngm ⁺ Cpnd per g Tiss | TBR | | | % Dose [†] in Total [†] Tissue [†] |
|--------------------|--------------------------------|--|--------------------|-----|--------------------|---|
| I. BLOOD | 4 | 89 +/- 6 | 1.000 | +/- | 0 | .312 +/- .020 |
| II. MAJOR TISSUES | | | | | | |
| SKIN: | | | | | | |
| Ear | 4 | 196 +/- 5 | 2.197 [†] | +/- | .151 | 1.626 +/- .084 |
| Neck | 4 | 147 +/- 33 | 1.672 | +/- | .477 | 1.229 +/- .300 |
| Hindlegs | 4 | 97 +/- 33 | 1.100 | +/- | .430 | .803 +/- .264 |
| Skin AVG | 4 | 147 +/- 20 | 1.656 | +/- | .333 | 1.220 +/- .183 |
| MUSCLE: | | | | | | |
| Neck | 4 | 60 +/- 11 | .682 | +/- | .167 | 1.669 +/- .300 |
| Abdomen | 4 | 77 +/- 33 | .876 | +/- | .422 | 2.123 +/- .869 |
| Hindlegs | 4 | 56 +/- 18 | .699 | +/- | .261 | 1.605 +/- .476 |
| Muscle AVG | 4 | 65 +/- 21 | .739 | +/- | .274 | 1.799 +/- .561 |
| ADIPOSE | | | | | | |
| Kidney | 4 | 1476 +/- 402 | 16.773 | +/- | 5.484 | 8.203 +/- 2.337 |
| Epididymal | 4 | 2267 +/- 264 | 25.327 | +/- | 1.997 | 12.559 +/- 1.537 |
| Mesenteric | 4 | 740 +/- 430 | 8.521 | +/- | 5.353 [†] | 4.100 +/- 2.334 |
| Adipose AVG | 4 | 1495 +/- 238 | 16.874 | +/- | 3.571 | 8.267 +/- 1.388 |
| LIVER: | 4 | 868 +/- 74 | 9.713 | +/- | .730 | 1.512 +/- .101 |
| III. OTHER TISSUES | | | | | | |
| Kidneys | 4 | 4005 +/- 441 | 45.032 | +/- | 6.814 | 1.656 +/- .252 |
| Bladder | 4 | 260 +/- 116 | 2.934 | +/- | 1.439 | .004 +/- .002 |
| Brain | 4 | 105 +/- 7 | 1.181 | +/- | .084 | .032 +/- .003 |

- All calculations are significant to 3 figures.
- TBR = Tissue:Blood Ratio
- † Adipose: Skin and Muscle Averages are the average of the averages for each subject.
- Original report Appendix has data from individual animals.

| | | | | | | | |
|---------------|--|---------------|-------|-----------|----------------------------|--------------|----------------------|
| STUDY ID: | H-4 | Length (hrs): | 72 | Route: | IV | Dose date: | 4-3-84 (MM-DD-YY) |
| SUBJECT ID'S: | R-13,R-14 R-15,R-16 | # of Subj: | 4 | Species: | RAT | Avg. Wt. (g) | 278 +/- 1 |
| | | Strain: | F344 | Age: | 103 DAYS | | |
| AVG DOSE Amt: | 2 mg/kg +/- .1 .5 mg Cpnd +/- 0 6.925e6 dpm +/- 2.200757e5 | Vehicle: | SERUM | Compound: | Hexachlorobutadiene (HCBD) | | |
| Spec. Act: | 13.8 dpm/ng ^{14}C -Cpnd | | | | | | MASTER2 |

Table 11

Total ^{14}C in Tissues 240 h After Intravenous Administration of 0.58 mg/kg
of [^{14}C]HCBD to Rats¹⁻⁴

| TISSUE | No. of Subjects Averaged | ng-meq Capd per g Tiss | TBR | | | % Dose in Total Tissue | | |
|--------------------|--------------------------------|------------------------------|--------|-----|-------|------------------------------|-----|------|
| I. BLOOD | 4 | 8 +/- 1 | 1.000 | +/- | 0 | .070 | +/- | .010 |
| II. MAJOR TISSUES | | | | | | | | |
| SKIN: | | | | | | | | |
| Ear | 4 | 8 +/- 1 | 1.006 | +/- | .074 | .215 | +/- | .027 |
| Neck | 4 | 7 +/- 0 | .808 | +/- | .072 | .171 | +/- | .012 |
| Hindfeet | 4 | 5 +/- 1 | .584 | +/- | .051 | .124 | +/- | .012 |
| Skin AVG | 4 | 7 +/- 1 | .799 | +/- | .039 | .170 | +/- | .012 |
| MUSCLE: | | | | | | | | |
| Neck | 4 | 5 +/- 1 | .574 | +/- | .079 | .405 | +/- | .046 |
| Abdomen | 4 | 4 +/- 1 | .514 | +/- | .120 | .368 | +/- | .109 |
| Hindleg | 4 | 5 +/- 1 | .400 | +/- | .104 | .432 | +/- | .112 |
| Muscle AVG | 4 | 5 +/- 1 | .563 | +/- | .054 | .402 | +/- | .073 |
| ADIPOSE | | | | | | | | |
| Kidney | 4 | 19 +/- 3 | 2.284 | +/- | .309 | .324 | +/- | .054 |
| Epididyma | 4 | 22 +/- 9 | 2.562 | +/- | .761 | .373 | +/- | .147 |
| Mesenteric | 4 | 16 +/- 4 | 1.961 | +/- | .339 | .281 | +/- | .070 |
| Adipose AVG | 4 | 19 +/- 5 | 2.269 | +/- | .401 | .326 | +/- | .088 |
| LIVER: | 4 | 67 +/- 5 | 8.166 | +/- | .642 | .465 | +/- | .044 |
| III. OTHER TISSUES | | | | | | | | |
| Kidneys | 4 | 347 +/- 42 | 42.101 | +/- | 2.707 | .476 | +/- | .063 |
| Bladder | 4 | 6 +/- 2 | .784 | +/- | .197 | .001 | +/- | 0 |
| Brain | 4 | 8 +/- 1 | .929 | +/- | .081 | .010 | +/- | .001 |

