



June 27, 2005

Sue Shallal, Ph.D.
Designated Federal Officer
U.S. EPA Science Advisory Board
Via e-mail: shallal.suhair@epa.gov

Re: PFOA Review Panel
*Submission of Pathology Working Group Report
on Mammary Tumors in Chronic Study of PFOA*

Dear Dr. Shallal:

We are submitting for the PFOA Panel's consideration a copy of a recently-completed Pathology Working Group (PWG) report examining the mammary findings from the 3M (Sibinski et al. 1983) chronic study on PFOA. (Experimental Pathology Laboratories, Inc., "Pathology Peer Review and Pathology working Group Review of Mammary Glands from a Chronic Feeding Study in Rats with PFOA," June 17, 2005.) The pathology review was a joint project of the 3M Medical Department and DuPont Haskell Laboratory.

The report concludes (p. 12):

The PWG concluded that the incidence of mammary gland neoplasms in the study was not affected by chronic dietary administration of PFOA. The morphologic appearance, overall incidence and distribution of the neoplasms observed in treated and control animals were similar.

The chronic study included a control group and two dose groups which received 30 or 300 ppm in the diet. The slides were retained, and were made available to the reviewing pathologist, Dr. Gabrielle Willson. Dr. Willson reexamined all sections of mammary gland from all female rats in all dose groups. Dr. Jerry Hardisty of Experiental Pathology Laboratories then convened a Pathology Working Group including Dr. Willson, Dr. Ray Brown and Dr. Ernest McConnell to determine a consensus diagnosis for all neoplastic lesions diagnosed by either the original study pathologist or the reviewing pathologist and to determine the toxicologic significance of the incidence of mammary gland neoplasms present in the female rats in the PFOA study. The Pathology Working Group examined the slides without knowledge of the treatment group of the animals, and applied diagnostic criteria and nomenclature of the Society of Toxicological Pathologists (Mann et al. 1996).

The primary difference between the original reported findings and the PWG results involved findings initially reported as lobular hyperplasia which the PWG classified as fibroadenoma. There were minor differences in classification of other findings. Dr. David Gaylor performed statistical analyses on the findings for the PWG. The PWG report states:

- There were no statistically significant differences in the incidence of fibroadenoma, adenocarcinoma, total benign neoplasms or total malignant neoplasms between control and treated animals using Fisher's Exact Test for pairwise comparison.
- Combining benign and malignant neoplasms is not recommended. However, even if combined in this study, there was no significant difference between control and treated groups. (p. 11)
- None of the tumor types or combinations of tumor types exhibited statistically significant survival-adjusted dose-response trends. (p. 20)
- There was no increase in tumor multiplicity or incidence with dose between control and treated groups. (p. 11)
- The morphologic appearance of neoplasms in treated groups was similar to those observed in the control group, indicating that treatment did not affect the phenotype of the neoplasms in the study. (p. 11)
- The incidence of mammary gland neoplasms in the study is similar to historical control data for untreated Crl:CD female Sprague Dawley rats in 104-week studies, as reported in the literature. (pp. 11-12)

Respectfully submitted,



Larry R. Zobel, M.D., M.P.H.
Staff Vice President and Medical Director

Enclosure

cc: EPA AR-226 Docket
Dr. Jennifer Seed
Dr. Robert Rickard