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SPONSOR: 3M Company

TEST MATERIAL: Fluorad<sup>®</sup> Fluorochemical FC-143

SUBJECT: Acute Oral Toxicity (LD<sub>50</sub>)  
Study in Rats.



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Date: May 5, 1978

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I. SYNOPSIS

Based upon the data obtained, the acute oral LD<sub>50</sub> values and 95% confidence limits were calculated to be as follows:

Male Rats: 680 (399 - 1157) mg/kg.

Female Rats: 430 (295 - 626) mg/kg.

Combined Male and Female Rats: 540 (389 - 749) mg/kg.

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## II. TEST MATERIAL

The test material was received from the 3M Company, St. Paul, Minnesota on October 24, 1977. It was identified as "Fluorad<sup>®</sup> Fluorochemical FC-143, 3M Stock No. 98-0211-0008-0, Lot 340" and was received as a white powder.

III. METHOD

Twenty-five male and 25 female rats of the Charles River CD strain (obtained from Charles River Breeding Laboratories, Inc., Portage, Michigan), weighing from 180 to 221 grams, were used for this study. The rats were housed by sex in groups of 5 rats per cage, in hanging wire-mesh cages in temperature and humidity controlled quarters. They were maintained in accordance with the recommendations contained in H.E.W. Publication No. 74-23 (N.I.H.) entitled "Guide for the Care and Use of Laboratory Animals". Water and Purina Laboratory Chow were available ad libitum, except for an overnight period immediately preceding oral administration during which food, but not water, was withheld.

The test material was administered orally by gavage as an emulsion in 40% acetone/60% corn oil at the following dosage levels to male and female rats: 100, 215, 464, 1000 and 2150 mg/kg.

Five rats of each sex were used at each dosage level. Volumes of 10 ml/kg of body weight were administered at all dosage levels.

All rats were observed for mortality and pharmacotoxic signs during the first four hours after dosing, at 24 hours and daily thereafter for a total of 14 days. Body weights were recorded immediately prior to dosing (control weight) and at 7 and 14 days. All rats which died on study were subjected to gross necropsy examination as were all survivors at the end of the 14 day observation period.

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## IV. RESULTS

### A. MORTALITY AND LD<sub>50</sub> VALUES:

#### Dose - Mortality Data

| Dosage<br>Level<br>mg/kg | Number of Deaths |   |      |   |   |   |   |   |      |   |   |   |   |   |      |        | Total<br>Mortalities |       |  |
|--------------------------|------------------|---|------|---|---|---|---|---|------|---|---|---|---|---|------|--------|----------------------|-------|--|
|                          | Hrs              |   | Days |   |   |   |   |   |      |   |   |   |   |   |      |        |                      |       |  |
|                          | 0-4              |   | 1    | 2 | 3 | 4 | 5 | 6 | 7-14 |   |   |   |   |   |      |        |                      |       |  |
|                          | M                | F | M    | F | M | F | M | F | M    | F | M | F | M | F | Male | Female | Total                |       |  |
| 100                      |                  |   |      |   |   |   |   |   |      |   |   |   |   |   | 1    | 1/5    | 0/5                  | 1/10  |  |
| 215                      |                  |   |      |   |   |   |   |   |      |   |   |   |   |   |      | 0/5    | 0/5                  | 0/10  |  |
| 464                      |                  |   |      |   | 2 | 2 |   |   |      | 1 |   |   |   |   |      | 2/5    | 3/5                  | 5/10  |  |
| 1000                     |                  |   |      | 2 | 2 | 2 |   | 1 | 1    |   |   |   |   |   |      | 3/5    | 5/5                  | 8/10  |  |
| 2150                     | 1                | 3 | 4    | 2 |   |   |   |   |      |   |   |   |   |   |      | 5/5    | 5/5                  | 10/10 |  |

#### The Acute Oral LD<sub>50</sub> Values and 95% Confidence Limits

Male Rats: 680 (399 - 1157) mg/kg.

