

*p*-ニトロアニソールのマウスを用いた経口投与による  
2 週 間 毒 性 試 験（混 餌 試 験）報 告 書

試験番号：0361

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## TABLES

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TABLE 1 EXPERIMENTAL DESIGN AND MATERIALS AND METHODS  
IN THE 2-WEEK FEED STUDY OF p-NITROANISOLE

| 2-week study                        |                                                                                                                     |
|-------------------------------------|---------------------------------------------------------------------------------------------------------------------|
| <Method of Administration>          | Mixed feed                                                                                                          |
| <Number of Groups>                  | Male 6, Female 6                                                                                                    |
| <Size of Groups>                    | 5 males and 5 females of each group                                                                                 |
| <Animals>                           |                                                                                                                     |
| Strain and Species                  | Crj:BDF <sub>1</sub> MOUSE                                                                                          |
| Animal Source                       | Charles River Japan, Inc.                                                                                           |
| Duration Held Before Study          | 2 wk                                                                                                                |
| Age When Placed on Study            | 6 wk                                                                                                                |
| Age When Killed                     | 8 wk                                                                                                                |
| <Doses>                             |                                                                                                                     |
| <Male>                              | 0, 5000, 10000, 20000, 40000 or 50000 ppm                                                                           |
| <Female>                            | 0, 5000, 10000, 20000, 40000 or 50000 ppm                                                                           |
| <Duration of Dosing>                | 7d/wk for 2wk                                                                                                       |
| <Animal Maintenance>                |                                                                                                                     |
| Feed                                | CRF-1 (Oriental Yeast Co., Ltd.)<br>Sterilized by $\gamma$ -ray<br>Available <i>ad libitum</i>                      |
| Water                               | Filtrated and sterilized by ultraviolet ray<br>Automatic watering system<br>Available <i>ad libitum</i>             |
| Animal per Cage                     | Single (stainless steel wire)                                                                                       |
| Animal Room Environment             | Barrier system<br>Temperature : 23±2°C<br>Humidity : 55±15%<br>Fluorescent light 12h/d<br>15~17 room air changes /h |
| <Type and Frequency of Observation> |                                                                                                                     |
| Clinical Sign                       | Observed 0-0, 1-1, 1-3, 1-7, 2-3, and 2-7 (wk-d)                                                                    |
| Body Weight                         | Weighed 0-0, 1-1, 1-3, 1-7, 2-3, and 2-7 (wk-d)                                                                     |
| Food Consumption                    | Weighed 1-3, 1-7, 2-3, and 2-7 (wk-d)                                                                               |

TABLE 1 EXPERIMENTAL DESIGN AND MATERIALS AND METHODS  
(Continued) IN THE 2-WEEK FEED STUDY OF p-NITROANISOLE

| 2-week study                  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |
|-------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <Hematology>                  | Red blood cell (RBC), Hemoglobin, Hematocrit,<br>Mean corpuscular volume (MCV),<br>Mean corpuscular hemoglobin (MCH),<br>Mean corpuscular hemoglobin concentrate (MCHC),<br>Platelet, White blood cell (WBC), Differential WBC,                                                                                                                                                                                                                                                                                                                                                                                                                 |
| <Biochemistry>                | Total protein, Albumin, A/G ratio,<br>Total bilirubin, Glucose, Total cholesterol<br>Phospholipid, Glutamic oxaloacetic transaminase (GOT),<br>Glutamic pyruvic transaminase (GPT),<br>Lactate dehydrogenase (LDH),<br>$\gamma$ -Glutamyl transpeptidase (G-GTP),<br>Creatine phosphokinase (CPK),<br>Urea nitrogen, Sodium, Potassium, Chloride,<br>Calcium, Inorganic phosphorus.                                                                                                                                                                                                                                                             |
| <Urinalysis>                  | None                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
| <Necropsy>                    | Necropsy performed on all animals.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |
| <Organ Weight>                | Organ weight measurement performed on at least<br>five animals per sex per group at sacrifice<br>The following organs were weighed;<br>thymus, adrenal, testis, ovary, heart, lung,<br>kidney, spleen, liver, and brain.                                                                                                                                                                                                                                                                                                                                                                                                                        |
| <Histopathologic Examination> | Histopathologic examination performed on at least<br>two animals per sex per group.<br>The following organs were examined;<br>skin, nasal cavity, nasopharynx, larynx, trachea, lung, bone marrow,<br>lymph node, thymus, spleen, heart, tongue, salivary gland, esophagus,<br>stomach, small intestine, large intestine, liver, gall bladder, pancreas,<br>kidney, urinary bladder, pituitary, thyroid, parathyroid, adrenal, testis,<br>epididymis, seminal vesicle, prostate, ovary, uterus, vagina,<br>mammary gland, brain, spinal cord, peripheral nerve,<br>eye, Harderian gland, muscle, bone, other organs/tissues with gross lesions. |

