

## ADME NTP Study S0141 Firemaster 680

The contract laboratory used FF-680 as an abbreviation for the test article.

Firemaster 680 is a synonym for 1,2-Bis(2,4,6-tribromophenoxy)ethane.

Sex/Species: adult male F344 rats.

Vehicles: oral, corn oil; dosed feed, Purina rodent chow in meal form.

CASRN 37853-59-1

Radiolabeled with carbon-14 in the ring; 1,2-Bis(2,4,6-tribromophenoxy)ethane, [ring-<sup>14</sup>C]-

### Studies Performed:

- Single day dosed feed study in rats (0.05, 0.5 or 5 percent) with sacrifice at circa 96 hours (hr) postdose. (N=4)
- 10-day repeat dosed feed study (0.05 percent) in rats with animals having access to dosed diet on days 0 to 10, and sacrificed on day 10. (N=5)
- Single 200 mg/kg oral gavage dose in rats with sacrifice 6 hours postdose (bile collection study). (N=4)

[<sup>14</sup>C]FF-680 was administered for one day at 0.169% in the diet (meal plus gelatin feed sticks) to an additional group of three male rats, used for the collection of expired radioactivity up to 48 hours after the start of administration. No radioactivity was detected in the expired air.

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| <b>Table 1: Urinary excretion of <sup>14</sup>C radioactivity by male Fischer 344 rats after administration of [<sup>14</sup>C]FF-680 in the diet for one day</b> |                                                             |            |           |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------|------------|-----------|
| <b>Time (hr)<sup>a</sup></b>                                                                                                                                      | <b>Concentration in feed (%)</b>                            |            |           |
|                                                                                                                                                                   | <b>0.05</b>                                                 | <b>0.5</b> | <b>5</b>  |
|                                                                                                                                                                   | <b>Mean ± SD dose excreted (%)<sup>b,c</sup></b>            |            |           |
| 0-18                                                                                                                                                              | 0.3 ± 0.0                                                   | 0.2 ± 0.1  | 0.2 ± 0.1 |
| 18-24                                                                                                                                                             | 0.1 ± 0.0                                                   | 0.0 ± 0.1  | 0.0 ± 0.0 |
| 24-48                                                                                                                                                             | 0.3 ± 0.1                                                   | 0.1 ± 0.0  | 0.1 ± 0.0 |
| 48-72                                                                                                                                                             | 0.1 ± 0.1                                                   | 0.0 ± 0.0  | 0.0 ± 0.0 |
| 72-96                                                                                                                                                             | 0.0 ± 0.0                                                   | 0.0 ± 0.0  | 0.0 ± 0.0 |
|                                                                                                                                                                   | <b>Mean ± SD dose excreted (cumulative %)<sup>b,c</sup></b> |            |           |
| 0-18                                                                                                                                                              | 0.3 ± 0.0                                                   | 0.2 ± 0.1  | 0.2 ± 0.1 |
| 0-24                                                                                                                                                              | 0.4 ± 0.0                                                   | 0.2 ± 0.1  | 0.2 ± 0.1 |
| 0-48                                                                                                                                                              | 0.7 ± 0.1                                                   | 0.3 ± 0.0  | 0.3 ± 0.1 |
| 0-72                                                                                                                                                              | 0.7 ± 0.1                                                   | 0.3 ± 0.0  | 0.3 ± 0.1 |
| 0-96                                                                                                                                                              | 0.7 ± 0.1                                                   | 0.3 ± 0.0  | 0.3 ± 0.1 |

<sup>a</sup>Time after the start of administration of [<sup>14</sup>C]FF-680 in the diet.

<sup>b</sup>Mean of data from four rats.

<sup>c</sup>For the purpose of calculating a mean ± SD, urine samples in which the radioactivity in 100 µl sample is less than twice the background of the system, or where the total radioactivity in the urine collected at a particular time interval is less than 0.1% of the dose, is considered to contain zero.

