3M General Offices

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April 27, 2005

Ms. Rose Allison
U S. Environmental Protection Agency
EPA East Building
1201 Constitution Avenue, N.W.
Washington, DC 20004

Subject: **Perfluorobutane sulfonate study reports associated with PMN submissions to the US EPA**

Dear Ms. Allison:

Provided below is the content of a memo from John Butenhoff, 3M Toxicology, dated April 26, 2005 and outlining the reasons for additional histopathology review of tissues from the 90-day oral toxicity study with the rat. The attached report from Dr. Cohen, submitted in 2004, will also be added to the 90-day oral toxicity study in next update of the Perfluorobutane sulfonate study reports CD.

> "In the 90-day oral toxicity study of PFBS in rats (Argus 418-026), histopathological review of kidneys by light microscopy reported minimal to mild kidney observations of primarily tubular hyperplasia and papillary edema in the high dose group (600 mg/k/d). In order to obtain an expert opinion on the relationship of these observations to PFBS treatment, the kidney slides were sent to Dr Samuel Cohen at the University of Nebraska Medical Center for his review Dr Cohen was blinded to the treatment regimen associated with each slide. His conclusion, detailed in the attached letter report dated June 18, 2004, was that there was no renal effect secondary to treatment.
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> John L. Butenhoff, Ph D., CIH, DABT
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Please feel free to contact me if you have any questions.

Regards,

Jay F. Schulz
Regulatory Affairs Specialist
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Contains No CBI

University of Nebraska Medical Center

NEBRASKA'S HEALTH SCIENCE CENTER

PATHOLOGY AND MICROBIOLOGY

June 18, 2004

John L. Butenhoff, Ph.D.
3M Corporate Toxicology and Regulatory Services
3M Center, Building 0220-02-E-02
St. Paul, Minnesota 55144-1000

Dear John,

I have completed examining the kidney tissue slides that were sent to me. I will try to summarize my findings. Please let me know if there is any additional detail that you need regarding either of these or if you would like to discuss them further.

The slides that I received were labeled Argus study 418-026. They included one or two slides for each of the animals with at least two sections of kidney available for each animal for examination. One slide (animal no. 14883) was broken upon arrival, but it was still possible to evaluate the kidney section on the slide.

My overall impression is that there are no significant treatment-related effects in these kidneys. I did not receive a code of sections indicating which animals belonged to which treatment groups, so I will refer only to the individual animal numbers for the few findings that I did observe.

There were occasional animals that showed mild interstitial, chronic inflammation, but this is a finding that is quite common in CD rats of this age. I do not believe that these are treatment related. A few animals had specific changes that I also do not believe are treatment related as they occur sporadically and in individual rats, and are relatively common renal changes in rats.

In animal 14860, there was focal calcification at the fornix of the papilla and the renal pelvis with adjoining urothelial metaplasia of the papilla and hyperplasia of the transitional epithelium. This was quite mild in degree. This also is a common finding in CD rats as it is in many strains of rats. Animal 14926 had also a small area similar to this in the renal pelvis.

In animal 14890, there was a focal area of papillary necrosis at the tip of the papilla, but I did not see any other abnormalities, including any evidence of tubular or urothelial hyperplasia. Although less common in rats, this is also not an infrequent finding.

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In animal 14895, there was an area of medullary calcification of a slight degree. This also is extremely common in CD rats, and if anything, I was surprised that there wasn't more evidence of it in more of the other rats. Calcification of the medulla or of the cortical medullary junction has been written about extensively as a spontaneous finding in rats. A similar finding was present in animal 14906, and was present at a somewhat greater extent than in animal 14895. Nevertheless, as is usually seen in such animals, there was no reaction around the calcification.

Animal no. 14923 showed numerous and extensive changes in one of the kidneys with extensive tubular dilatation in the cortex and medulla, extensive papillary necrosis with adjoining urothelial metaplasia and hyperplasia. There are also areas of acute inflammation and extensive areas of chronic inflammation. My overall impression of this animal is that there was obstruction of the lower urinary tract with resulting hydroureter and hydronephrosis, and consequent pyelonephritis. In rats, this is most frequently seen in association with urinary tract calculi, which may be present transiently but can produce long-term effects.

In summary, I cannot find any consistent changes in these rats, and my overall conclusion is that there is no renal effect secondary to treatment.

Please let me know when and to whom you want me to send these slides. In the meantime, I will keep them in my office.

Sincerely yours,

Samuel M. Cohen, M.D., Ph.D.
Professor and Chair, Pathology and Microbiology
Havlik-Wall Professor of Oncology

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