



Technology  
& Engineering

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March 27, 2008

US EPA Office of Pollution Prevention and Toxics  
EPA East Building Room 6428  
Attn: Section 8(e)  
1201 Constitution Avenue, NW  
Washington, DC 20004

Contain NO CBI

Dear 8(e) Coordinator:

This letter is to inform you of the results from a two-generation oral OECD 416 study conducted with p-toluenesulfonamide (CAS #70-55-3) by Notox, the Netherlands, on behalf of Axcentive SARL, France. The test article was administered to rats in the diet at dose levels of 0, 1000, 3000 or 10,000 ppm (equivalent to 52-78 mg/kg/day for males and 75-161 mg/kg/day for females; 165-237 mg/kg/day for males and 232-499 mg/kg/day for females; and 566-832 mg/kg/day for males and 733-1631 mg/kg/day for females, respectively).

p-TSA administered in the diet of male and female rats, at concentrations of 1000, 3000 or 10000 ppm, induced F<sub>0</sub> and F<sub>1</sub>-parental effects (lower body weights and weight gain with corresponding organ weight changes) at 3000 and 10000 ppm and effects, to the pups (lower body weights for F<sub>1</sub> and F<sub>2</sub> pups with corresponding organ weight changes), related to decreased body weights of the dams and a delay in vaginal opening and balanopreputial separations for F<sub>1</sub> pups at 10000 ppm. Reproduction and breeding parameters were unaffected for both generations for treatment up to 10000 ppm.

The following findings were reported:

F<sub>0</sub> Generation

1000 ppm: No treatment related findings.

3000 ppm: Decreased body weight and body weight gain were reported as well as decreased terminal body weights at necropsy which resulted in increased relative organ weights of the brain and kidneys. These changes were most likely associated with decreased body weights and in the absence of microscopic findings in reproductive organs, were not considered a sign of toxicity.



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Akzo Nobel Inc.  
525 West Van Buren Street  
Chicago, Illinois 60607-3835  
Tel. (312) 554 7000  
Fax (312) 544 7125

10000 ppm: Decreased body weights and body weight gain were reported as well as decreased terminal body weights at necropsy which resulted in increased relative organ weight changes of the brain, liver, kidneys, seminal vesicles, adrenals and spleen. These changes were most likely associated with decreased body weights and in the absence of microscopic findings in reproductive organs, were not considered a sign of toxicity.

#### F<sub>1</sub> Pups

1000 ppm: No treatment related findings.

3000 ppm: No treatment related findings.

10000 ppm: During the first seven days of lactation, pups exhibited slightly lower body weights when compared to controls. The slightly lower weights were considered to have been caused by the lower body weights of their dams. From day 14 of lactation, body weights were statistically significantly lower. These changes were likely associated with the pups beginning to switch to feed. At necropsy (day 21 postpartum) pups exhibited a statistically significantly decreased terminal body weights, decreased absolute weights of the brain, spleen and thymus and increased relative weights of the brain. These changes were most likely associated with decreased body weights in this group during lactation and not considered a sign of toxicity. There was a delay in the mean day of vaginal opening (evaluated beginning on postnatal day 25) and balanopreputial separation (evaluated beginning on postnatal day 35). The mean body weights, on the day of acquisition, for females in this group were comparable to female controls weights while the mean body weights of males were statistically significantly less than the mean body weights for control males.

#### F<sub>1</sub> Generation

1000 ppm: No treatment related findings.

3000 ppm: Body weights and body weight gain and terminal body weights at necropsy were decreased which resulted in decreased absolute spleen weights and increased relative weights of the brain. These changes were most likely associated with decreased body weights and in the absence of microscopic findings in reproductive organs, were not considered a sign of toxicity.

10000 ppm: Body weights and body weight gains were decreased as was food consumption for females during the last week of pregnancy. Terminal body weights at necropsy were decreased which resulted in decreased absolute weights of the brain, liver and spleen and increased relative weights of the brain, kidneys, testes, prostate and seminal vesicles, pituitary gland, adrenals and spleen. These changes were most likely associated with decreased body weights and in the absence of microscopic findings in reproductive organs, were not considered a sign of toxicity.

F2 Pup Development

1000 ppm: No treatment related effects

3000 ppm: No treatment related effects

10000 ppm: Lower body weights for male and female pups were observed from day 1 of lactation on wards. This was considered to be due to the lower body weights of their dams. This group exhibited decreased terminal body weights at necropsy, decreased absolute weights of the brain, spleen and thymus and increased relative weight of the brain. Females had a slightly decreased relative thymus weight. These changes were most likely associated with decreased body weights during lactation and were not considered a sign of toxicity.

Please contact me at (312) 544-7061 with any questions.

Sincerely,

A handwritten signature in cursive script that reads "Louette J. Rausch".

Louette J. Rausch,  
Senior Staff Toxicologist  
Akzo Nobel Services Inc./T&E  
525 W. Van Buren  
Chicago, IL 60607

From: Origin ID: GYYA (312)544-7005  
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Akzo Nobel  
525 W Van Buren Street



Chicago, IL 60607

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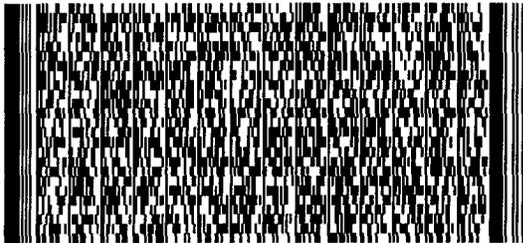


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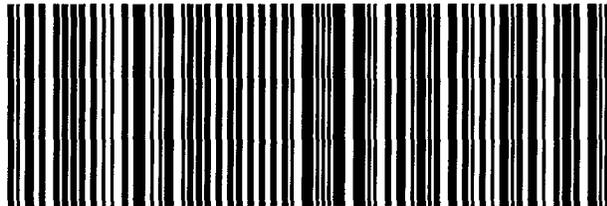
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