

US EPA ARCHIVE DOCUMENT



*This change was given orally to Karen Cannon today via telephone.* CASWELL FILE

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY  
WASHINGTON, D.C. 20460

*E. Wilson*  
B-6-90 008272

MAR -4 1991

MEMORANDUM

OFFICE OF PESTICIDES AND TOXIC SUBSTANCES

SUBJECT: Dithiopyr -- Data from Subchronic Feeding Studies, Submitted under MRID No. 416895-01 and -02

Chemical (Caswell) 7470  
RD Record No. S 36589  
HED Project 1-0153

FROM: Irving Mauer, Ph.D., Geneticist  
Toxicology Branch-I (IRS)  
Health Effects Division (H7509C)

*Irving Mauer*  
12-18-90

TO: Eugene Wilson, PM 23  
Herbicide-Fungicide Branch  
Registration Division (H7505C)

THRU: Karl P. Baetcke, Ph.D., Chief  
Toxicology Branch-I (IRS)  
Health Effects Division (H7509C)

*Karl P. Baetcke*  
2/21/91

Registrant: Monsanto, St. Louis MO

Request : Under cover of November 12, 1990, the registrant has submitted the following tox. studies for review and evaluation:

- (1) Dithiopyr (MON-7200): Subchronic Feeding Study in Rats (Study No. ET-86-187, Final Report dated May 17, 1986), designated R.D. No. 1022 (EPA MRID No. 41689501)
- (2) Dithiopyr (MON-7200): Subchronic Feeding Study in Dogs (Study No. ET-86-376, Final Report dated June 7, 1988), designated R.D. No. 1024 (EPA MRID No. 41689502), .....

... both performed for Monsanto by the Institute of Environmental Toxicology (ET), Tokyo (Japan).

RD requests that these studies be reviewed expeditiously, said expedite request to be forthcoming from the Director's office.

Dietary Effects of Dithiopyr (MON-7200) Fed Fischer-344 Rats (12/Sex/Group) for 13 Weeks<sup>1/</sup> (cont'd)

| Observation                | Dose Level (ppm) |      |      |      |      |        |        |        |        |        |   |   |      |   |  |
|----------------------------|------------------|------|------|------|------|--------|--------|--------|--------|--------|---|---|------|---|--|
|                            | 0                |      |      | 10   |      |        | 100    |        |        | 1000   |   |   | 5000 |   |  |
|                            | M                | F    | M    | F    | M    | F      | M      | F      | M      | F      | M | F | M    | F |  |
| <u>Clinical Chemistry:</u> |                  |      |      |      |      |        |        |        |        |        |   |   |      |   |  |
| ALP                        | 250              | 177  | 255  | 168  | 227* | 160    | 231    | 142*   | 576**  | 302*   |   |   |      |   |  |
| GGTP                       | 1.3              | 1.1  | 1.2  | 0.9  | 1.2  | 0.9    | 1.3    | 0.9    | 2.5**  | 2.6**  |   |   |      |   |  |
| TP                         | 6.27             | 6.06 | 6.27 | 6.05 | 6.22 | 6.40*  | 6.63** | 6.49** | 6.30   | 6.89** |   |   |      |   |  |
| Alb                        | 3.09             | 3.15 | 3.04 | 3.13 | 3.05 | 3.55** | 3.38*  | 3.35   | 3.79** | 4.07** |   |   |      |   |  |
| Glob                       | 3.18             | 2.91 | 3.23 | 2.91 | 3.17 | 2.86   | 3.26   | 3.13** | 2.52** | 2.81   |   |   |      |   |  |
| Glu                        | 146              | 124  | 131  | 121  | 134  | 117    | 150    | 126    | 118**  | 135*   |   |   |      |   |  |
| T. Chol.                   | 39               | 64   | 40   | 64   | 43   | 70**   | 62**   | 83**   | 67**   | 102**  |   |   |      |   |  |
| TG                         | 75               | 37   | 75   | 36   | 71   | 30**   | 55     | 36     | 21**   | 22**   |   |   |      |   |  |
| BUN                        | 15.2             | 14.9 | 15.3 | 15.9 | 14.7 | 14.8   | 16.8   | 15.0   | 18.6** | 21.4** |   |   |      |   |  |
| Creat.                     | 0.64             | 0.67 | 0.65 | 0.66 | 0.61 | 0.63   | 0.64   | 0.66   | 0.45** | 0.59** |   |   |      |   |  |
| T. Bil.                    | 0.12             | 0.12 | 0.13 | 0.12 | 0.13 | 0.12   | 0.14   | 0.12   | 0.16** | 0.11   |   |   |      |   |  |
| Na                         | 147              | 146  | 147  | 146  | 147  | 146    | 146    | 145    | 144**  | 144    |   |   |      |   |  |
| K                          | 3.32             | 3.32 | 3.14 | 3.09 | 3.36 | 2.96   | 3.36   | 3.05   | 3.76** | 3.42   |   |   |      |   |  |
| P                          | 4.9              | 3.6  | 4.9  | 3.4  | 5.0  | 3.7    | 5.1    | 3.6    | 5.5**  | 4.2    |   |   |      |   |  |
| <u>Gross Pathology:</u>    |                  |      |      |      |      |        |        |        |        |        |   |   |      |   |  |
| Enl. liver                 | 0                | 0    | 0    | 0    | 0    | 0      | 5*     | 1      | 12**   | 12**   |   |   |      |   |  |
| Dk. kidneys                | 0                | 0    | 0    | 0    | 0    | 0      | 0      | 0      | 9**    | 12**   |   |   |      |   |  |
| Pale adrenals              | 0                | 0    | 0    | 0    | 0    | 0      | 0      | 0      | 12**   | 0      |   |   |      |   |  |

<sup>1/</sup> Selected (positive) findings extracted from Tables 1 through 28 and Appendices 1 through 22 of the Final Report (ET-86-187).