1.. All calculations are significant to 3 figures.

2.. TBR = Tissue:Blood Ratio

3.. Adipose, Skin and Muscle Averages are the average of the averages for each subject.

4.. Original report Appendix has data from individual animals.

| | | | |
|---|-------------------|--------------------------------------|--|
| STUDY ID: HCB-5 | Length (hrs): 240 | Route: IV | Dose date: 05-01-84 (MM-DD-YY) |
| SUBJECT ID'S: R17,R18 R19,R20 | # of Subj: 4 | Species: RAT Strain: F344 | Aug. Wt. (g) 223 +/- 1 Age: 95 DAYS |
| AVG DOSE Amt: 1 mg/kg +/- 0 .1 mg Capd +/- 0 9.8375e6 dpm +/- 1.49772e5 | Vehicle: SERUM | Compound: Hexachlorobutadiene (HCBD) | |
| Spec. Act: 76.2 dpm/mg ^{14}C -Capd | | | |

Table 12

Total ^{14}C in Tissues 240 h After Oral Administration of 0.70 mg/kg
of [^{14}C]HCBd to Rats¹⁻⁴

| TISSUE | No. of Subjects Averaged | ngmgs Caps per g Tiss | TBR | | | % Dose in Total Tissue | | |
|--------------------|--------------------------------|-----------------------------|--------|-----|-------|------------------------------|-----|-------|
| I. BLOOD | 4 | 9 +/- 1 | 1.000 | +/- | 0 | .076 | +/- | .0071 |
| II. MAJOR TISSUES | | | | | | | | |
| SKIN: | | | | | | | | |
| Ear | 4 | 7 +/- 1 | .805 | +/- | .143 | .145 | +/- | .018 |
| Neck | 4 | 6 +/- 1 | .708 | +/- | .166 | .127 | +/- | .020 |
| Hindlegs | 4 | 4 +/- 1 | .519 | +/- | .133 | .073 | +/- | .018 |
| Skin AVG | 4 | 6 +/- 1 | .677 | +/- | .141 | .121 | +/- | .017 |
| MUSCLE: | | | | | | | | |
| Neck | 4 | 4 +/- 1 | .506 | +/- | .147 | .300 | +/- | .070 |
| Abdomen | 4 | 4 +/- 0 | .509 | +/- | .008 | .308 | +/- | .030 |
| Hindleg | 4 | 5 +/- 1 | .543 | +/- | .133 | .323 | +/- | .056 |
| Muscle AVG | 4 | 4 +/- 1 | .519 | +/- | .093 | .311 | +/- | .032 |
| ADIPOSE | | | | | | | | |
| Kidney | 4 | 14 +/- 4 | 1.686 | +/- | .503 | .206 | +/- | .068 |
| Epididymal | 4 | 27 +/- 6 | 3.261 | +/- | 1.060 | .390 | +/- | .111 |
| Mesenteric | 4 | 14 +/- 2 | 1.720 | +/- | .403 | .206 | +/- | .039 |
| Adipose AVG | 4 | 19 +/- 3 | 2.223 | +/- | .572 | .267 | +/- | .061 |
| LIVER: | 4 | 88 +/- 8 | 10.353 | +/- | 1.073 | .481 | +/- | .063 |
| III. OTHER TISSUES | | | | | | | | |
| Kidneys | 4 | 409 +/- 24 | 48.519 | +/- | 6.799 | .474 | +/- | .068 |
| Bladder | 4 | 8 +/- 5 | .949 | +/- | .476 | .001 | +/- | 0 |
| Brain | 4 | 8 +/- 1 | .997 | +/- | .152 | .008 | +/- | .0011 |

