



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

11/19/84

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OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

Caswell # 11

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) *WFB 11/15/84*

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> <u>mg/kg/day</u>	<u>EPL's data</u> <u>(10/12/84)</u>		<u>Monsanto's data</u> <u>(2/12/84)</u>	
	<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. Burin

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Dosage mg/kg/day	No. of tissues examined and incidence of animals with tumors:	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										
Nasal turbinate tumors																															
		61	25	17	46	44	42	47	42	44	47	45	48	46	49	46	47	41	45	42	48										
°adenoma																															
		42	11	10	19	0	0	0	0	0	1	15	14	0	0	0	0	0	10	4	23	10									
°adenocarcinoma																															
		7	2	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	0	0									
Stomach																															
		68	31	20	49	50	50	50	50	50	49	48	49	50	50	50	50	50	50	50	50	50									
°malignant tumors																															
		3	19	0	1	0	0	0	0	1	0	0	0	0	0	0	0	0	1	17	23										
- mixed carcinosarcoma																															
		2	6	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	1	11	17									
- undifferentiated sarcoma																															
		-	5	-	1	-	-	-	1	-	-	-	-	-	-	-	-	-	-	-	-	-									
- undifferentiated carcinoma																															
		-	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-									
- adenocarcinoma																															
		-	3	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-									
- leiomyosarcoma																															
		-	3	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-									
- Anaplastic sarcoma																															
		1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-									
- Osteosarcoma																															
		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-									
Thyroid																															
		70	31	20	49	49	49	50	49	49	49	47	48	49	50	44	49	46	50	49											
°C-cell adenoma carcinoma																															
		4	3	1	2	5	2	3	2	7	4	6	3	4	2	5	3	2	4	7	3										
		0	0	0	1	0	0	0	0	1	0	0	1	0	1	0	1	0	1	0	0										
°Follicular adenoma carcinoma																															
		8	4	1	3	2	1	4	1	3	0	4	2	1	0	0	0	1	2	11	2										
		10	0	1	1	1	3	0	1	1	1	2	1	0	0	0	0	0	0	2											
Brain																															
		70	31	20	49	50	50	50	50	49	49	50	50	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	0	0										
Liver																															
		70	31	20	49	50	50	50	50	50	50	49	50	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	1	3										
°Nodular hyperplasia																															
		0	1	0	1	0	0	0	0	0	0	1	0	2	0	2	0	1	2	4	1										
°Carcinoma																															
		2	2	0	1	2	0	1	1	2	0	2	0	0	0	0	0	0	0	0	0										

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

** After 10/12/74 EPL Ambrosini

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

*GI: animals maintained on treated diets for 2-years, maintained on treated diets for only 5 to 6 months.