This change was given
Orally to Keven Cannon
Today via telephone.

CASWELL FILE

E. Wilson 2-6-90

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

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)
RD Record No. S
HED Project 1-0153

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

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)

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[1/] (cont'd)

Observation	Dose Level (ppm)									
	0		10		100		1000		5000	
	M	F	M	F	M	F	M	F	M	F
Clinical Chemistry:										
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
Gross Pathology:										
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

[1/] 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[1/] (cont'd)

Observation	Dose Level (ppm)									
	0		10		100		1000		5000	
	M	F	M	F	M	F	M	F	M	F
Absolute Organ Wt:										
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*	39.6	60.4**
Histopathology: (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**

[1/] 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 $p < 0.01$.