TABLE 2 SURVIVAL ANIMAL NUMBERS AND BODY WEIGHT CHANGES OF MALE MICE  
IN THE 2-WEEK FEED STUDY OF p-NITROANISOLE

| Week-day<br>on Study                                                 | Control |                          |     | 5000ppm |                      |                   | 10000ppm |                      |                   | 20000ppm |                      |                   | 40000ppm |                      |                   | 50000ppm |                      |                   |
|----------------------------------------------------------------------|---------|--------------------------|-----|---------|----------------------|-------------------|----------|----------------------|-------------------|----------|----------------------|-------------------|----------|----------------------|-------------------|----------|----------------------|-------------------|
|                                                                      | Av.Wt.  | No. of<br>Surviv.<br><5> |     | Av.Wt.  | % of<br>cont.<br><5> | No. of<br>Surviv. | Av.Wt.   | % of<br>cont.<br><5> | No. of<br>Surviv. | Av.Wt.   | % of<br>cont.<br><5> | No. of<br>Surviv. | Av.Wt.   | % of<br>cont.<br><5> | No. of<br>Surviv. | Av.Wt.   | % of<br>cont.<br><5> | No. of<br>Surviv. |
| 0-0                                                                  | 23.7    | (5)                      | 5/5 | 23.6    | (5)                  | 100               | 23.7     | (5)                  | 100               | 23.6     | (5)                  | 100               | 23.6     | (5)                  | 100               | 23.6     | (5)                  | 100               |
| 1-1                                                                  | 23.9    | (5)                      | 5/5 | 23.3    | (5)                  | 97                | 22.7     | (5)                  | 95                | 21.5     | (5)                  | 90                | 21.1     | (5)                  | 88                | 20.4     | (5)                  | 85                |
| 1-3                                                                  | 24.1    | (5)                      | 5/5 | 23.7    | (5)                  | 98                | 23.6     | (5)                  | 98                | 21.3     | (5)                  | 88                | 19.0     | (5)                  | 79                | 17.8     | (5)                  | 74                |
| 1-7                                                                  | 24.6    | (5)                      | 5/5 | 24.0    | (5)                  | 98                | 24.3     | (5)                  | 99                | 22.1     | (5)                  | 90                | 15.3     | (5)                  | 62                | 15.4     | (1)                  | 63                |
| 2-3                                                                  | 25.3    | (5)                      | 5/5 | 24.4    | (5)                  | 96                | 24.7     | (5)                  | 98                | 22.3     | (5)                  | 88                | 14.7     | (2)                  | 58                | -        | (0)                  | -                 |
| 2-7                                                                  | 26.2    | (5)                      | 5/5 | 25.5    | (5)                  | 97                | 26.0     | (5)                  | 99                | 24.1     | (5)                  | 92                | -        | (0)                  | -                 | -        | (0)                  | -                 |
| < > : No.of effective animals, ( ) : No.of measured animals Av.Wt.:g |         |                          |     |         |                      |                   |          |                      |                   |          |                      |                   |          |                      |                   |          |                      |                   |