1.1 All calculations are significant to 3 figures.

2.1 TBR = Tissue:Blood Ratio

3.1 Adipose, Skin and Muscle Averages are the average of the averages for each subject.1

4.1 Original report Appendix has data from individual animals.

| | | | | | | | |
|---------------|--|---------------|----------|-----------|----------------------------|--------------|------------------------|
| STUDY ID: | HCBd-6 | Length (hrs): | 240 | Route: | ORAL | Dose date: | 05-01-84 (MM-DD-YY) |
| SUBJECT ID'S: | R-21, R-22 R-23, R-24 | # of Subj: | 4 | Species: | RAT | Avg. Wt. (g) | 228 +/- 1 |
| | | Strain: | F344 | Age: | 95 DAYS | | |
| AVG DOSE Amt: | 1 mg/kg +/- .1 .2 mg Caps +/- 0 1.175e7 cps +/- 1.170114e6 | Vehicle: | CORN OIL | Compound: | Hexachlorobutadiene (HCBd) | | |
| Spec. Act: | 73.41dpm/mg ^{14}C -Caps | | | | | | |

Table 13

Total ^{14}C in Tissues 240 h After Intravenous Administration of 27 mg/kg
of [^{14}C]HCB₂D to Rats¹⁻⁴

| TISSUE | No. of Subjects Averaged | ng-req Capd per g Tiss | TBR | | | % Dose in Total Tissue | |
|--------------------|--------------------------------|------------------------------|--------|-----|--------|------------------------------|----------|
| I. BLOOD | 4 | 772 +/- 41 | 1.000 | +/- | 0 | .179 | +/- .010 |
| II. MAJOR TISSUES | | | | | | | |
| SKIN: | | | | | | | |
| Ear | 4 | 367 +/- 36 | .475 | +/- | .030 | .203 | +/- .021 |
| Neck | 4 | 256 +/- 25 | .331 | +/- | .025 | .141 | +/- .014 |
| Hindqtrs | 4 | 186 +/- 50 | .239 | +/- | .055 | .103 | +/- .028 |
| Skin AVG | 4 | 270 +/- 29 | .349 | +/- | .022 | .149 | +/- .017 |
| MUSCLE: | | | | | | | |
| Neck | 4 | 217 +/- 20 | .283 | +/- | .035 | .400 | +/- .037 |
| Abdomen | 4 | 198 +/- 9 | .257 | +/- | .014 | .365 | +/- .017 |
| Hindleg | 4 | 165 +/- 45 | .213 | +/- | .051 | .305 | +/- .084 |
| Muscle AVG | 4 | 194 +/- 9 | .251 | +/- | .004 | .357 | +/- .019 |
| ADIPOSE | | | | | | | |
| Kidney | 4 | 612 +/- 145 | .791 | +/- | .174 | .226 | +/- .055 |
| Epididymal | 4 | 1323 +/- 460 | 1.726 | +/- | .641 | .489 | +/- .179 |
| Mesenteric | 4 | 519 +/- 60 | .673 | +/- | .077 | .191 | +/- .025 |
| Adipose AVG | 4 | 818 +/- 199 | 1.064 | +/- | .276 | .302 | +/- .075 |
| LIVER: | 4 | 2158 +/- 78 | 2.801 | +/- | .127 | .284 | +/- .020 |
| III. OTHER TISSUES | | | | | | | |
| Kidneys | 4 | 11075 +/- 1511 | 14.375 | +/- | 1.977 | .308 | +/- .015 |
| Bladder | 4 | 5325 +/- 10208 | 6.703 | +/- | 12.625 | .014 | +/- .026 |
| Brain | 4 | 445 +/- 38 | .604 | +/- | .068 | .011 | +/- .001 |

1.1 All calculations are significant to 3 figures.

2.1 TBR = Tissue:Blood Ratio

3.1 Adipose, Skin and Muscle Averages are the average of the averages for each subject.

4.1 Original report Appendix has data from individual animals.

| | | | | | | | |
|---------------|---|---------------|-------|-----------|----------------------------|--------------|------------------------|
| STUDY ID: | HCB2-7 | Length (hrs): | 240 | Route: | IV | Dose date: | 06-11-84 (MM-DD-YY) |
| SUBJECT ID'S: | R-25, R-26 R-27, R-28 | # of Subj: | 4 | Species: | RAT | Avg. Wt. (g) | 247 +/- 2 |
| | | Strain: | F344 | Age: | 100 DAYS | | |
| AVG DOSE Amt: | 27 mg/kg +/- .5 6.8 mg Capd +/- .1 1.0113e7 dpm +/- 1.18145e5 | Vehicle: | SERUM | Compound: | Menzchlorobutadiene (HCB2) | | |
| Spec. Act: | 1.511dpm/ng ^{14}C -Capd | | | | | | |

Table 14

Total ^{14}C in Tissues 240 h After Oral Administration of 34 mg/kg
of [^{14}C]HCBd to Rats¹⁻⁴

