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TSCA Document Control Officer (7407M)  
EPA East – Room 6428 Attn: Section 8(e)  
Office of Pollution Prevention and Toxics  
U.S. Environmental Protection Agency  
1201 Constitution Ave., NW  
Washington, DC 20004-3302



8EHQ-0311-18289A

DCN: 88110000173

Subject: TSCA 8(e) Submission



Dear Sir/Madam:

Arkema Inc. (Arkema) is making this submission to the U.S. Environmental Protection Agency (EPA) pursuant to Toxic Substances Control Act (TSCA) Section 8(e) on behalf of the Organosulfur REACH Group (OSRG) Consortium Product Group members<sup>1</sup>. The submission provides information from two repeated oral (gavage) studies in rats with di-tert-Bu polysulfides (CAS Registry Number 68937-96-2) as the test material.

Di-tert-Bu polysulfides (CAS Registry Number 68937-96-2) is the subject of the OSRG Consortium Product Group's efforts to register the substance within the REACH program.

#### 4-Week Toxicity Study by the Oral Route in Rats Followed by a 2-Week Treatment-Free Period

The toxicity of the test material was evaluated in Sprague-Dawley rats following daily oral administration for 4 weeks at dose-levels of 33, 100 or 300 mg/kg/day. At the end of the treatment period five animals per sex from the vehicle control (0.5% carboxymethylcellulose in purified water) group and the high-dose group were kept for a 2-week treatment-free period.

At 300 mg/kg/day, the only test item-related clinical sign was ptyalism, observed on several occasions in almost all animals. Lower body weight gain was observed at the end of the treatment period in both sexes (-14% in males; -25 % in females, when compared with controls). Higher body weight gain was observed in high dose animals during the treatment-free period. Food consumption was unaffected throughout the study. Lower red blood cell parameters [including erythrocyte count, hemoglobin level, mean cell hemoglobin concentration and packed cell volume] were observed, together with higher mean cell volume and mean cell hemoglobin level. These changes were associated with higher reticulocyte count (3.6-fold in males and 5.2-fold in females) and were indicative of regenerative anemia. Slightly higher neutrophil counts were observed. At the end of the treatment-free period, normalization of the above parameters was observed but higher hemoglobin level and packed cell volume were observed in both sexes when compared to controls. Blood biochemistry changes at the end of the treatment period were no longer observed at the end of the treatment-free period. Increased kidney, liver and spleen weights were noted at the end of the treatment were observed with a lower severity when compared to those recorded at the end of treatment period, thus indicating partial reversibility. Microscopic non-adverse changes were seen in the kidneys of males (hyaline droplets and brown pigment in cortex), liver (hepatocellular hypertrophy, brown pigment in Kupffer cells and hemopoiesis), spleen (hemopoiesis, brown pigment and congestion), bone marrow

<sup>1</sup> OSRG Consortium Product Group members include: Arkema France, Chevron Phillips Chemicals International N.V. and Chevron Phillips Chemical Company LP.

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(increased erythroid and/or myeloid cell numbers) and forestomach (hyperkeratosis, acanthosis and inflammation). At the end of the treatment-free period, partial reversibility of these changes was noted.

At 100 mg/kg/day, lower body weight gain was observed in females during the treatment period. At hematology investigations, similar changes as in high-dose animals were observed, but with a lower severity. Increased kidney, liver and spleen weights were recorded at the end of the treatment period and correlated with macroscopic enlargement of the kidney and liver. Microscopic non-adverse changes were seen in the kidneys of males, liver, spleen, bone marrow, and forestomach.

At 33 mg/kg/day, no relevant clinical changes were observed. Microscopic non-adverse changes were seen in the kidneys of males, in the liver and spleen of females.

In summary:

The test item was generally well-tolerated at all dose-levels tested. The dose-related changes in hematology parameters were indicative of a slight and reversible regenerative anemia and correlated at pathology with extramedullary hemopoiesis in the spleen and increased erythroid cells in the bone marrow. These latter findings were considered to be a compensatory effect, secondary to the test material-related effect on red blood cells.

At 33 or 100 mg/kg/day, none of these changes were considered to be adverse, taking into consideration their limited amplitude, the reversibility observed at the dose level of 300 mg/kg/day and/or the absence of associated degenerative changes.

#### Reproduction-Developmental Toxicity Screening Test by the Oral Route in Rats

The objective of this study was to evaluate the potential toxic effects of the test material following daily oral administration to male and female rats from before mating, through mating and, for the females, through gestation until day 4 *post-partum*. The study was conducted as a reproduction/developmental screening test according to OECD 421 guideline and GLP.

Three groups of 10 male and 10 female Sprague-Dawley rats received the test material (purity 97.29%) daily, 2 weeks before mating and through mating and, for the females, through gestation until day 4 *post-partum*. The dose-levels were 25, 75 or 150 mg/kg/day. Another group of 10 males and 10 females received the vehicle, 0.5% aqueous carboxymethylcellulose in purified water, under the same experimental conditions and acted as a control group. The dosing volume was 5 mL/kg/day.

In conclusion, the test material was generally well tolerated at all dose-levels tested. The dose-related changes induced among hematology parameters were indicative of a slight and regenerative anemia and correlated at pathology with extramedullary hemopoiesis in the spleen. At 150 mg/kg/day, the increased incidence and/or severity of the changes observed at pathology and hematology parameters were considered to be adverse.

At 25 or 75 mg/kg/day, none of these changes were considered to be adverse, taking into consideration their limited amplitude, the absence of associated degenerative changes and/or the reversibility observed at the dose-level of 300 mg/kg/day in the concurrent 28-day oral toxicity study described above.

Based on the results of this study:

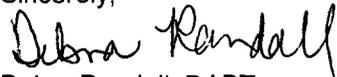
1. the No Observed Adverse Effect Level (NOAEL) for parental toxicity was considered to be 75 mg/kg/day based on the significant regenerative anemia observed at 150 mg/kg/day;
2. the No Observed Effect Level (NOEL) for reproductive performance (mating and fertility) was considered to be 150 mg/kg/day; and
3. the NOEL for toxic effects on the offspring was 75 mg/kg/day based on the lower body weight gain of the pups at 150 mg/kg/day.

Nothing in this letter is considered confidential business information by Consortium members.

The Consortium has not made a determination at this time that any significant risk of injury to human health or to the environment is presented by these findings. This information is submitted in accordance with the Consortium's understanding of guidance issued by EPA indicating EPA's interpretation of Section 8(e) of the Toxic Substances Control Act or, where it is not clear that reporting criteria have been met, it is submitted as a precautionary measure and because it is information in which EPA may have an interest.

Questions regarding this submission may be directed to me at 215-419-5890 or via e-mail at [debra.randall@arkema.com](mailto:debra.randall@arkema.com).

Sincerely,

A handwritten signature in black ink that reads "Debra Randall". The signature is written in a cursive, flowing style.

Debra Randall, DABT  
Manager, Product Safety

