

Recovery of Radioactivity 48 Hours Following Single Intravenous Administration of 0.3 mg/kg [¹⁴C]Dicyclohexylcarbodiimide to Male Fischer 344 Rats – Study D^a

Dose Recovered in Excreta (%)

| End of Collection Period (h) | Urine ^b CPDE ^c | Cage Rinse CPDE | Feces CPDE | Volatile Organics ^d CPDE | CO ₂ ^d CPDE | Total CPDE |
|------------------------------|--------------------------------------|-----------------|------------|-------------------------------------|-----------------------------------|------------|
| 8 | 33.1 ± 3.8 | NC ^e | NC | NC | NC | 33.1 ± 3.8 |
| 24 | 51.7 ± 2.3 | NC | 15.7 ± 2.5 | NC | NC | 67.4 ± 3.8 |
| 48 | 54.3 ± 2.4 | 1.0 ± 0.3 | 20.0 ± 3.1 | NC | NC | 75.6 ± 3.9 |

Distribution in Tissues (48 hours)

| Tissue | ng-eq per g tissue Mean | ng-eq per g tissue SD | TBR ^f Mean | TBR SD | % Dose in Total Tissue ^g Mean | % Dose in Total Tissue SD |
|----------------------|-------------------------|-----------------------|-----------------------|--------|--|---------------------------|
| Adipose | 221.0 | 69.9 | 90.5 | 33.5 | 5.1 | 1.6 |
| Bladder | 23.7 | 7.7 | 9.7 | 3.6 | 0.004 | 0.002 |
| Blood | 2.5 | 0.2 | Unity | – | 0.043 | 0.004 |
| Brain | 66.9 | 4.0 | 26.9 | 1.5 | 0.17 | 0.01 |
| Heart | 157.0 | 18.1 | 63.5 | 11.3 | 0.17 | 0.01 |
| Jugular Vein | 55.9 | 9.7 | 22.9 | 6.5 | 0.018 | 0.004 |
| Kidney | 143.0 | 5.6 | 58.0 | 6.9 | 0.36 | 0.03 |
| Liver | 35.5 | 1.4 | 14.3 | 1.5 | 0.45 | 0.03 |
| Lung | 37.6 | 2.9 | 15.2 | 1.6 | 0.046 | 0.003 |
| Muscle | 30.4 | 3.1 | 12.2 | 0.7 | 4.8 | 0.5 |
| Skin | 26.3 | 4.3 | 10.6 | 2.1 | 1.5 | 0.3 |
| Spleen | 44.4 | 5.9 | 17.8 | 1.6 | 0.04 | 0.01 |
| Testes | 13.8 | 0.6 | 5.6 | 0.7 | 0.054 | 0.003 |
| Carcass ^h | NA ⁱ | – | NA | – | 0.9 | 1.3 |

^aAll values expressed as mean ± standard deviation (SD) (N = 5). The target dose was 0.3 mg dicyclohexylcarbodiimide/kg body weight. The actual dose delivered was 0.3 ± 0.01 mg/kg (11.3 ± 0.3 μCi/animal). Rats were surgically fitted with indwelling jugular cannulae for serial blood withdrawal. This study has toxicokinetic data (blood concentration time course) also. At all intravenous (iv) dose levels, signs of toxicity were evident (tremor, convulsions, lethargy, piloerection, etc.), but no mortality was associated with any of the iv dose levels studied.

^bUrine values include methanol rinse of the urine flask.

^cCPDE = Cumulative percent dose excreted.

^dVolatile organics and CO₂ in exhaled breath.

^eNC = not collected. No collection was scheduled for this time interval.

^fTBR = Tissue/Blood ratio.

^gPercent Dose was calculated using the following values for the mass of total tissue, expressed as percent of body weight: adipose, 7.0%; blood, 5.2%; muscle, 48%; and skin, 17%.

^hCarcass values are based on the residual digested carcass after the removal of the listed tissues (i.e., percent dose measured in skin, adipose, muscle (Studies C and D), and blood was subtracted from the total percent dose measured in the carcass).

ⁱNA = not applicable