TABLE 3 SURVIVAL ANIMAL NUMBERS AND BODY WEIGHT CHANGES OF FEMALE MICE  
IN THE 2-WEEK FEED STUDY OF p-NITROANISOLE

| Week-day<br>on Study                                                 | Control |                          |     | 5000ppm |                      |                   | 10000ppm |                      |                   | 20000ppm |                      |                   | 40000ppm |                      |                   | 50000ppm |                      |                   |
|----------------------------------------------------------------------|---------|--------------------------|-----|---------|----------------------|-------------------|----------|----------------------|-------------------|----------|----------------------|-------------------|----------|----------------------|-------------------|----------|----------------------|-------------------|
|                                                                      | Av.Wt.  | No. of<br>Surviv.<br><5> |     | Av.Wt.  | % of<br>cont.<br><5> | No. of<br>Surviv. | Av.Wt.   | % of<br>cont.<br><5> | No. of<br>Surviv. | Av.Wt.   | % of<br>cont.<br><5> | No. of<br>Surviv. | Av.Wt.   | % of<br>cont.<br><5> | No. of<br>Surviv. | Av.Wt.   | % of<br>cont.<br><5> | No. of<br>Surviv. |
| 0-0                                                                  | 18      | (5)                      | 5/5 | 17.8    | (5)                  | 100               | 17.8     | (5)                  | 100               | 17.8     | (5)                  | 100               | 17.8     | (5)                  | 100               | 17.8     | (5)                  | 100               |
| 1-1                                                                  | 18      | (5)                      | 5/5 | 17      | (5)                  | 96                | 16.6     | (5)                  | 94                | 15.9     | (5)                  | 90                | 15.3     | (5)                  | 86                | 15.1     | (5)                  | 85                |
| 1-3                                                                  | 18      | (5)                      | 5/5 | 17.9    | (5)                  | 102               | 17.9     | (5)                  | 102               | 15.8     | (5)                  | 90                | 12.7     | (5)                  | 72                | 12.3     | (5)                  | 70                |
| 1-7                                                                  | 18      | (5)                      | 5/5 | 18      | (5)                  | 98                | 18.3     | (5)                  | 99                | 16.8     | (5)                  | 91                | 10.9     | (1)                  | 59                | -        | (0)                  | -                 |
| 2-3                                                                  | 19      | (5)                      | 5/5 | 18.8    | (5)                  | 101               | 18.8     | (5)                  | 101               | 17.8     | (5)                  | 95                | -        | (0)                  | -                 | -        | (0)                  | -                 |
| 2-7                                                                  | 19      | (5)                      | 5/5 | 19.7    | (5)                  | 104               | 20.1     | (5)                  | 106               | 20.1     | (5)                  | 106               | -        | (0)                  | -                 | -        | (0)                  | -                 |
| < > : No.of effective animals, ( ) : No.of measured animals Av.Wt.:g |         |                          |     |         |                      |                   |          |                      |                   |          |                      |                   |          |                      |                   |          |                      |                   |

