

US EPA ARCHIVE DOCUMENT

11-13-84



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

004091

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: Alachlor (Lasso), EPA Reg. #524-316, EPL's
Re-Evaluation of Nasal cavity Lesions in a
2-year chronic study in rats # ML-80-186
(8002184), by Monsanto

TO: Robert Taylor
Product Manager (25)
Registration Division (TS-767C)

FROM: Amal Mahfouz, Ph.D. *Amal Mahfouz 11/10/84*
Toxicology Branch
Hazard Evaluation Division (TS-769C)

THRU: Laurence D. Chitlik, DABT *LDC 11/13/84*
Head, Review Section V
Toxicology Branch
Hazard Evaluation Division (TS-769C)

and

William L. Burnam, Chief
Toxicology Branch
Hazard Evaluation Division (TS-769C)

Submucosal nasal hyperplasia was noted in a recently submitted and reviewed low dose chronic feeding/oncogenic study in rats with Alachlor, see page 22 of my 4/17/84 review of this study (study # ML-80-186 by Monsanto, Environmental Health Laboratory, 2/12/84).

The Agency requested a histological re-evaluation of the above mentioned finding in order to determine if these lesions were hyperplasia or neoplasia. A histological re-evaluation of tissues of the nasal cavity was performed by Experimental Pathology Laboratories, Inc. (EPL) at the Research Triangle Park facility. The newly submitted EPL report dated 10/12/84 (which was forwarded to the Toxicology Branch on 11/1/84) indicated that the submucosal nasal lesions were not neoplastic lesions.

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However, this report reflected a slight increase in the previously reported incidences of papillary adenoma at 15 mg/kg/day dosage level (papillary adenoma was also reported as respiratory epithelium adenoma in the original final report of study # ML-80-186). The updated incidences of this nasal tumor is presented in the table below:

Study # ML-80-186 (800218)

Incidences of Nasal Turbinate Tumors (adenoma)

<u>Dosage</u> mg/kg/day	<u>EPL's data</u> (10/12/84)		<u>Monsanto's data</u> (2/12/84)	
	<u>Males</u>	<u>Females</u>	<u>Males</u>	<u>Females</u>
0.0	0/44	0/42	0/45	0/42
0.5	0/47	0/42	0/48	0/44
2.5	0/44	1/47	0/45	1/47
15.0	15/45	14/48	11/45	9/48

Please note that the EPL data need to be included in the 2 tables on pages 23 and 24 of my 10/24/84 review of the special chronic study (high dose), # ML-80-224, by Monsanto. Copies of these 2 pages (with the updated incidences of nasal turbinate tumors in study # ML-80-186) are attached to this memo.

Attachment: 2

cc: R. Engler
B. Litt
G. Rurin

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Dosage mg/kg/day	Study #ML-80-224		Study #ML-80-186 **						Study #BD-77-421									
	126	GIII*	0	.5	2.5	15	0	14	42	126								
No. of tissues examined and incidence of animals with tumors:	M	F	M	F	M	F	M	F	M	F	M	F						
<u>Nasal turbinate tumors</u>	61	25	17	46	44	42	47	42	44	47	46	47	41	45	42	48		
°adenoma	42	11	10	19	0	0	0	0	1	15	14	0	0	0	10	4	23	10
°adenocarcinoma	7	2	0	1	0	0	0	0	0	0	0	0	0	0	1	1	0	0
<u>Stomach</u>	68	31	20	49	50	50	50	50	49	48	49	50	50	50	50	50	50	50
°malignant tumors	3	19	0	1	0	0	1	0	0	0	0	0	0	0	0	1	17	23
- mixed carcinosarcoma	2	6	-	-	-	-	-	-	-	-	-	-	-	-	-	-	1	11
- undifferentiated sarcoma	-	5	-	1	-	-	1	-	-	-	-	-	-	-	-	-	-	-
- undifferentiated carcinoma	-	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
- adenocarcinoma	-	3	-	-	-	-	-	-	-	-	-	-	-	-	-	-	2	1
- Leiomyosarcoma	-	3	-	-	-	-	-	-	-	-	-	-	-	-	-	-	1	1
- Anaplastic sarcoma	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
- Osteosarcoma	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	3	4
<u>Thyroid</u>	70	31	20	49	49	49	49	49	49	47	48	49	50	44	49	46	50	49
°C-cell adenoma	4	3	1	2	5	2	3	2	7	4	6	3	4	2	5	3	2	4
carcinoma	0	0	0	1	0	0	0	1	0	0	0	1	0	1	0	0	1	0
°Follicular adenoma	8	4	1	3	2	1	4	1	3	0	4	2	1	0	0	1	2	11
carcinoma	10	0	1	1	1	3	0	1	1	1	2	1	0	0	0	0	0	2
<u>Brain</u>	70	31	20	49	50	50	50	50	49	49	50	50	50	50	50	50	50	50
°Neuroepithelioma	1	1	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
<u>Liver</u>	70	31	20	49	50	50	50	50	50	49	50	50	50	50	50	50	50	50
°Hepatoma	3	1	0	0	1	0	0	1	0	0	0	0	1	0	0	0	2	1
°Nodular hyperplasia	0	1	0	1	0	0	0	0	0	0	1	0	2	0	1	1	2	4
°Carcinoma	2	2	0	1	2	0	1	2	0	0	2	0	0	0	0	0	0	0