Female Rats: 430 (295 - 626) mg/kg.

Combined Male and Female Rats: 540 (389 - 749) mg/kg.

#### Slope

Male Rats: 1.00.

Female Rats: 1.00.

Combined Male and Female Rats: 1.00.

#### Statistical References

<sup>1</sup>Weil, C. S. 1952. Tables for Convenient Calculation of Median Effective Dose and Instruction in Their Use. Biometrics, 8: 249-263.

<sup>2</sup>Thompson, W. R. and Weil, C. S. 1952. On the Construction of Tables for Moving Average Interpolation. Biometrics, 8: 51-54.

<sup>3</sup>Eby, R. 1957. Statistical Tables for Dose Evaluation, Report No. 5711. Miles-Ames Research Laboratory, Elkhart, Indiana.

### B. PHARMACOTOXIC SIGNS:

The following pharmacotoxic signs were observed during the 14 day observation period: (see Table 1).

**NUMBER OF RATS SHOWING PHARMACOTOXIC  
SIGNS AND TIME [HOUR] (DAY) OBSERVED**

**TABLE - 1.**

**COMPOUND - FC-143:**

**MALES**

| OBSERVATION            | 100 mg/kg                     | 215 mg/kg                            | 464 mg/kg                            | 1000 mg/kg                                         | 2150 mg/kg                 |
|------------------------|-------------------------------|--------------------------------------|--------------------------------------|----------------------------------------------------|----------------------------|
| Normal                 | 3 (2 - 12),<br>4 (13 - 14)    | 4 (2 - 5),<br>5 (6 - 14)             | 2 (2 - 5),<br>3 (6 - 14)             | 2 (6 - 14)                                         |                            |
| Ptosis                 | 2 (1)                         | 2 (1)                                | 3 (1)                                | 1 [1], 3 (1)                                       |                            |
| Piloerection           |                               |                                      |                                      | 1 (1)                                              |                            |
| Hypoactivity           | 5 [1, 2 1/2, 4],<br>5 (1)     | 5 [1, 2 1/2, 4],<br>5 (1), 1 (2 - 3) | 5 [1, 2 1/2, 4],<br>5 (1), 1 (2 - 3) | 5 [1, 2 1/2, 4],<br>5 (1), 3 (2 - 3),<br>2 (4 - 5) | 5 [1, 2 1/2], 4 [4]        |
| Decreased Limb<br>Tone | 3 [1], 4 [2 1/2, 4],<br>3 (1) | 4 [1, 2 1/2], 3 [4],<br>3 (1)        | 2 [1], 3 [2 1/2],<br>5 [4], 5 (1)    | 2 [1, 2 1/2], 4 [4],<br>5 (1), 1 (2 - 3)           | 5 [2 1/2], 4 [4]           |
| Ataxia                 | 4 [1], 5 [2 1/2],<br>2 [4]    | 4 [1], 3 [2 1/2, 4]                  | 3 [1], 2 [2 1/2, 4],<br>1 (1)        | 2 [1], 3 [2 1/2, 4],<br>5 (1), 1 (2 - 3)           | 3 [1], 5 [2 1/2],<br>4 [4] |
| Corneal Opacity        | 2 (1 - 6), 1 (7 - 12)         | 2 (1), 1 (2 - 5)                     | 2 (1), 1 (2 - 5)                     | 4 (1)                                              |                            |
| Death                  | 1 (7)                         |                                      | 2 (2)                                | 2 (2), 1 (4)                                       | 1 [4], 4 (1)               |
|                        |                               |                                      |                                      |                                                    |                            |
|                        |                               |                                      |                                      |                                                    |                            |
|                        |                               |                                      |                                      |                                                    |                            |
|                        |                               |                                      |                                      |                                                    |                            |
|                        |                               |                                      |                                      |                                                    |                            |

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**NUMBER OF RATS SHOWING PHARMACOTOXIC  
SIGNS AND TIME [HOUR] (DAY) OBSERVED**