| TISSUE | No. of Subjects Averaged | ng-mg Capd per g Tiss | TBR | | | % Dose in Total Tissue | |
|--------------------|--------------------------------|-----------------------------|--------|-----|-------|------------------------------|----------|
| I. BLOOD | 4 | 288 +/- 71 | 1.000 | +/- | 0 | .053 | +/- .012 |
| II. MAJOR TISSUES | | | | | | | |
| SKIN: | | | | | | | |
| Ear | 4 | 267 +/- 75 | .925 | +/- | .082 | .118 | +/- .031 |
| Neck | 4 | 220 +/- 47 | .775 | +/- | .260 | .097 | +/- .020 |
| Hindqtrs | 4 | 165 +/- 52 | .572 | +/- | .088 | .073 | +/- .022 |
| Skin AVG | 4 | 218 +/- 50 | .764 | +/- | .104 | .096 | +/- .021 |
| MUSCLE: | | | | | | | |
| Neck | 4 | 191 +/- 46 | .666 | +/- | .059 | .281 | +/- .064 |
| Abdomen | 4 | 174 +/- 44 | .605 | +/- | .044 | .256 | +/- .061 |
| Hindleg | 4 | 202 +/- 110 | .686 | +/- | .255 | .296 | +/- .157 |
| Muscle AVG | 4 | 189 +/- 65 | .652 | +/- | .111 | .277 | +/- .091 |
| ADIPOSE | | | | | | | |
| Kidney | 4 | 600 +/- 329 | 2.004 | +/- | .610 | .176 | +/- .093 |
| Epididymal | 4 | 1803 +/- 1499 | 5.895 | +/- | 3.492 | .527 | +/- .429 |
| Peritoneic | 4 | 480 +/- 210 | 1.627 | +/- | .342 | .141 | +/- .059 |
| Adipose AVG | 4 | 961 +/- 675 | 3.175 | +/- | 1.475 | .281 | +/- .193 |
| LIVER: | 4 | 2061 +/- 662 | 7.125 | +/- | 1.157 | .238 | +/- .061 |
| III. OTHER TISSUES | | | | | | | |
| Kidneys | 4 | 12388 +/- 2835 | 43.164 | +/- | 3.655 | .274 | +/- .065 |
| Bladder | 4 | 285 +/- 226 | .916 | +/- | .497 | .001 | +/- 0 |
| Brain | 4 | 335 +/- 82 | 1.165 | +/- | .128 | .007 | +/- .002 |

- All calculations are significant to 3 figures.
- TBR = Tissue:Blood Ratio
- Adipose, Skin and Muscle Averages are the average of the averages for each subject.
- Original report Appendix has data from individual animals.

| | | | | | | | |
|---------------|---|---------------|----------|-----------|-----------------------------|--------------|------------------------|
| STUDY ID: | HCBDE | Length (hrs): | 240 | Route: | ORAL | Dose date: | 06-11-84 (MM-DD-YY) |
| SUBJECT ID'S: | R-29, R-30 R-31, R-32 | # of Subj: | 4 | Species: | RAT | Avg. Wt. (g) | 252 +/- 1 |
| | | Strain: | F344 | Age: | 100 DAYS | | |
| AVG DOSE Amt: | 34 mg/kg +/- .4 8.5 mg Capd +/- 0 1.145e7 dpm +/- 1.73251e5 | Vehicle: | CORN OIL | Compound: | Hexachlorobutadiene (HCBd). | | |
| Spec. Act: | 1.34 dpm/ng ^{14}C -Capd. | | | | | | MASTER2 |

Table 15

Total ^{14}C in Tissues 72 h After Oral Administration of 166 mg/kg
of [^{14}C]HCB₂D to Rats Pretreated with Antibiotics¹⁻⁴

| TISSUE | No. of Subjects Averaged | ng- ¹⁴ C Capd per g Tiss | TBR | | | % Dose in Total Tissue |
|----------------------|--------------------------------|--|--------|------------------|-------|------------------------------|
| I. BLOOD | 4 | 18254 +/- 4368 | 1.000 | +/- | 0 | .692 +/- .155 |
| II. MAJOR TISSUES | | | | | | |
| SKIN: | | | | | | |
| Ear | 4 | 32134 +/- 8273 | 1.768 | +/- | .232 | 2.906 +/- .7231 |
| Neck | 4 | 17263 +/- 6398 | .907 | +/- | .273 | 1.555 +/- ¹ .746 |
| Hindqtrs | 4 | 10514 +/- 2670 | .575 | +/- | .025 | .9491 +/- .229 |
| Skin AVG | 4 | 19970 +/- 6063 | 1.084 | +/- | .104 | 1.803 +/- .925 |
| MUSCLE: | | | | | | |
| Neck | 4 | 11545 +/- 5041 | .617 | +/- | .145 | 3.472 +/- 1.471 |
| Abdomen | 4 | 9040 +/- 3368 | .491 | +/- ¹ | .119 | 2.729 +/- 1.004 |
| Hindleg | 4 | 11209 +/- 4514 | .595 | +/- | .111 | 3.365 +/- ¹ 1.318 |
| Muscle AVG | 4 | 10598 +/- 4362 | .567 | +/- | .098 | 3.189 +/- 1.187 |
| ADIPOSE | | | | | | |
| Kidney | 4 | 228947 +/- 76318 | 12.681 | +/- | 3.668 | 13.844 +/- 4.592 |
| Epididymal | 4 | 254998 +/- 58094 | 14.295 | +/- | 3.478 | 15.417 +/- 3.567 |
| Mesenteric | 4 | 184618 +/- 71896 | 9.9541 | +/- | 1.645 | 11.208 +/- 4.156 |
| Adipose AVG | 4 | 223521 +/- 64274 | 12.310 | +/- | 2.282 | 13.487 +/- 3.786 |
| LIVER: | 4 | 81352 +/- 16442 | 4.494 | +/- | .266 | 1.469 +/- .246 |
| III. OTHER TISSUES | | | | | | |
| Kidneys ¹ | 4 | 95576 +/- 8229 | 5.428 | +/- | 1.121 | .637 +/- .040 |
| Bladder | 4 | 23926 +/- 7523 | 1.361 | +/- | .537 | .006 +/- ¹ .001 |
| Brain | 4 | 9200 +/- 1755 | .514 | +/- | .086 | .033 +/- .009 |