**Table 2: Fecal excretion of <sup>14</sup>C radioactivity by male Fischer 344 rats after administration of [<sup>14</sup>C]FF-680 in the diet for one day**

| Time (hr) <sup>a</sup> | Concentration in feed (%)                                   |            |            |
|------------------------|-------------------------------------------------------------|------------|------------|
|                        | 0.05                                                        | 0.5        | 5          |
|                        | <b>Mean ± SD dose excreted (%)<sup>b</sup></b>              |            |            |
| 0-18                   | 23.2 ± 9.3                                                  | 19.9 ± 2.5 | 18.5 ± 2.4 |
| 18-24                  | 15.2 ± 2.9                                                  | 11.4 ± 5.4 | 9.5 ± 1.3  |
| 24-48                  | 51.6 ± 9.5                                                  | 45.6 ± 6.1 | 52.5 ± 2.7 |
| 48-72                  | 8.4 ± 3.9                                                   | 5.0 ± 2.6  | 8.7 ± 1.1  |
| 72-96                  | 1.2 ± 0.5                                                   | 2.9 ± 2.3  | 2.1 ± 2.2  |
|                        | <b>Mean ± SD dose excreted (cumulative %)<sup>b,c</sup></b> |            |            |
| 0-18                   | 23.2 ± 9.3                                                  | 19.9 ± 2.5 | 18.5 ± 2.4 |
| 0-24                   | 38.2 ± 11.9                                                 | 31.3 ± 7.5 | 28.0 ± 1.2 |
| 0-48                   | 89.9 ± 2.6                                                  | 76.9 ± 2.6 | 80.5 ± 2.4 |
| 0-72                   | 98.3 ± 1.5                                                  | 81.8 ± 4.8 | 89.2 ± 2.8 |
| 0-96                   | 99.5 ± 1.6                                                  | 84.7 ± 4.4 | 91.3 ± 2.3 |

<sup>a</sup>Time after the start of administration of [<sup>14</sup>C]FF-680 in the diet.

<sup>b</sup>Mean of data from four rats.

**Table 3: Daily urinary and fecal excretion of  $^{14}\text{C}$  radioactivity by male Fischer 344 rats after administration of [ $^{14}\text{C}$ ]FF-680 in the diet at 0.05% for ten days**

| Time (day) <sup>a</sup> | Cumulative % dose (mean $\pm$ SD) <sup>b,c</sup> |                |
|-------------------------|--------------------------------------------------|----------------|
|                         | Urine                                            | Feces          |
| 0-1                     | 0.2 $\pm$ 0.1                                    | 34.3 $\pm$ 7.1 |
| 0-2                     | 0.3 $\pm$ 0.0                                    | 56.0 $\pm$ 4.4 |
| 0-3                     | 0.3 $\pm$ 0.0                                    | 63.2 $\pm$ 2.8 |
| 0-4                     | 0.4 $\pm$ 0.1                                    | 68.2 $\pm$ 1.6 |
| 0-5                     | 0.4 $\pm$ 0.1                                    | 70.9 $\pm$ 1.4 |
| 0-6                     | 0.4 $\pm$ 0.0                                    | 71.8 $\pm$ 1.2 |
| 0-7                     | 0.4 $\pm$ 0.0                                    | 72.0 $\pm$ 0.7 |
| 0-8                     | 0.4 $\pm$ 0.0                                    | 73.1 $\pm$ 1.6 |
| 0-9                     | 0.4 $\pm$ 0.0                                    | 74.4 $\pm$ 1.1 |
| 0-10                    | 0.4 $\pm$ 0.0                                    | 74.9 $\pm$ 1.0 |

<sup>a</sup>Time after the start of administration of [ $^{14}\text{C}$ ]FF-680 in the diet.

<sup>b</sup>Mean  $\pm$  SD of data from five rats.

<sup>c</sup>Data calculated as a percentage of the total radioactivity consumed up to sample collection time.

**Table 4: Concentration of [ $^{14}\text{C}$ ]FF-680 equivalents in bile of male Fischer 344 rats after oral administration of [ $^{14}\text{C}$ ]FF-680 at 200 mg/kg**

| Time (min) | Concentration (nmol/g)<br>Mean $\pm$ SD |
|------------|-----------------------------------------|
| 0-15       | a                                       |
| 15-30      | a                                       |
| 30-45      | 2.33 $\pm$ 2.07 <sup>b</sup>            |
| 45-60      | 2.33 $\pm$ 2.28 <sup>b</sup>            |
| 60-90      | 3.31 $\pm$ 3.19 <sup>b</sup>            |
| 90-120     | 5.49 $\pm$ 5.66 <sup>b</sup>            |
| 120-180    | 10.21 $\pm$ 8.86 <sup>b</sup>           |
| 180-240    | 15.85 $\pm$ 14.07 <sup>b</sup>          |
| 240-300    | 17.70 $\pm$ 17.68 <sup>b</sup>          |
| 300-360    | 19.47 $\pm$ 22.78 <sup>b</sup>          |

<sup>a</sup>Mean  $\pm$  SD not calculable because radioactivity in all samples was less than twice background for the system.