*GI: animals maintained on treated diets for 2-year; GIII: animals maintained on treated diets for only 5 to 6 months.

** After the 10/17/74 EPL administration.

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Dosage mg/kg/day	Study #ML-80-224				Study #ML-80-186**					Study #BD-77-421										
	GI*		GIII*		0		.5		2.5		15		0		14		42		126	
	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F
No. of tissues examined and % incidence of animals with tumors:	61	25	17	46	44	42	47	42	44	47	45	48	46	49	46	47	41	45	42	48
Nasal turbinate tumors	69	44	59	41	0	0	0	2	33	29	0	0	0	0	0	0	24	9	55	21
°adenoma	12	8	0	2	0	0	0	0	0	0	0	0	0	0	0	0	2	2	0	0
°carcinoma	68	31	20	49	50	50	50	50	49	48	49	50	50	50	50	50	50	50	50	50
Stomach	4	61	0	2	0	0	0	2	0	0	0	0	0	0	0	0	0	2	34	46
°malignant tumors	3	19	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	22	34
- mixed carcinosarcoma	-	16	-	2	-	-	-	2	-	-	-	-	-	-	-	-	-	-	-	-
- undifferentiated sarcoma	-	3	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
- undifferentiated carcinoma	-	10	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	4	2
- adenocarcinoma	-	10	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	2	2
- Leiomyosarcoma	1	3	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
- Anaplastic sarcoma	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	8
- Osteosarcoma	70	31	20	49	49	49	50	49	49	49	49	47	48	49	50	44	49	46	50	49
Thyroid	6	10	5	4	10	4	6	4	14	8	12	6	8	4	10	7	4	9	14	6
°C-cell adenoma	0	0	0	2	0	0	0	2	0	0	0	0	2	0	2	0	0	2	0	0
carcinoma	11	13	5	6	4	2	8	2	6	0	8	4	2	0	0	0	2	4	22	4
°Follicular adenoma	14	0	5	2	2	6	0	2	2	4	2	2	0	0	0	0	0	0	4	4
carcinoma	70	31	20	49	50	50	50	50	49	49	49	49	50	50	50	50	50	50	50	50
Brain	1	3	0	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
°Neuroepithelioma*	70	31	20	49	50	50	50	50	50	50	50	49	50	50	50	50	50	50	50	50
Liver	4	3	0	0	2	0	0	2	0	0	0	0	2	0	0	0	4	2	2	6
°Hepatoma	0	3	0	2	0	0	0	0	0	0	0	2	0	4	0	2	2	4	8	2
°Nodular hyperplasia	3	7	0	2	4	0	2	2	2	0	0	4	0	0	0	0	0	0	0	0
°Carcinoma																				

*GI: animals maintained on treated diets for 2-year; GIII: animals maintained on treated diets for only 5 to 6 months.

** After EPL's corrections.