1.1 All calculations are significant to 3 figures.1

2.1 TBR = Tissue:Blood Ratio

3. Adipose: Skin and Muscle Averages are the average of the averages for each subject.1

4. Original report Appendix has data from individual animals.

| | | | | | | | |
|---------------|---|---------------|----------|--------------|--|------------|------------------------|
| STUDY ID: | HCB ₂ D-9 | Length (hrs): | 72 | Route: | ORAL;ANTB | Dose date: | 08-20-84 (MM-DD-YY) |
| SUBJECT ID'S: | R-33;R-34;R-35 # of Subj: 4 R-36 | Species: | RAT | Avg. Wt. (g) | 2421 +/- 4 | Age: | 90 DAYS |
| AUG DOSE Amt: | 166 mg/kg +/- 6.3 38.6 mg Capd +/- 1.1 1.0255e7 dpm +/- 2.424184e51 | Vehicle: | CORN OIL | Compound: | Hexachlorobutadiene (HCB ₂ D) | | |
| Spec. Act: | .254 dpm/ng ¹⁴ C-Capd | | | | | | |

Table 16

Total ^{14}C in Tissues 240 h After Intravenous Administration of 1.86 mg/kg of [^{14}C]HCBd to Rats Pretreated with Antibiotics¹⁻⁴

| TISSUE | No. of Subjects Averaged | ngms Capd per g Tiss | TBR | % Dose in Total Tissue |
|-------------------|--------------------------|----------------------|------------------|------------------------|
| I. BLOOD | 4 | 149 +/- 6 | 1.000 +/- 0 | .507 +/- .016 |
| II. MAJOR TISSUE | | | | |
| SKIN: | | | | |
| Ear | 4 | 226 +/- 28 | 1.515 +/- .183 | 1.827 +/- .183 |
| Neck | 4 | 169 +/- 8 | .994 +/- .064 | 1.222 +/- .075 |
| Forelimbs | 4 | 105 +/- 8 | .704 +/- .064 | .849 +/- .052 |
| Skin AVG | 4 | 160 +/- 11 | 1.071 +/- .068 | 1.293 +/- .054 |
| MUSCLE: | | | | |
| Neck | 4 | 81 +/- 13 | .545 +/- .089 | 2.191 +/- .327 |
| Abdomen | 4 | 62 +/- 12 | .415 +/- .081 | 1.673 +/- .334 |
| Hindlimb | 4 | 65 +/- 11 | .433 +/- .075 | 1.740 +/- .256 |
| Muscle AVG | 4 | 69 +/- 6 | .465 +/- .039 | 1.848 +/- .109 |
| ADIPOSE | | | | |
| Kidney | 4 | 1041 +/- 161 | 6.979 +/- 1.152 | 5.601 +/- .758 |
| Epididymus | 4 | 1845 +/- 160 | 12.394 +/- 1.533 | 9.954 +/- .975 |
| Mesenteric | 4 | 614 +/- 65 | 4.112 +/- .639 | 3.306 +/- .305 |
| Adipose AVG | 4 | 1167 +/- 102 | 7.828 +/- .890 | 6.287 +/- .506 |
| LIVER: | 4 | 915 +/- 57 | 6.143 +/- .654 | 1.957 +/- .134 |
| III. OTHER TISSUE | | | | |
| Kidneys | 4 | 3741 +/- 403 | 25.079 +/- 3.213 | 1.754 +/- .130 |
| Bladder | 4 | 252 +/- 106 | 1.913 +/- .769 | .010 +/- .005 |
| Spleen | 4 | 130 +/- 17 | .868 +/- .116 | .034 +/- .002 |

- All calculations are significant to 3 figures.
- TBR = Tissue:Blood Ratio
- Adipose, Skin and Muscle Averages are the average of the averages for each subject.
- Original report Appendix has data from individual animals.

| | | | | | | | |
|---------------|------------------------------------|---------------|-----------|-----------|---------------------------|--------------|------------------------|
| STUDY ID: | HR-1 | Length (hrs): | 240 | Route: | IV | Dose date: | 05-14-84 (19-00-YY) |
| SUBJECT ID'S: | A243, A247 A249, A246 | # of Subj: | 4 | Species: | RA7 | Avg. Wt. (g) | 213 +/- 6 |
| | | Strain: | F344 | Age: | 88 DAYS | | |
| AVG DOSE Act: | 2 mg/kg +/- .1 .4 mg Capd +/- 0 | Vehicle: | 10XPG/SEF | Compound: | Hexachlorobutadiene (HCB) | | |
| | 5.323e6 dpm +/- 1.203E13e5 | | | | | | |
| Spec. Act: | 13.5 dpm/ng ^{14}C -Capd | | | | | | |

