

ORIGINAL

TSCA NON-CONFIDENTIAL BUSINESS INFORMATION

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COMMENTS:

DOES NOT CONTAIN CBI



January 20, 2011

TSCA Confidential Business Information Center (7407M)
EPA East - Room 6428 Attn: Section 8(e)
U.S. Environmental Protection Agency
1200 Pennsylvania Avenue, NW
Washington, DC 20460-0001

Attention: TSCA 8(e) Coordinator

RE: Information Acquired During Study with 4,4'-methylenedianiline ("MDA" CASRN 101-77-9) and Formaldehyde, oligomeric reaction products with aniline ("oligomeric MDA, PMDA" CAS RN 25214-70-4)

Dear TSCA 8(e) Coordinator:

The American Chemistry Council's Diisocyanates Panel (Panel), on behalf of its members,¹ is submitting the following data to EPA pursuant to Section 8(e) of the Toxic Substances Control Act (TSCA). This letter transmits two reports regarding antiandrogenic activity observed for the test substances 4,4'-methylenedianiline ("MDA," CASRN 101-77-9) and Formaldehyde, oligomeric reaction products with aniline ("oligomeric MDA, PMDA" CAS RN 25214-70-4). Existing guidance is not sufficient to determine whether this information is reportable under TSCA Section 8(e); therefore no determination has been made as to whether a significant risk of injury to health or the environment is actually presented by the findings.

The objective of the *in vitro* studies was to determine the androgenic and antiandrogenic potential of the test substance using a Yeast Androgen Screening (YAS) assay. Since this is an *in vitro* system, designed as a screening assay, the results of the *in vitro* testing may not necessarily indicate that such a potential may also exist in mammals. The YAS assay was not included by the USEPA for its Endocrine Disrupter Screening Program (EDSTAC Final Report, August 1998)².

The study author summarizes the results of the studies as follows:

¹ The Diisocyanates Panel members are Bayer MaterialScience LLC, BASF Corporation, Huntsman and The Dow Chemical Company.

² EDSTAC [Endocrine Disruptor Screening and Testing Advisory Committee]. Final Report: Volume 1, August 1998.



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“4,4’-MDA: Testing for Potential Androgenic and Antiandrogenic Activity Using the YAS-ASSAY [AR] (Yeast Androgen Screening)”

The test substance 4,4’-MDA showed no androgenic activity in comparison to dihydrotestosterone under the experimental conditions. The test substance 4,4’-MDA showed clear antiandrogenic activity in comparison to hydroxyflutamide under the experimental conditions. A reproducible inhibition of the androgen effect compared to 10^{-09} mol/L 5α -dihydrotestosterone (suppression of expected color development) was observed at concentrations from about 10^{-05} mol/L and higher. Thus, under the experimental conditions chosen here, it is concluded that 4,4’-MDA did not exert androgenic effects while antiandrogenic effects were observed in the YAS assay using the hAR yeast strain, but only at relatively high test concentration(s).

“Formaldehyde, oligomeric reaction products with aniline (oligomeric MDA, PMDA) Testing for Potential Androgenic and Antiandrogenic Activity Using the YAS-ASSAY [AR] (Yeast Androgen Screening)”

The test substance Formaldehyde, oligomeric reaction products with aniline (oligomeric MDA, PMDA) showed no androgenic activity in comparison to dihydrotestosterone under the experimental conditions. The test substance showed clear antiandrogenic activity in comparison to hydroxyflutamide under the experimental conditions. A reproducible inhibition of the androgen effect compared to $5*10^{-09}$ mol/L 5α -dihydrotestosterone (suppression of expected color development) was observed at 10^{-4} mol/L. Thus, under the experimental conditions chosen here, it is concluded that Formaldehyde, oligomeric reaction products with aniline (oligomeric MDA, PMDA) did not exert androgenic effects while it exerted antiandrogenic effects in the Yeast Androgen Screening (YAS) assay using the hAR yeast strain, but only at the highest test concentration.

While being submitted in accordance with TSCA 8(e), the Panel has made no determination as to whether a substantial risk of injury to health or the environment is actually presented by these findings. However, the Panel is aware that EPA could consider this information to constitute a substantial risk: therefore, it is being submitted to EPA under 8(e) out of an abundance of caution. This submission should therefore discharge any 8(e) responsibilities that might exist, and should be processed in accordance with EPA’s “substantial risk” procedures.

If you have any questions, please contact me, the Diisocyanates Panel Manager, at 202-249-6721, or at sahar_osman-sypher@americanchemistry.com.

Sincerely,

Sahar Osman-Sypher

Sahar Osman-Sypher
Manager, Diisocyanates Panel

TSCA 8(e) Submission
Diisocyanates Panel
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Attachments:

Reports Provided on CD-ROM

4,4'-MDA: Testing for Potential Androgenic and Antiandrogenic Activity Using the YAS-ASSAY [AR] (Yeast Androgen Screening)

Formaldehyde, oligomeric reaction products with aniline (oligomeric MDA, PMDA) Testing for Potential Androgenic and Antiandrogenic Activity Using the YAS-ASSAY [AR] (Yeast Androgen Screening)