<sup>b</sup>For the purpose of calculating a mean  $\pm$  SD, samples in which the radioactivity was less than twice background for the system were considered to contain zero nmol/g.

**Table 5: Biliary excretion of <sup>14</sup>C radioactivity by male Fischer 344 rats after oral administration of [<sup>14</sup>C]FF-680 at 200 mg/kg**

| <b>Time (min)</b> | <b>Dose excreted (%)<sup>a</sup><br/>Mean ± SD</b> |
|-------------------|----------------------------------------------------|
| 0-15              | 0.00 ± 0.00                                        |
| 15-30             | 0.00 ± 0.00                                        |
| 30-45             | 0.00 ± 0.00                                        |
| 45-60             | 0.00 ± 0.00                                        |
| 60-90             | 0.00 ± 0.00                                        |
| 90-120            | 0.00 ± 0.00                                        |
| 120-180           | 0.01 ± 0.01                                        |
| 180-240           | 0.01 ± 0.01                                        |
| 240-300           | 0.01 ± 0.01                                        |
| 300-360           | 0.01 ± 0.01                                        |
|                   | <b>Dose excreted (cumulative %)</b>                |
| 0-15              | 0.00 ± 0.00                                        |
| 0-30              | 0.00 ± 0.00                                        |
| 0-45              | 0.00 ± 0.00                                        |
| 0-60              | 0.00 ± 0.00                                        |
| 0-90              | 0.00 ± 0.00                                        |
| 0-120             | 0.00 ± 0.00                                        |
| 0-180             | 0.01 ± 0.01                                        |
| 0-240             | 0.02 ± 0.02                                        |
| 0-300             | 0.03 ± 0.03                                        |
| 0-360             | 0.04 ± 0.04                                        |

<sup>a</sup> For the purpose of calculating a mean ± SD, the samples in which the radioactivity was less than twice background for the system were considered to contain zero nmol/g.

**Table 6: Concentration of [<sup>14</sup>C]FF-680 equivalents in tissues of male Fischer 344 rats at ca. 96 hr after the start of administration of [<sup>14</sup>C]FF-680 in the diet for one day**

| Tissue          | Concentration in feed (%)                     |                          |                          |
|-----------------|-----------------------------------------------|--------------------------|--------------------------|
|                 | 0.05                                          | 0.5                      | 5                        |
|                 | Mean ± SD concentration (nmol/g) <sup>a</sup> |                          |                          |
| Blood           | — <sup>b</sup>                                | —                        | —                        |
| Liver           | —                                             | —                        | —                        |
| Kidney          | —                                             | —                        | —                        |
| Heart           | —                                             | —                        | —                        |
| Lung            | —                                             | —                        | —                        |
| Brain           | —                                             | —                        | —                        |
| Adipose tissue  | 0.38 ± 0.10                                   | —                        | 1.73 ± 3.45 <sup>c</sup> |
| Skeletal muscle | —                                             | —                        | —                        |
| Skin            | 0.15 ± 0.04                                   | —                        | —                        |
| Spleen          | —                                             | —                        | —                        |
| Thymus          | 0.44 ± 0.20                                   | 0.36 ± 0.73 <sup>c</sup> | —                        |
| Testes          | —                                             | —                        | —                        |

<sup>a</sup>Mean of data from four rats.

<sup>b</sup>Mean ± SD not calculable because all samples were less than twice background for the system.

<sup>c</sup>Values are below the minimum quantifiable limit because only one rat showed quantifiable level of <sup>14</sup>C. The other three were considered to contain zero nmol/g.

**Table 7: Percentage of dose of [<sup>14</sup>C]FF-680 equivalents in tissues of male Fischer 344 rats at ca. 96 hr after the start of administration of [<sup>14</sup>C]FF-680 in the diet for one day**

| Tissue          | Concentration in feed (%)       |     |             |
|-----------------|---------------------------------|-----|-------------|
|                 | 0.05                            | 0.5 | 5           |
|                 | Mean ± SD (% dose) <sup>a</sup> |     |             |
| Blood           | — <sup>b</sup>                  | —   | —           |
| Liver           | —                               | —   | —           |
| Kidney          | —                               | —   | —           |
| Heart           | —                               | —   | —           |
| Lung            | —                               | —   | —           |
| Brain           | —                               | —   | —           |
| Adipose tissue  | 0.09 ± 0.01                     | —   | 0.01 ± 0.01 |
| Skeletal muscle | —                               | —   | —           |
| Skin            | 0.06 ± 0.01                     | —   | —           |
| Spleen          | —                               | —   | —           |
| Thymus          | —                               | —   | —           |
| Testes          | —                               | —   | —           |
| Total           | 0.15 ± 0.02                     | —   | 0.01 ± 0.01 |

<sup>a</sup> Mean of data from four rats.