Table 17

Total ^{14}C Found in the GI Tract After Administration of ^{14}C -HCBP (% Dose \pm S.D.)^a to Rats

| Organ | Dose (mg/kg): Route: Sacrifice Time (days): | 166 Oral ^c 3 | 166 Oral 3 | 34 Oral 10 | 5.8 Oral 3 | 2.1 Oral 3 | 0.70 Oral 10 | 27 IV 3 | 1.8 IV 3 | 1.9 ^b IV 3 | 0.58 IV 10 |
|-------------------------|---|-------------------------------|------------------|-------------------|------------------|------------------|--------------------|-------------------|-----------------|-----------------------------|--------------------|
| Stomach | | | | | | | | | | | |
| Tissue | | 0.698 \pm 0.24 | - | 0.002 \pm 0.001 | - | - | 0.004 \pm 0.0005 | 0.003 \pm 0.000 | - | 0.04 \pm 0.01 | 0.0005 \pm 0.001 |
| Contents | | 11.2 \pm 7.8 | - | 0.001 \pm 0.001 | - | - | 0.002 \pm 0.003 | 0.004 \pm 0.003 | - | - | 0.002 \pm 0.0006 |
| Tissue + Contents | | - | 7.42 \pm 4.27 | - | 1.01 \pm 1.66 | 0.09 \pm 0.04 | - | - | 0.06 \pm 0.01 | - | - |
| Cecum | | | | | | | | | | | |
| Tissue | | 2.00 \pm 0.53 | - | 0.003 \pm 0.001 | - | - | 0.004 \pm 0.0005 | 0.003 \pm 0.001 | - | 0.12 \pm 0.03 | 0.005 \pm 0.0006 |
| Contents | | 31.0 \pm 7.4 | - | 0.02 \pm 0.01 | - | - | 0.03 \pm 0.02 | 0.02 \pm 0.01 | - | - | 0.03 \pm 0.005 |
| Tissue + Contents | | - | 35.8 \pm 12.4 | - | 1.04 \pm 0.33 | 1.02 \pm 0.25 | - | - | 0.95 \pm 0.12 | - | - |
| Small Intestines | | | | | | | | | | | |
| Tissue | | 1.50 \pm 0.22 | - | 0.006 \pm 0.002 | - | - | 0.02 \pm 0.005 | 0.008 \pm 0.002 | - | 0.12 \pm 0.01 | 0.02 \pm 0.005 |
| Contents | | 1.47 \pm 0.76 | - | 0.01 \pm 0.00 | - | - | 0.02 \pm 0.006 | 0.009 \pm 0.00 | - | - | 0.02 \pm 0.00 |
| Tissue + Contents | | - | 3.75 \pm 1.77 | - | 0.49 \pm 0.14 | 0.45 \pm 0.10 | - | - | 0.51 \pm 0.08 | - | - |
| Large Intestines | | | | | | | | | | | |
| Tissue | | 0.802 \pm 0.22 | - | 0.004 \pm 0.002 | - | - | 0.007 \pm 0.002 | 0.007 \pm 0.002 | - | 0.08 \pm 0.03 | 0.007 \pm 0.003 |
| Contents | | 2.89 \pm 1.1 | - | 0.01 \pm 0.01 | - | - | 0.01 \pm 0.005 | 0.008 \pm 0.002 | - | - | 0.03 \pm 0.005 |
| Tissue + Contents | | - | 4.37 \pm 4.38 | - | 0.25 \pm 0.77 | 0.33 \pm 0.05 | - | - | 0.37 \pm 0.10 | - | - |

^a Data for individual animals are in the original report Appendix.^b Animals were treated by oral gavage with ampicillin at 200 mg/kg daily for four days prior to HCBP dosing.^c Animals were pretreated with lincomycin and neomycin at 100 mg/kg daily for four days prior to dosing with HCBP.

Table 18. Cumulative Excretion of Total ^{14}C After Oral Administration of ^{14}C -HCBD to B6C3F1, Male Mice (% Dose)