TABLE 4 FOOD CONSUMPTION CHANGES OF MALE MICE IN THE 2-WEEK FEED STUDY OF p-NITROANISOLE

| Week-day<br>on Study                                                 | Control |                          |     | 1250ppm |                      |                   | 2500ppm |                      |                   | 5000ppm |                      |                   | 10000ppm |                      |                   | 20000ppm |                      |                   |
|----------------------------------------------------------------------|---------|--------------------------|-----|---------|----------------------|-------------------|---------|----------------------|-------------------|---------|----------------------|-------------------|----------|----------------------|-------------------|----------|----------------------|-------------------|
|                                                                      | Av.FC.  | No. of<br>Surviv.<br><5> |     | Av.FC.  | % of<br>cont.<br><5> | No. of<br>Surviv. | Av.FC.  | % of<br>cont.<br><5> | No. of<br>Surviv. | Av.FC.  | % of<br>cont.<br><5> | No. of<br>Surviv. | Av.FC.   | % of<br>cont.<br><5> | No. of<br>Surviv. | Av.FC.   | % of<br>cont.<br><5> | No. of<br>Surviv. |
| 1-3                                                                  | 4.1     | (5)                      | 5/5 | 3.2     | (5)                  | 78                | 3.5     | (5)                  | 85                | 2.3     | (5)                  | 56                | 2        | (5)                  | 49                | 2.2      | (5)                  | 54                |
| 1-7                                                                  | 4.0     | (5)                      | 5/5 | 3.7     | (5)                  | 92                | 4.1     | (5)                  | 103               | 3.7     | (5)                  | 92                | 3.4      | (5)                  | 85                | 1.4      | (1)                  | 35                |
| 2-3                                                                  | 4.1     | (5)                      | 5/5 | 3.7     | (5)                  | 90                | 4.1     | (5)                  | 100               | 3.6     | (5)                  | 88                | 1.2      | (1)                  | 29                | -        | (0)                  | -                 |
| 2-7                                                                  | 4.1     | (5)                      | 5/5 | 3.8     | (5)                  | 93                | 4.1     | (5)                  | 100               | 3.9     | (5)                  | 95                | -        | (0)                  | -                 | -        | (0)                  | -                 |
| < > : No.of effective animals, ( ) : No.of measured animals Av.FC.:g |         |                          |     |         |                      |                   |         |                      |                   |         |                      |                   |          |                      |                   |          |                      |                   |

TABLE 5 FOOD CONSUMPTION CHANGES OF FEMALE MICE IN THE 2-WEEK FEED STUDY OF p-NITROANISOLE

| Week-day<br>on Study                                                 | Control |                          |     | 1250ppm |                      |                   | 2500ppm |                      |                   | 5000ppm |                      |                   | 10000ppm |                      |                   | 20000ppm |                      |                   |
|----------------------------------------------------------------------|---------|--------------------------|-----|---------|----------------------|-------------------|---------|----------------------|-------------------|---------|----------------------|-------------------|----------|----------------------|-------------------|----------|----------------------|-------------------|
|                                                                      | Av.FC.  | No. of<br>Surviv.<br><5> |     | Av.FC.  | % of<br>cont.<br><5> | No. of<br>Surviv. | Av.FC.  | % of<br>cont.<br><5> | No. of<br>Surviv. | Av.FC.  | % of<br>cont.<br><5> | No. of<br>Surviv. | Av.FC.   | % of<br>cont.<br><5> | No. of<br>Surviv. | Av.FC.   | % of<br>cont.<br><5> | No. of<br>Surviv. |
| 1-3                                                                  | 3.5     | (5)                      | 5/5 | 3.8     | (5)                  | 109               | 3.7     | (5)                  | 106               | 3.2     | (5)                  | 91                | 1.2      | (5)                  | 34                | 0.9      | (4)                  | 26                |
| 1-7                                                                  | 3.6     | (5)                      | 5/5 | 3.9     | (5)                  | 108               | 3.8     | (5)                  | 106               | 4.8     | (5)                  | 133               | 0.7      | (1)                  | 19                | -        | (0)                  | -                 |
| 2-3                                                                  | 3.4     | (5)                      | 5/5 | 3.8     | (5)                  | 112               | 4.0     | (5)                  | 118               | 5.2     | (5)                  | 153               | -        | (0)                  | -                 | -        | (0)                  | -                 |
| 2-7                                                                  | 3.3     | (5)                      | 5/5 | 4.0     | (5)                  | 121               | 4.0     | (5)                  | 121               | 3.6     | (5)                  | 109               | -        | (0)                  | -                 | -        | (0)                  | -                 |
| < > : No.of effective animals, ( ) : No.of measured animals Av.FC.:g |         |                          |     |         |                      |                   |         |                      |                   |         |                      |                   |          |                      |                   |          |                      |                   |