5/23/82

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

001884

MEMORANDUM

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

TO: Robert Taylor (25)
Registration Division (TS-767)
and
Residue Chemistry Branch
Hazard Evaluation Division (TS-769)

SUBJECT: Bladex; PP#9F2232; Bladex in/on Soybeans; 2-Year Mouse Oncogenicity Study CASWELL#188C
Accession Nos: 247295-298

Recommendations:

1) The following studies are required to support the requested tolerances:

(a) rat teratology
(b) rabbit teratology

2) The mouse oncogenicity study is acceptable as Core-Minimum Data. Bladex was not oncogenic to mice up to 1000 ppm in the diet.

Review:

1) A 2-Year Feeding Study of Bladex in Mice (Sittingbourne Research Centre Report#SBGR. 81.171; December, 1981)

Test Material: Bladex technical; Batch No. 8-21-0-0

Bladex was fed to male and female CD mice for up to 2 years at dietary concentrations of 0, 10, 25, 250 and 1000 ppm. The experimental design is shown below:

Bladex Technical ppm in diet	Number of Mice Male	Female
0	100	100
10	50	50
25	50	50
1000	50	50

1 of 3

Criteria evaluated included toxic signs, mortality, body weight and food consumption. At necropsy, organs were weighed, and gross and microscopic examination of organs and tissues was performed.

Terminal blood samples were taken for hematology and clinical chemistry analyses.

Statistical analyses of the data were performed.

Results:

No specific treatment-related toxic signs were noted but in females of the 250 and 1000 ppm groups, poor condition and skin sores were observed more frequently than in other groups. There were dose-related decreases in body weight of both sexes from 10-1000 ppm during the study and at termination. The frequency of reduced food consumption was also dose-related. Survival was greater than 50% for both sexes of all groups at 15 months. Male survival was unaffected by treatment but survival in the 250 and 1000 ppm female groups was lower than in the female controls. Relative brain weight was increased for the 250 and 1000 ppm males and females. Relative liver weight was increased for the 250 and 1000 ppm females. Relative heart weight was increased for the 1000 ppm males and females.

Relative kidney weight was increased for the 1000 ppm females and relative testes weight was increased in the 1000 ppm males.

Significant decrease in blood glucose and increase in total protein was noted in the female of the 1000 ppm group.

Anemia was present in the 1000 ppm female. Decrease in both absolute and differential leucocyte values were present in both males and females at 250 and 1000 ppm.

The onset, type and incidence of tumors was comparable between the control and treated groups.

The table below shows the incidences of the different types of lymphoreticular tumors:

		INCIDENCE OF TUMORS									
		MALES					FEMALES				
	Dietary conc. (ppm)	0	10	25	250	1000	0	10	25	250	1000
TUMORS	Number of Animals	100	50	50	50	50	100	50	50	50	50
Lymphoreticular Tissues											
Lymphoblastic lymphosarcoma		5	1	1	2	3	9	5	3	6	4
Reticulum cell sarcoma		2	2	1	2	3	3	4	4	3	3
Stem cell leucemia		1	1		1	1	1			2	1
Myeloid leucemia		1	1	1	1		1	1			
Erythroblastic sarcoma					1		1				
Spleen - Hemangiosarcoma		1	4	2			1				
Spleen - Hemangioendothelioma							1				
Popliteal L.N. - Hemangiosarcoma						1					

When the incidence of tumors of individual sites was subjected to statistical analysis, the only statistically significant conclusion related to splenic hemangiosarcomas in male mice. This inference was due to the increase in incidence of the 10 ppm group. Since no splenic hemangiosarcomas were identified in males fed dietary concentrations of 250 and 1000 ppm and no tumors of this type, of this site, were recorded in any females fed the test compound, it is concluded that the above observation is a chance occurrence and of no biological significance.

Conclusion:

Bladex technical was not oncogenic to mice at dietary levels up to 1000 ppm.

Classification: Core-Minimum Data

5/18/82

William Dykstra, Ph.D WRD for LDC
Toxicology Branch
Hazard Evaluation Division (TS-769)

TS-769:th:TOX/HED:WDykstra:5-18-82:Rm. 820:77395:card 5