| Dose (mg/kg) | 2.0 ^b | | | | 24 ^c | | | | 50 ^c | | | | |
|--------------|------------------|------------------------------------|--|--------------------|-----------------|-------------|------------------------------------|--------------------|-----------------|------------------------|------------------------------------|--------------------------|--------------------------|
| | Urine | Breath ^e (volatiles) | Breath ^e (CO ₂) ₂ | Feces ^f | Total | Urine | Breath ^e (volatiles) | Feces ^f | Total | Urine | Breath ^e (volatiles) | Feces ^f | Total |
| 0-6 | 11.2 ± 2.8 | | | | 11.2 ± 2.8 | 5.2 ± 2.0 | | | 5.2 ± 2.0 | 0.8 ± 0.3 | | | 0.8 ± 0.3 |
| 6-122 | 21.0 ± 4.2 | 5.2 ± 1.4 | 1.8 ± 0.1 | | 28.0 ± 3.2 | 12.1 ± 0.52 | 6.3 ± 1.0 | | 18.4 ± 1.4 | 1.6 ± 0.1 | 6.2 ± 1.2 | | 7.7 ± 1.2 |
| 12-24 | 25.8 ± 4.6 | 7.3 ± 2.1 | 2.4 ± 0.3 | 45.3 ± 2.2 | 80.8 ± 2.3 | 15.5 ± 0.4 | 9.0 ± 0.5 | 40.2 ± 2.6 | 65.0 ± 2.9 | 2.0 ± 0.2 | 8.8 ± 1.6 | 18.4 ± 8.2 | 29.2 ± 8.7 |
| 24-302 | 27.9 ± 4.8 | 7.8 ± 2.2 | 2.5 ± 0.4 | | 83.5 ± 3.1 | 16.3 ± 0.6 | 9.8 ± 0.4 | | 66.2 ± 2.7 | 2.2 ± 0.2 | 9.9 ± 2.2 | | 30.4 ± 8.8 |
| 30-482 | 29.2 ± 4.8 | 8.0 ± 2.3 | 2.6 ± 0.4 | 49.1 ± 1.8 | 88.9 ± 3.4 | 17.3 ± 1.1 | 10.2 ± 0.3 | 48.1 ± 5.2 | 75.6 ± 6.0 | 2.4 ± 0.2 | 10.8 ± 2.3 | 27.6 ± 12.1 | 40.8 ± 12.9 |
| 48-542 | 29.8 ± 4.9 | | | | 89.4 ± 3.5 | 17.6 ± 1.2 | | | 75.9 ± 6.12 | 2.5 ± 0.2 | | | 40.9 ± 12.9 |
| 54-722 | 30.2 ± 4.9 | | | 49.7 ± 1.7 | 90.4 ± 3.52 | 17.9 ± 1.2 | | 49.1 ± 5.52 | 77.1 ± 6.62 | 2.7 ± 0.4 | | 28.0 ± 12.3 | 41.8 ± 13.2 |
| 72-962 | 30.5 ± 5.0 | | | 50.3 ± 1.8 | 91.4 ± 3.32 | 18.2 ± 1.2 | | 50.0 ± 5.52 | 78.3 ± 6.42 | 3.6 ± 0.2 ^d | | 30.2 ± 20.3 ^d | 44.4 ± 19.4 ^d |
| 96-1202 | 30.7 ± 5.0 | | | 50.6 ± 1.8 | 91.9 ± 3.4 | 18.9 ± 1.6 | | 50.9 ± 5.12 | 79.9 ± 6.3 | 4.0 ± 0.2 ^d | | 32.2 ± 22.0 ^d | 46.7 ± 21.5 ^d |
| 120-144 | 30.9 ± 5.0 | | | 50.8 ± 1.8 | 92.2 ± 3.4 | 19.2 ± 1.5 | | 51.4 ± 5.12 | 80.8 ± 6.2 | 4.4 ± 0.5 ^d | | 32.7 ± 21.8 ^d | 47.6 ± 21.3 ^d |
| 144-1682 | 31.0 ± 5.0 | | | 51.0 ± 1.8 | 92.5 ± 3.3 | 19.5 ± 1.5 | | 52.0 ± 5.22 | 81.6 ± 6.3 | 4.7 ± 0.4 ^d | | 33.5 ± 21.3 ^d | 48.8 ± 20.8 ^d |
| 168-1922 | 31.1 ± 5.0 | | | 51.1 ± 1.8 | 92.8 ± 3.42 | 19.7 ± 1.5 | | 52.3 ± 5.22 | 82.1 ± 6.2 | 5.0 ± 0.6 ^d | | 34.5 ± 21.5 ^d | 50.1 ± 21.1 ^d |
| 192-2162 | 31.2 ± 5.0 | | | 51.3 ± 1.7 | 93.0 ± 3.3 | 19.9 ± 1.5 | | 52.5 ± 5.22 | 82.6 ± 6.3 | 5.2 ± 0.7 ^d | | 34.8 ± 21.6 ^d | 50.6 ± 21.3 ^d |
| 216-2402 | 31.3 ± 5.0 | | | 51.4 ± 1.6 | 93.3 ± 3.4 | 20.1 ± 1.5 | | 52.6 ± 5.22 | 82.9 ± 6.3 | 5.4 ± 0.8 ^d | | 35.1 ± 21.5 ^d | 51.2 ± 21.3 ^d |

^a See original report Appendix for data from individual mouse units.

^b Values are averages ± S.D. for four mouse units. Each mouse unit contained 3 mice, except where

^c Values are averages ± S.D. for four mouse units. However, since individual mice were dying at various times during the experiment, percent dose excreted was calculated from dpm excreted by remaining mice divided by the dose given to remaining mice.

^d Values are averages ± range for two mouse units. One mouse unit contained two mice; the other unit contained one mouse.

^e Breath samples were collected through 48 hrs only. First breath collection was 0-12 hrs.

^f Feces collection was in 24-hr intervals.

