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

OFFICE OF
PREVENTION, PESTICIDES, AND
TOXIC SUBSTANCES

TXR NO. 0052000

MEMORANDUM

DATE: July 16, 2003

SUBJECT: PHMB Cancer Peer Review: Pathology Working Group (PWG) Peer Review of Proliferative Vascular Lesions in Male and Female Rats

PC code: 111801

FROM: Jessica Kidwell, Executive Secretary, Cancer Assessment Review Committee
Science Information Management Branch
Health Effects Division (7509C)

Jessica Kidwell

TO: William Burnam, Chair, Cancer Assessment Review Committee
Immediate Office
Health Effects Division (7509C)

Attached please find Dr. Pletcher's memo (dated July 16, 2003) confirming the validity of the PWG peer review (MRID No. 44042801) of proliferative vascular lesions in male and female rats dosed with PHMB.

cc: Jonathan Chen

MEMORANDUM

TO: Jessica Kidwell
Health Effects Division
Environmental Protection Agency (EPA)

FROM: John M. Pletcher, DVM, MPH, DACVP
EPA Consulting Pathologist
Pathology Associates (PAI), A Division of Charles River Laboratories

DATE: 16 July, 2003

SUBJECT: Pathology Working Group Peer Review of Proliferative Vascular Lesions in Male and Female Rats

I have completed my review of Dr. William M. Busey's report entitled as above and dated May 13, 1996. Dr. Busey served as the PWG's Chairperson and Dr. Jerry Hardisty did the Peer Review of all sections containing proliferative vascular lesions in the liver from the 512 (256 males and 256 females) rats that comprised the four groups of an oncogenicity study of PHMB entitled, Polyhexamethylene Biguanide (PHMB): Two Year Feeding Study in Rats. The study (CTL Study No. PR0936) was conducted by the Zeneca (now Syngenta) Central Toxicology Laboratory in the United Kingdom. The purpose of the Peer Review/PWG process was to determine the incidence of proliferative vascular neoplasms of the liver following currently accepted nomenclature and diagnostic criteria and to discuss the relevance, for purposes of risk assessment, of the hepatic vascular neoplasms that occurred in the study. The PWG was conducted in Research Triangle Park (NC) on 16 April, 1996.

Six experienced toxicological pathologists were assembled to conduct the PWG including the Study Pathologist from Zeneca/Syngenta (Dr. Mervyn Robinson) and the Reviewing Pathologist (Dr. Hardisty), as well as two observers. Based on Dr. Busey's report, both the Peer Review and the PWG were conducted in accordance with EPA pesticide Regulation (PR) Notice 94-5 (EPA, 1994).

The conclusion of the PWG was that the overall weight of evidence indicated that the slightly higher number of Group 4 male and female rats having vascular neoplasms in the liver was not associated with the dietary administration of PHMB. It was the unanimous opinion of the PWG that the liver vascular neoplasms were incidental, a result of biological variation. This conclusion was based on the lack of evidence of an increased incidence of non-neoplastic vascular changes that would be indicative of a pre-neoplastic process; the low and predominantly benign incidence of liver vascular neoplasms in the study; and the lack of precursor lesions similar to that observed in other compounds such as tetrafluoroethylene, vinyl fluoride and

quinoline, chemicals that are known to produce vascular neoplasms. Moreover, the incidences of vascular neoplasms at other sites in the rats of the study in question were not treatment-related.

I cannot find fault with the conduct or constitution of the PWG nor its conclusion and, therefore, I recommend that the finding of this report be considered valid.

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Chemical:	**Poly(iminoimidocarbonyliminoimidocarbony**
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