\*Significantly different from control at  $p < 0.05$ .

\*\*Significantly different from control at  $p < 0.01$ .

Dietary Effects of Dithiopyr (MON-7200) Fed Fischer-344 Rats (12/Sex/Group) for 13 Weeks<sup>1/</sup> (cont'd)

| Observation                  | Dose Level (ppm) |      |        |      |      |        |         |        |         |         |   |   |      |   |  |
|------------------------------|------------------|------|--------|------|------|--------|---------|--------|---------|---------|---|---|------|---|--|
|                              | 0                |      |        | 10   |      |        | 100     |        |         | 1000    |   |   | 5000 |   |  |
|                              | M                | F    | M      | M    | F    | M      | M       | F      | M       | M       | F | M | M    | F |  |
| <u>Absolute Organ Wt:</u>    |                  |      |        |      |      |        |         |        |         |         |   |   |      |   |  |
| Brain (mg)                   | 1893             | 1733 | 1911   | 1739 | 1867 | 1759   | 1907    | 1776   | 1785**  | 1735    |   |   |      |   |  |
| Pit. (mg)                    | 8.8              | 11.9 | 8.8    | 12.1 | 9.0  | 12.1   | 8.5     | 13.0   | 7.1**   | 9.9     |   |   |      |   |  |
| Thyroid (mg)                 | 15.0             | 11.8 | 16.5   | 12.3 | 15.6 | 13.7   | 18.3**  | 14.3*  | 17.7*   | 18.9*   |   |   |      |   |  |
| Thymus (mg)                  | 173              | 163  | 178    | 174  | 169  | 176    | 170     | 168    | 107**   | 132*    |   |   |      |   |  |
| Heart (mg)                   | 869              | 581  | 880    | 580  | 880  | 581    | 894     | 613*   | 690**   | 591     |   |   |      |   |  |
| Liver (g)                    | 7.79             | 4.35 | 7.83   | 4.28 | 7.98 | 5.38** | 10.25** | 5.21** | 14.58** | 11.70** |   |   |      |   |  |
| Kidneys (mg)                 | 1876             | 1155 | 1886   | 1168 | 1907 | 1231*  | 2054*   | 1267** | 1971    | 1473**  |   |   |      |   |  |
| Spleen (mg)                  | 552              | 377  | 560    | 405  | 567  | 397    | 538     | 391    | 354**   | 320**   |   |   |      |   |  |
| Testes (mg)                  | 2769             | --   | 2815   | --   | 2826 | --     | 2862    | --     | 2897    | --      |   |   |      |   |  |
| Ovaries (mg)                 | --               | 57.7 | --     | 60.1 | --   | 62.4   | --      | 67.2** | --      | 60.8    |   |   |      |   |  |
| Adrenals (mg)                | 42.5             | 53.9 | 47.1** | 54.3 | 44.2 | 58.5*  | 46.3*   | 58.2*  | --      | 60.4**  |   |   |      |   |  |
| <u>Histopathology:</u>       |                  |      |        |      |      |        |         |        |         |         |   |   |      |   |  |
| (No.)                        |                  |      |        |      |      |        |         |        |         |         |   |   |      |   |  |
| Lung (foam cells)            | 0                | 0    | 0      | 0    | 0    | 0      | 0       | 0      | 7**     | 0       |   |   |      |   |  |
| Liver                        |                  |      |        |      |      |        |         |        |         |         |   |   |      |   |  |
| - Swelling                   | 0                | 0    | 0      | 0    | 0    | 12**   | 12**    | 12**   | 12**    | 12**    |   |   |      |   |  |
| - Granule                    | 0                | 1    | 0      | 3    | 0    | 0      | 0       | 1      | 3       | 2       |   |   |      |   |  |
| - Bile duct proliferation    | 0                | 0    | 0      | 0    | 0    | 0      | 1       | 1      | 1       | 7*      |   |   |      |   |  |
| Kidneys                      |                  |      |        |      |      |        |         |        |         |         |   |   |      |   |  |
| - Tubul. atrophy             | 8                | 1    | 9      | 1    | 11   | 1      | 12      | 6*     | 12      | 12**    |   |   |      |   |  |
| - Casts                      | 0                | 0    | 1      | 0    | 0    | 0      | 9*      | 1      | 11**    | 12**    |   |   |      |   |  |
| Thyroid                      |                  |      |        |      |      |        |         |        |         |         |   |   |      |   |  |
| - Hypertrophy                | 0                | 0    | 0      | 0    | 0    | 2      | 7*      | 6*     | 11**    | 12**    |   |   |      |   |  |
| Adrenal cortical hypertrophy | 0                | 0    | 0      | 0    | 0    | 2      | 0       | 5*     | 12**    | 8**     |   |   |      |   |  |

<sup>1/</sup> Selected (positive) findings extracted from Tables 1 through 28 and Appendices 1 through 22 of the Final Report (ET-86-187).

\*Significantly different from control at p < 0.05.

\*\*Significantly different from control at p < 0.01.