<sup>b</sup> Mean ± SD not calculable because all samples were less than twice background for the system.

**Table 8: Concentration and percentage of [<sup>14</sup>C]FF-680 equivalents in tissues of male Fischer 344 rats at ten days after the start of administration of [<sup>14</sup>C]FF-680 at 0.05% in the diet for ten days**

| Tissue          | Mean ± SD <sup>a</sup>   |                      |
|-----------------|--------------------------|----------------------|
|                 | nmol/g                   | Fraction of dose (%) |
| Blood           | 0.44 ± 0.09              | 0.01 ± 0.00          |
| Liver           | 0.52 ± 0.03              | — <sup>b</sup>       |
| Kidney          | 1.64 ± 0.30              | —                    |
| Heart           | 0.40 ± 0.04              | —                    |
| Lung            | 0.40 ± 0.03              | —                    |
| Brain           | 0.02 ± 0.03 <sup>c</sup> | —                    |
| Spleen          | 0.17 ± 0.02              | —                    |
| Testes          | 0.13 ± 0.02              | —                    |
| Skin            | 1.09 ± 0.09              | 0.04 ± 0.01          |
| Adipose tissue  | 3.19 ± 0.58              | 0.06 ± 0.01          |
| Skeletal muscle | 0.38 ± 0.21              | 0.04 ± 0.02          |
| Thymus          | 0.95 ± 0.14              | —                    |
| Stomach         | 15.33 ± 8.72             | 0.02 ± 0.01          |
| Intestines      | 4.51 ± 1.10              | 0.02 ± 0.01          |
| Total %         |                          | 0.17 ± 0.02          |

<sup>a</sup> Mean ± SD of data from five rats.

<sup>b</sup> Mean ± SD not calculable because radioactivity in all samples was <0.01% of the dose.

<sup>c</sup> Radioactivity in four of the five samples was less than twice background for the system. For the purpose of calculating a mean ± SD, the samples in which the radioactivity was less than twice background for the system were considered to contain zero nmol/g.



**Table 9: Recovery of <sup>14</sup>C radioactivity at ca. 96 hr after the start of administration of [<sup>14</sup>C]FF-680 in the diet of male Fischer 344 rats for one day**

| Sample <sup>b</sup> | Concentration in feed (%)                 |            |            |
|---------------------|-------------------------------------------|------------|------------|
|                     | 0.05                                      | 0.5        | 5          |
|                     | Mean ± SD dose recovered (%) <sup>a</sup> |            |            |
| Urine               | 0.7 ± 0.1                                 | 0.3 ± 0.0  | 0.3 ± 0.1  |
| Feces               | 99.5 ± 1.6                                | 84.7 ± 4.4 | 91.3 ± 2.2 |
| Cage rinse          | 0.6 ± 0.6                                 | 0.5 ± 0.2  | 0.3 ± 0.1  |
| Tissues             | 0.2 ± 0.1                                 | <0.1       | <0.1       |
| Total               | 101.0 ± 1.9                               | 85.5 ± 4.5 | 91.8 ± 2.4 |

<sup>a</sup>Mean of data from four rats.

<sup>b</sup>Urine and feces were collected up to the time of sacrifice, at ca. 96 hr. At sacrifice, tissues and cage rinse were collected.

**Table 10: Recovery of <sup>14</sup>C radioactivity at ca. ten days after the start of administration of [<sup>14</sup>C]FF-680 at 0.05% concentration in the diet of male Fischer 344 rats for ten days**

| Sample <sup>a</sup> | Mean ± SD dose recovered (%)                       |
|---------------------|----------------------------------------------------|
| Urine               | 0.4 ± 0.0                                          |
| Feces               | 74.9 ± 1.0                                         |
| Intestinal contents | 4.8 ± 0.9                                          |
| Cage rinse          | 7.6 ± 2.6 <sup>b</sup>                             |
| Tissues             | 0.2 ± 0.0                                          |
| Total               | 86.4 ± 3.7 <sup>c</sup><br>87.7 ± 2.5 <sup>d</sup> |

<sup>a</sup>Urine and feces were collected every 24 hr and at sacrifice. At sacrifice, tissues and cage rinse were collected.

<sup>b</sup>Mean ± SD calculated from four samples due to loss of one sample.

<sup>c</sup>Mean ± SD calculated for data from all rats.

<sup>d</sup>Mean ± SD calculated from the four rats that had all the samples.