**TABLE - 1. (Cont.)**

**COMPOUND - FC-143:**

**FEMALES**

| OBSERVATION             | 100 mg/kg                     | 215 mg/kg                         | 464 mg/kg                                       | 1000 mg/kg                                  | 2150 mg/kg                 |
|-------------------------|-------------------------------|-----------------------------------|-------------------------------------------------|---------------------------------------------|----------------------------|
| Normal                  | 5 (2 - 14)                    | 5 (2 - 14)                        | 2 (4 - 14)                                      |                                             |                            |
| Ptosis                  |                               |                                   | 3 (1)                                           | 2 (1)                                       |                            |
| Piloerection            |                               |                                   |                                                 | 3 (1), 1 (2)                                |                            |
| Hypothermic<br>to Touch |                               |                                   | 1 (2 - 3)                                       |                                             |                            |
| Hypoactivity            | 5 [1, 2 1/2, 4],<br>5 (1)     | 5 [1, 2 1/2, 4],<br>5 (1)         | 5 [1, 2 1/2, 4],<br>5 (1), 3 (2 - 3)            | 5 [1, 2 1/2, 4],<br>3 (1), 1 (2)            | 5 [1, 2 1/2], 2 [4]        |
| Decreased<br>Limb Tone  | 4 [1, 2 1/2], 3 [4],<br>3 (1) | 1 [1], 2 [2 1/2],<br>3 [4], 3 (1) | 1 [1], 2 [2 1/2],<br>5 [4], 5 (1),<br>2 (2 - 3) | 2 [1], 4 [2 1/2],<br>5 [4], 3 (1),<br>1 (2) | 5 [2 1/2], 2 [4]           |
| Ataxia                  | 4 [1], 5 [2 1/2],<br>3 [4]    | 4 [1, 2 1/2, 4 ]                  | 2 [1, 2 1/2], 3 [4],<br>3 (1), 2 (2 - 3)        | 4 [1, 2 1/2], 5 [4],<br>3 (1), 1 (2)        | 1 [1], 5 [2 1/2],<br>2 [4] |
| Corneal Opacity         |                               |                                   |                                                 | 1 (1)                                       |                            |
| Death                   |                               |                                   | 2 (2), 1 (4)                                    | 2 (1), 2 (2), 1 (3)                         | 3 [4], 2 (1)               |
|                         |                               |                                   |                                                 |                                             |                            |
|                         |                               |                                   |                                                 |                                             |                            |
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**C. BODY WEIGHTS:**

The following body weights were obtained during the 14 day observation period:

