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

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AUG 9 1988

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: Maneb Data Call-In; Update - Translation of German Document; Urinary Bladder Effects

TO: Lois Rossi
Product Manager (21)
Registration Division (TS-767C)

FROM: Linda L. Taylor, Ph.D. *Linda Taylor 8/4/88*
Toxicology Branch, Section III
Hazard Evaluation Division (TS-769C)

THROUGH: Marcia van Gemert, Ph.D. *Marcia van Gemert 8/4/88*
Section III, Head
Toxicology Branch, HED (TS-769C)

and

Theodore M. Farber, Ph.D.
Chief, Toxicology Branch, HED (TS-769C) *Theodore M. Farber*

Chemical: Maneb
Caswell No.: 539
Record No.: 229207
Project No.: 9-0844
Registrant: Pennwalt Corporation
Action Requested: Review of paper submitted in support of the 31-month rat chronic feeding study.

Comment: Pennwalt Corporation has submitted a translation of the German paper cited in the 31-month rat chronic feeding study, as requested. This paper was cited as relevant to the findings of the chronic study (particularly those relating to the urinary bladder). The title of the paper is "On The Problems of Nephrotoxicity Caused by Human Drugs." This reviewer fails to see the relevance of this paper. It states that, in effect, without data from human testing, effects in laboratory animals are meaningless, or difficult to interpret.

Following a discussion of the urinary bladder data with Dr. Blaughter (EPA pathologist), it was determined that further clarification of the urinary bladder data is needed.

In an amendment to the final report regarding the findings of the toxicity

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bladder, the Study Director indicated that the papillomas, precancerous dysplasia, and inceptive carcinomas described for the control and high-dose groups in the original final report should be compared with the term - partly papillary-like hyperplasia, used to describe the findings in the other three dose groups in the amended final report (examinations performed by a different pathologist than the one who examined the control and high-dose groups).

The attached tables list the urinary bladder findings (for males only). Table A lists the findings for the control and high-dose groups (from the original final report), and Table B lists those for the other dose levels (from the amendment).

The Registrant should be requested to submit the urinary bladder findings for the control and high-dose males using the terminology used for the lower dose groups. A description of the morphological criteria used to classify the lesions should also be submitted, along with a comparison of the original findings.

No change in the classification of this study can be made at this time pending submission of these data.

TABLE A

Animal #	Urinary Bladder Finding	Week of Dissection
CONTROL MALES (11)		
3	precancerous dysplasia	132
4	precancerous dysplasia	93
14	precancerous epithelial dysplasia	103
19	carcinoma	120
20	cysto-papillary tumor	114
29	precancerous dysplasia	90
32	precancerous dysplasia	132
33	precancerous dysplasia	100
60	precancerous dysplasia	132
HIGH-DOSE MALES (17)		
4	precancerous dysplasia papilloma	132
8	precancerous dysplasia	122
9	precancerous dysplasia	132
14	pavement carcinoma	132
19	papilloma	177
	increased epithelial dysplasia	
20	moderate epithelial dysplasia	104
22	moderate epithelial dysplasia ulcus	113
23	moderate epithelial dysplasia	93
31	increased epithelial dysplasia ulcus	132
32	precancerous dysplasia ulcus	122
35	precancerous dysplasia ulcus	122
39	squamous epithelial carcinoma	95
41	papilloma	137
44	precancerous dysplasia	127
50	precancerous dysplasia	104
51	precancerous dysplasia	132
54	precancerous dysplasia	111
50	precancerous dysplasia ulcus, myopathy	132
65	moderate epithelial dysplasia ulcus	132
66	moderate epithelial dysplasia	93
69	carcinoma of squamous epithelium	124
71	precancerous dysplasia	97

TABLE B

006838

Animal #	Urinary Bladder Finding	Week of Dissection
LOW-DOSE MALES (II)		
12	mucosal hyperplasia	128
19	papillary mucosal hyperplasia	131
29	hemorrhagic cystitis	130
44	mucosal hyperplasia	132
54	mucosal hyperplasia	129
62	mucosal hyperplasia	91
66	mucosal hyperplasia	122
LOW-DOSE MALES (III)		
1	inflammatory infiltration	123
3	hemorrhagic cystitis	125
11	ectasia	97
18	mucosal hyperplasia	106
54	mucosal hyperplasia	130
67	mucosal hyperplasia	131
68	mucosal hyperplasia	130
MID-DOSE MALES (IV)		
10	mucosal hyperplasia	128
32	hemorrhagic cystitis	132
44	mucosal hyperplasia	130
48	mucosal hyperplasia	132
62	mucosal hyperplasia	132
63	papillary mucosal hyperplasia	132
65	mucosal hyperplasia	131