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

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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) *Hyw 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> 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. Burin

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*	GI**	GI**	GI**	0	.5	2.5	15	**	0	14	42	126								
	<u>Nasal turbinate tumors</u>	M 61	F 25	M 17	F 46	M 44	F 42	M 47	F 42	M 44	F 47	M 45	F 48	M 46	F 49	M 46	F 47	M 41	F 45	M 42	F 48	
	° adenoma	42	11	10	19	0	0	0	0	1	15	14	0	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
	<u>Stomach</u>	68	31	20	49	50	50	50	50	49	48	49	50	50	50	50	50	50	50	50	50	50
	° malignant tumors	3	19	0	1	0	0	0	1	0	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	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	2	
	- leiomyosarcoma	-	3	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	1	
	- Anaplastic sarcoma	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
	- Osteosarcoma	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	3	
	<u>Thyroid</u>	70	31	20	49	49	49	50	49	49	47	48	49	50	50	44	49	46	50	49	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	
	° Follicular adenoma carcinoma	8	4	1	3	2	1	4	1	3	0	4	2	1	0	0	0	1	2	11	2	
	° Follicular carcinoma	10	0	1	1	1	3	0	1	1	1	2	1	0	0	0	0	0	0	2	2	
	<u>Brain</u>	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	
	<u>Liver</u>	70	31	20	49	50	50	50	50	50	49	50	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	1	0	1	0	2	0	1	2	4	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; GI\*\* animals maintained on treated diets for only 6 months.  
 \*\* After 10/12/74 EPL Ambviss.

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

\*GI: animals maintained on treated diets for 2-year; GIIT: animals maintained on treated diets for only 6 to 6 months.  
 \*\*After UPL's corrections.