| <u>Dosage Level (mg/kg)</u> | <u>Individual Rat Number</u> | <u>Sex</u> | <u>Control Weight (grams)</u> | <u>7 Day Weight (grams)</u> | <u>14 day Weight (grams)</u> |
|-----------------------------|------------------------------|------------|-------------------------------|-----------------------------|------------------------------|
| 100                         | 76888                        | Male       | 194                           | 242                         | 296                          |
|                             | 76889                        | Male       | 189                           | 228                         | 275                          |
|                             | 76890                        | Male       | 210                           | Died                        | Died                         |
|                             | 76891                        | Male       | 190                           | 240                         | 285                          |
|                             | 76892                        | Male       | 198                           | 246                         | 304                          |
|                             | 76908                        | Female     | 198                           | 217                         | 240                          |
|                             | 76909                        | Female     | 192                           | 212                         | 226                          |
|                             | 76910                        | Female     | 186                           | 208                         | 227                          |
|                             | 76911                        | Female     | 204                           | 225                         | 244                          |
|                             | 76912                        | Female     | 188                           | 191                         | 212                          |
|                             | 76893                        | Male       | 214                           | 266                         | 318                          |
|                             | 76894                        | Male       | 213                           | 267                         | 330                          |
| 215                         | 76895                        | Male       | 212                           | 254                         | 312                          |
|                             | 76896                        | Male       | 210                           | 252                         | 290                          |
|                             | 76897                        | Male       | 203                           | 234                         | 298                          |
|                             | 76913                        | Female     | 195                           | 218                         | 243                          |
|                             | 76914                        | Female     | 182                           | 203                         | 232                          |
|                             | 76915                        | Female     | 190                           | 209                         | 230                          |
|                             | 76916                        | Female     | 185                           | 205                         | 222                          |
|                             | 76917                        | Female     | 182                           | 203                         | 236                          |
|                             | 76898                        | Male       | 215                           | Died                        | Died                         |
|                             | 76899                        | Male       | 202                           | 249                         | 330                          |
|                             | 76900                        | Male       | 216                           | 239                         | 296                          |
|                             | 76901                        | Male       | 218                           | Died                        | Died                         |
| 464                         | 76902                        | Male       | 200                           | 245                         | 302                          |
|                             | 76918                        | Female     | 180                           | 200                         | 227                          |
|                             | 76919                        | Female     | 180                           | Died                        | Died                         |
|                             | 76920                        | Female     | 182                           | 204                         | 223                          |
|                             | 76921                        | Female     | 192                           | Died                        | Died                         |
|                             | 76922                        | Female     | 194                           | Died                        | Died                         |
|                             | 76903                        | Male       | 188                           | 208                         | 270                          |
|                             | 76904                        | Male       | 194                           | Died                        | Died                         |
|                             | 76905                        | Male       | 192                           | Died                        | Died                         |
|                             | 76906                        | Male       | 186                           | Died                        | Died                         |
|                             | 76907                        | Male       | 192                           | 223                         | 290                          |
|                             |                              |            |                               |                             |                              |

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| <u>Dosage<br/>Level<br/>(mg/kg)</u> | <u>Individual<br/>Rat Number</u> | <u>Sex</u> | <u>Control<br/>Weight<br/>(grams)</u> | <u>7 Day<br/>Weight<br/>(grams)</u> | <u>14 Day<br/>Weight<br/>(grams)</u> |
|-------------------------------------|----------------------------------|------------|---------------------------------------|-------------------------------------|--------------------------------------|
| 1000                                | 76923                            | Female     | 202                                   | Died                                | Died                                 |
|                                     | 76924                            | Female     | 180                                   | Died                                | Died                                 |
|                                     | 76925                            | Female     | 184                                   | Died                                | Died                                 |
|                                     | 76926                            | Female     | 198                                   | Died                                | Died                                 |
|                                     | 76927                            | Female     | 196                                   | Died                                | Died                                 |
| 2150                                | 77208                            | Male       | 206                                   | Died                                | Died                                 |
|                                     | 77209                            | Male       | 213                                   | Died                                | Died                                 |
|                                     | 77210                            | Male       | 208                                   | Died                                | Died                                 |
|                                     | 77211                            | Male       | 211                                   | Died                                | Died                                 |
|                                     | 77212                            | Male       | 213                                   | Died                                | Died                                 |
|                                     | 77213                            | Female     | 221                                   | Died                                | Died                                 |
|                                     | 77214                            | Female     | 213                                   | Died                                | Died                                 |
|                                     | 77215                            | Female     | 217                                   | Died                                | Died                                 |
|                                     | 77216                            | Female     | 219                                   | Died                                | Died                                 |
|                                     | 77217                            | Female     | 206                                   | Died                                | Died                                 |

D. NECROPSY FINDINGS:

Gross necropsy observations were noted as indicated on pages 9, 10 and 11.

