

## ADME NTP Study S0191 2-Chloronitrobenzene

The contract laboratory abbreviation for the test article is 2-CNB.

Species: adult male F344 rats.

Vehicles: dermal, acetone

CASRN 88-73-3

Radiolabeled with carbon-14 in the ring; 2-Chloronitrobenzene, [Ring-<sup>14</sup>C]

2-Chloronitrobenzene Groups in Study Performed:

1. 0.65 mg/kg single dermal administration with dose site covered and sacrifice 72 hours postdose. (n=3)
2. 6.5 mg/kg single dermal administration with dose site covered and sacrifice 72 hours postdose. (n=3)
3. 65 mg/kg single dermal administration with dose site covered and sacrifice 72 hours postdose. (n=3)

This study determining cumulative excretion is part of a series of NTP studies conducted in the same laboratory on the disposition and metabolism of 2-chloronitrobenzene in male F344 rats.

S0104 – 11-day repeat 65 mg/kg 2-CNB oral gavage administration to 9 week old rats (186-203 g at randomization).

S0364 – single oral dosing of 2.0, 20, or 200 mg/kg 2-CNB to 11 week old rats (198-231 g at the time of randomization).

S0365 – 11-day repeat 65 mg/kg 2-CNB oral administration to geriatric rats (approximately 19 months old and 406-483 g at randomization).

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**Table 1: Urinary excretion of <sup>14</sup>C radioactivity by male Fischer 344 rats after dermal administration of [<sup>14</sup>C]2-CNB at 0.65, 6.5 and 65 mg/kg**

Time (hr)	Dose level (mg/kg)		
	0.65	6.5	65
	Dose excreted (%) <sup>a</sup>		
0-4	1.9 ± 1.5	2.5 ± 0.9	0.4 ± 0.8
4-8	4.0 ± 1.9	9.8 ± 5.6	7.0 ± 1.5
8-24	10.2 ± 1.0	8.5 ± 1.6	10.4 ± 2.3
24-48	3.0 ± 1.2	2.6 ± 0.7	7.4 ± 5.3
48-72	1.5 ± 0.7	1.1 ± 0.2	2.3 ± 0.6
	Dose excreted (cumulative %)		
0-4	1.9 ± 1.5	2.5 ± 0.9	0.4 ± 0.8
0-8	5.8 ± 2.9	12.3 ± 4.8	7.4 ± 1.0
0-24	16.0 ± 3.9	20.8 ± 6.3	17.8 ± 3.3
0-48	19.0 ± 5.0	23.4 ± 6.3	25.2 ± 4.3
0-72	20.5 ± 5.7	24.4 ± 6.2	27.5 ± 3.7

<sup>a</sup>Values are means of data from three animals ± SD.

**Table 2: Fecal excretion of  $^{14}\text{C}$  radioactivity by male Fischer 344 rats after dermal administration of [ $^{14}\text{C}$ ]2-CNB at 0.65, 6.5 and 65 mg/kg**

Time (hr)	Dose level (mg/kg)		
	0.65	6.5	65
	<b>Dose excreted (%)<sup>a</sup></b>		
0-4	0.2 ± 0.3	0.0 ± 0.0	0.0 ± 0.0
4-8	0.3 ± 0.6	0.2 ± 0.4	0.1 ± 0.1
8-24	4.4 ± 2.5	8.8 ± 2.7	5.2 ± 2.3
24-48	4.5 ± 1.2	4.5 ± 1.0	4.1 ± 0.7
48-72	1.7 ± 0.5	1.0 ± 0.1	2.3 ± 0.5
	<b>Dose excreted (cumulative %)</b>		
0-4	0.2 ± 0.3	0.0 ± 0.0	0.0 ± 0.0
0-8	0.5 ± 0.5	0.2 ± 0.4	0.1 ± 0.1
0-24	4.9 ± 2.6	9.1 ± 2.3	5.2 ± 2.4
0-48	9.4 ± 3.3	13.6 ± 3.2	9.3 ± 2.8
0-72	11.0 ± 3.3	14.6 ± 3.2	11.7 ± 2.8

<sup>a</sup>Values are means ± SD of data from three animals.

**Table 3: Collection of <sup>14</sup>C radioactivity in ethanol from male Fischer 344 rats after dermal administration of [<sup>14</sup>C]2-CNB at 0.65, 6.5 and 65 mg/kg**

Time (hr)	Dose level (mg/kg)		
	0.65	6.5	65
	<b>Dose excreted (%)<sup>a</sup></b>		
0-4	7.8 ± 9.0	5.3 ± 6.2	7.4 ± 7.8
4-8	3.3 ± 2.6	2.7 ± 2.8	4.7 ± 2.6
8-24	9.2 ± 3.0	8.5 ± 4.9	8.9 ± 2.9
24-32	2.6 ± 0.3	2.2 ± 0.6	3.1 ± 1.0
32-48	4.9 ± 0.7	4.3 ± 0.8	3.4 ± 1.0
48-56	1.9 ± 0.4	1.3 ± 0.1	1.5 ± 0.2
56-72	2.7 ± 0.9	2.3 ± 0.3	3.3 ± 0.1
	<b>Dose excreted (cumulative %)</b>		
0-4	7.8 ± 9.0	5.3 ± 6.2	7.4 ± 7.8
0-8	11.1 ± 11.6	8.0 ± 9.0	12.1 ± 10.1
0-24	20.3 ± 14.5	16.5 ± 13.8	21.0 ± 7.4
0-32	22.9 ± 14.4	18.7 ± 14.3	24.1 ± 8.3
0-48	27.8 ± 14.0	23.0 ± 14.5	27.5 ± 9.2
0-56	29.7 ± 13.6	24.3 ± 14.5	29.0 ± 9.1
0-72	32.3 ± 13.8	26.5 ± 14.7	32.3 ± 9.0

<sup>a</sup>Values are means ± SD of data from three animals.

**Table 4: Recovery of <sup>14</sup>C radioactivity at 72 hr after dermal application of [<sup>14</sup>C]2-CNB to male Fischer 344 rats at 0.65, 6.5 and 65 mg/kg**

Sample	Dose level (mg/kg)		
	0.65	6.5	65
	Mean ± SD dose recovered (%)		
Exposed skin	0.4 ± 0.2	0.7 ± 0.4	0.4 ± 0.1
Protective device	18.1 ± 5.0	4.9 ± 3.6	28.5 ± 8.6
Gauze	1.1 ± 0.7	0.3 ± 0.2	0.8 ± 0.3
Ethanol trap	32.3 ± 13.8	26.5 ± 14.7	32.3 ± 9.0
Urine	20.5 ± 5.7	24.4 ± 6.2	27.5 ± 3.7
Feces	11.0 ± 3.3	14.6 ± 3.2	11.7 ± 2.8
Cagewash	1.0 ± 0.2	1.0 ± 0.2	1.2 ± 0.2
Total unabsorbed <sup>a</sup>	51.9 ± 11.2	32.4 ± 18.2	62.0 ± 12.0
Total absorbed <sup>b</sup>	32.6 ± 8.7	40.0 ± 8.9	40.3 ± 5.3
Total recovered	84.5 ± 5.1	72.4 ± 9.8	102.3 ± 14.3

<sup>a</sup>Total unabsorbed represents radioactivity recovered in exposed skin, protective device, gauze, and ethanol traps.

<sup>b</sup>Total absorbed represents radioactivity recovered in urine, feces and cagewashings.