Table 19

Cumulative Excretion of Total ^{14}C After IV Administration of
19 mg/kg ^{14}C -HCBD to B6C3F1 Male Mice (% Dose)^a

| Time (hr) | Urine | Breath ^c | Feces ^d | Total |
|-----------|-------------------------|---------------------|-------------------------|-------------------------|
| 0-6 | 11.0 ± 1.4 | | | 11.0 ± 1.4 |
| 6-12 | 18.0 ± 1.0 | 7.0 ± 0.9 | | 25.0 ± 0.8 |
| 12-24 | 23.2 ± 0.9 | 9.4 ± 1.0 | 41.4 ± 3.4 | 74.0 ± 3.1 |
| 24-30 | 24.5 ± 1.2 | 10.0 ± 1.0 | | 75.9 ± 2.9 |
| 30-48 | 25.6 ± 1.4 | 10.4 ± 1.0 | 48.8 ± 0.8 | 84.8 ± 2.2 |
| 48-54 | 25.8 ± 1.5 | | | 85.2 ± 2.2 |
| 54-72 | 26.2 ± 1.5 | | 50.2 ± 1.0 | 86.9 ± 2.4 |
| 72-96 | 26.6 ± 1.6 | | 50.8 ± 1.0 | 87.8 ± 2.5 |
| 96-120 | 26.8 ± 1.6 | | 51.2 ± 1.0 | 88.4 ± 2.5 |
| 120-144 | 27.0 ± 1.6 | | 51.4 ± 0.9 | 88.8 ± 2.6 |
| 144-168 | 27.1 ± 1.7 ^b | | 51.6 ± 0.9 ^b | 89.2 ± 2.6 ^b |
| 168-192 | 27.3 ± 1.8 ^b | | 51.8 ± 0.9 ^b | 89.6 ± 2.6 ^b |
| 192-216 | 27.4 ± 1.8 ^b | | 51.9 ± 0.9 ^b | 89.7 ± 2.6 ^b |
| 216-240 | 27.6 ± 1.8 ^b | | 52.1 ± 0.9 ^b | 90.1 ± 2.5 ^b |

^aValues are averages ± S.D. for four mouse units. Each mouse unit contained 3 mice, except where noted. See original report Appendix for data from individual mouse units.

^bValues are averages ± S.D. for four mouse units. Three mouse units contained 3 mice; one mouse unit contained 2 mice.

^cBreath samples were collected through 48 hrs only. First breath collection was 0-12 hrs.

^dFeces collection was in 24-hr intervals.

Table 20. Average Percent Dose Excreted as ^{14}C -HCBD in Urine of B6C3F1 Male Mice After Administration of ^{14}C -HCBD

| Route | Dose | Time | % ^{14}C -HCBD in Urine Composite | Avg. % Dose Excreted | Avg. % Dose Excreted as ^{14}C -HCBD |
|-------|----------|---------|--|----------------------------|---|
| IV | 19 mg/kg | 0-6 hr | 24.2 | 11.0 \pm 1.4 | 2.66 |
| | | 6-12 hr | 20.5 | 6.97 \pm 1.2 | 1.43 |
| Oral | 2 mg/kg | 0-6 hr | 10.7 | 11.2 \pm 2.8 | 0.120 |
| | | 6-12 hr | 7.03 | 9.81 \pm 1.6 | 0.690 |
| Oral | 24 mg/kg | 0-6 hr | 23.6 | 5.20 \pm 2.0 | 1.23 |
| | | 6-12 hr | 21.0 | 6.88 \pm 1.6 | 1.44 |
| Oral | 50 mg/kg | 0-6 hr | 22.3 | 0.800 \pm 0.30 | 0.130 |
| | | 6-12 hr | 19.7 | 0.778 \pm 0.26 | 0.150 |

Table 21

Concentration of ^{14}C in B6C3F1 Mouse Tissues Ten Days After Oral
Administration of 2.0 mg [^{14}C]HCBd/kg^a

| Tissue | ng-eq HCBd per g tissue | TBR ^b | % Dose |
|-------------------------|-------------------------------|------------------|--------------------------|
| <u>Major Tissues</u> | | | |
| Blood | 31.2 ± 13.7 | 1.0 ± 0 | 0.12 ± 0.05 ^c |
| Skin | 49.3 ± 9.3 | 1.9 ± 1.0 | 0.36 ± 0.08 ^c |
| Muscle | 34.4 ± 4.1 | 1.3 ± 0.6 | 0.84 ± 0.11 ^c |
| Adipose | 43.7 ± 11.1 | 1.6 ± 0.7 | 0.21 ± 0.05 ^c |
| Liver | 65.6 ± 9.7 | 2.5 ± 1.3 | 0.16 ± 0.04 ^c |
| <u>GI Tract Tissues</u> | | | |
| Stomach | 13 ± 10 | 0.5 ± 0.4 | < 0.01 |
| Small Intestine | 6.4 ± 3.4 | 0.2 ± 0.2 | < 0.01 |
| Cecum | 37.1 ± 16.7 | 1.3 ± 0.5 | 0.01 |
| Large Intestine | 15.2 ± 10.6 | 0.4 ± 0.1 | < 0.01 |
| <u>Other Tissues</u> | | | |
| Kidney | 439 ± 96 | 17.1 ± 10.6 | 0.32 ± 0.07 |
| Bladder | 176 ± 133 | 3.8 ± 3.5 | 0.01 |
| Brain | 24.0 ± 2.9 | 0.9 ± 0.4 | 0.01 |

^aValues are averages + SD for four mouse units. Each mouse unit contained 3 mice. Original report Appendix has data from individual mouse units.

^bTissue:Blood Ratio.

^cBlood is assumed to be 8.4% of body weight; skin - 15%; muscle - 50%; adipose - 10%.