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## 1. Rats which died during the study period:

Dosage Level (mg/kg)  
Number Exhibiting Sign/Number Necropsied

| Gross Necropsy<br>Observations:                                   | 100  |        | 215  |        | 464  |        | 1000 |        | 2150 |        |
|-------------------------------------------------------------------|------|--------|------|--------|------|--------|------|--------|------|--------|
|                                                                   | Male | Female | Male | Female | Male | Female | Male | Female | Male | Female |
| Yellow stained<br>urogenital<br>region                            |      |        |      |        |      |        |      | 2/5    | 3/5  | 2/5    |
| Lungs, conges-<br>tion                                            | 1/1  |        |      |        | 2/2  | 1/3    | 2/3  | 4/5    | 4/5  | 5/5    |
| Lungs, pitted                                                     |      |        |      |        |      |        |      |        | 2/5  |        |
| Lungs, red<br>foci                                                |      |        |      |        |      |        |      |        |      | 1/5    |
| Stomach, dis-<br>tension                                          |      |        |      |        |      | 1/3    | 2/3  | 4/5    | 5/5  | 3/5    |
| Stomach,<br>fluid filled                                          |      |        |      |        |      | 1/3    |      |        | 5/5  | 4/5    |
| Stomach, mu-<br>cosa, hyper-<br>emia                              |      |        |      |        |      | 3/3    | 1/3  | 1/5    | 4/5  | 1/5    |
| Stomach, mu-<br>cosa, thick-<br>ened                              |      |        |      |        |      | 2/3    | 2/3  |        |      |        |
| Stomach, con-<br>tains dark<br>red fluid                          |      |        |      |        |      | 1/3    |      |        |      |        |
| Stomach, glan-<br>dular mucosa,<br>erosion                        |      |        |      |        |      | 1/3    |      |        |      |        |
| Stomach, con-<br>tains dark<br>red parti-<br>culate ma-<br>terial |      |        |      |        |      |        |      |        | 1/5  |        |
| Stomach, red<br>fluid filled                                      |      |        |      |        |      |        |      |        |      | 1/5    |

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| Gross Necropsy<br>Observations:    | Dosage Level (mg/kg)<br>Number Exhibiting Sign/Number Necropsied |        |      |        |      |        |      |        |      |        |
|------------------------------------|------------------------------------------------------------------|--------|------|--------|------|--------|------|--------|------|--------|
|                                    | 100                                                              |        | 215  |        | 464  |        | 1000 |        | 2150 |        |
|                                    | Male                                                             | Female | Male | Female | Male | Female | Male | Female | Male | Female |
| Intestines, red<br>fluid filled    |                                                                  |        |      |        |      |        |      |        | 2/5  | 1/5    |
| Liver, pale<br>coloration          |                                                                  |        |      |        |      |        |      |        | 1/5  |        |
| Partially,<br>cannibalized         | 1/1                                                              |        |      |        |      |        |      |        |      |        |
| Red stain<br>around nose/<br>mouth |                                                                  |        |      |        |      |        |      |        | 3/5  | 4/5    |

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## 2. Rats which were sacrificed following 14 days of observation:

|                                      | Dosage Level (mg/kg)                     |        |      |        |      |        |      |        |
|--------------------------------------|------------------------------------------|--------|------|--------|------|--------|------|--------|
|                                      | Number Exhibiting Sign/Number Necropsied |        |      |        |      |        |      |        |
|                                      | 100                                      |        | 215  |        | 464  |        | 1000 |        |
| Gross Necropsy Observations:         | Male                                     | Female | Male | Female | Male | Female | Male | Female |
| No gross lesions                     |                                          |        |      |        | 1/3  | 1/2    | 1/2  |        |
| Lungs, foci                          |                                          |        |      | 1/5    |      |        |      |        |
| Stomach, mucosa, thickened           | 4/4                                      | 5/5    | 5/5  | 4/5    | 2/3  | 1/2    | 1/2  |        |
| Stomach, glandular mucosa, hyperemia | 1/4                                      | 2/5    | 1/5  | 1/5    |      |        | 1/2  |        |
| Uterus, hydrometra                   |                                          | 1/5    |      | 2/5    |      |        |      |        |
| Kidneys, mottled coloration          | 2/4                                      | 2/5    | 3/5  | 4/5    | 1/3  |        | 1/2  |        |