September 29, 2009

Kathleen Stanton
Associate Director, Scientific Affairs
The Soap and Detergent Association
1500 K Street N.W.
Suite 300
Washington, DC 20005

Dear Ms. Stanton:

The Office of Pollution Prevention and Toxics is transmitting EPA's comments on the robust summaries and test plan for the Aluminum Alkoxides Category, posted on the ChemRTK HPV Challenge Program Web site on May15, 2008. I commend the Soap and Detergent Association for its commitment to the HPV Challenge Program.

EPA reviews test plans and robust summaries to determine whether the reported data and test plans will provide the data necessary to adequately characterize each SIDS endpoint. On its Challenge Web site, EPA has provided guidance for determining the adequacy of data and preparing test plans used to prioritize chemicals for further work.

EPA will post this letter and the enclosed comments on the HPV Challenge Web site within the next few days. As noted in the comments, we ask that the Association advise the Agency, within 60 days of this posting on the Web site, of any modifications to its submission.

Please send any electronic revisions or comments to the following e-mail addresses: oppt.ncic@epa.gov and chem.rtk@epa.gov. If you have any questions about this response, please contact me at 202-564-8617. Submit questions about the HPV Challenge Program through the "Contact Us" link on the HPV Challenge Program Web site pages or through the TSCA Assistance Information Service (TSCA Hotline) at (202) 554-1404. The TSCA Hotline can also be reached by e-mail at tsca-hotline@epa.gov.

I thank you for your submission and look forward to your continued participation in the HPV Challenge Program.

Sincerely,

/s/

Mark W. Townsend, Chief
HPV Chemicals Branch

Enclosure

cc: O. Hernandez
R. Lee
J. Willis

EPA Comments on Chemical RTK HPV Challenge Submission:
Aluminum Alkoxides Category

Summary of EPA Comments

The sponsor, The Soap and Detergent Association Aluminum Alkoxides Consortium, submitted a test plan and robust summaries to EPA for the Aluminum Alkoxides Category dated April 18, 2008. EPA posted the submission on the ChemRTK HPV Challenge Web site on May 15, 2008.

EPA has reviewed this submission and has reached the following conclusions:

1. Category Definition and Justification. These aspects of the submission are adequate except for an ambiguity in the category definition discussion.

2. Physical Chemical Properties. The submitter's approach is in general adequate for the purposes of the HPV Challenge Program. For the isopropyl derivative, available literature data need to be provided in a robust summary. The submitter needs to prepare robust summaries, with technical discussions where appropriate, to address the SIDS endpoints for alumina/aluminum hydroxide.

3. Environmental Fate. The submitter's approach is adequate for the purposes of the HPV Challenge Program except for hydrolysis. Additional data and/or an adequate technical discussion of hydrolysis, and available data for the isopropyl derivative, need to be added in robust summary format. Hydrolysis testing of the mixture may be needed.

4. Health Effects. Adequate data are available to address the SIDS endpoints for the purposes of the HPV Challenge Program. The submitter needs to address deficiencies in the robust summaries.

5. Ecological Effects. EPA reserves judgment on these endpoints pending receipt of better support for the hydrolysis claims underlying the submitter's approach.

EPA requests that the submitter advise the Agency within 60 days of any modifications to its submission and of a projected schedule for submission of a final package to the Challenge program.

EPA Comments on the Aluminum Alkoxides Category Challenge Submission

General

The submitter states that the hydrolysis of the sponsored substances results in the formation of the corresponding alcohol and alumina (Al_2O_3, CAS No.1344-28-1). Alumina formation depends on reaction conditions and may be initially minor. Aluminum hydroxide ($Al(OH)_3$, CAS No. 21645-51-2) is the expected initial aluminum hydrolysis product at pH 7, and its partially dehydrated form, AlO(OH), may also be present. They have different physicochemical properties which contribute to their individual toxicities. The submitter needs to address this issue and the potential toxicities of the different aluminum oxides.

Because the test plan states (p. 6) that the sponsored substances are intermediates in alcohol manufacture, the statement (p. 8) that the mixture is produced by a "two-stage oxidation process of alcohols" appears incorrect; "olefins" may have been intended instead of "alcohols."

Category Definition

The category consists of two substances -- 2-propanol, aluminum salt (Al isopropoxide, CAS No. 555-31-7) and an aluminum alkoxides mixture (CAS No. 68937-64-4) that includes the constituents $Al(OR_1)(OR_2)(OR_3)$, where R_1, R_2 and R_3 represent alkyl chains of the same or different lengths. The submitter lists the following constituents, all having $R_1 = R_2 = R_3$:

Ethanol, aluminum salt	CAS No. 555-75-9

1-Butanol, aluminum salt	CAS No. 3085-30-1
1-Hexanol, aluminum salt	CAS No. 23275-26-5
1-Octanol, aluminum salt	CAS No. 14624-13-6
1-Decanol, aluminum salt	CAS No. 26303-54-8
1-Dodecanol, aluminum salt	CAS No. 14624-15-8
1-Tetradecanol, aluminum salt	CAS No. 67905-32-2
1-Hexadecanol, aluminum salt	CAS No. 19141-82-3
1-Octadecanol, aluminum salt	CAS No. 3985-81-7
1-Eicosanol, aluminum salt	CAS No. 67905-31-1
1-Docosanol, aluminum salt	CAS No. 67905-30-0
1-Tetracosanol, aluminum salt	CAS No. 67905-29-7
1-Hexacosanol, aluminum salt	CAS No. 67905-28-6
1-Octacosanol, aluminum salt	CAS No. 67905-27-5
1-Triacontanol, aluminum salt	CAS No. 67905-26-4

While the test plan does indicate that all mixed isomers are present (such as $R_1 <> R_2 <> R_3$), other statements imply that only those in the above list are included. Editing to remove the ambiguity would reduce the potential for confusion.

Analog Justification

The submitter proposes characterizing the toxicity of the sponsored substances with data from the hydrolysis products. The submitter states that upon contact with water, the aluminum salts rapidly hydrolyze to alumina and, for the mixture, these corresponding linear alcohols:

Ethanol	CAS No. 64-17-5
1-Butanol	CAS No. 71-36-3
1-Hexanol	CAS No. 111-27-3
1-Octanol	CAS No. 111-87-5
1-Decanol	CAS No. 112-30-1
1-Dodecanol	CAS No. 112-53-8
1-Tetradecanol	CAS No. 112-72-1
1-Hexandecanol	CAS No. 36653-82-4
1-Octadecanol	CAS No. 112-92-5
1-Eicosanol	CAS No. 629-96-9
1-Docosanol	CAS No. 661-19-8
1-Tetracosanol	CAS No. 506-51-4
1-Hexacosanol	CAS No. 506-52-5
1-Octacosanol	CAS No. 557-61-9
1-Triacontanol	CAS No. 593-50-0

EPA agrees that using data for the hydrolysis products, alumina/aluminum hydroxide and the corresponding alcohol, to address the SIDS health effects endpoints and some physical chemical and environmental fate endpoints for the sponsored substances is reasonable for the purposes of the HPV Challenge program. EPA reserves judgment as to the suitability of the approach for ecological effects.

Health effects. Direct health effects testing of such reactive substances as aluminum alkoxides is impractical. Thus, for these endpoints, the submitter's approach using data on the hydrolysis products is reasonable.

Ecological effects. In EPA's Inert Exemption reassessment of aluminum isopropoxide (http://www.epa.gov/opprd001/inerts/aluminumisopropoxide.pdf), a hydrolysis study on a mixture of that substance and 2-butanol, aluminum salt (CAS No. 2269-22-9) concluded that the mixture was completely hydrolyzed in 25 seconds. While this supports the claim of rapid hydrolysis for lower molecular weight mixture components, the submission contains assertions but no supporting data as to the relative rates of hydrolysis of the higher molecular weight components under environmental conditions. The higher

molecular weight mixture components may hydrolyze more slowly because of lower solubility and/or lower reactivity. A test plan discussion of hydrolysis of silicon alkoxides for comparison purposes did not identify the alkyl groups present and did not state half-life values. The test plan does not state how the information on mixture component distribution was determined; if done by an analytical procedure involving hydrolysis, then details of that procedure could shed some light on the reaction and possibly support the submitter's assertions of uniformly rapid hydrolysis of all components.

If such information is lacking, the submitter needs to perform a hydrolysis study designed to determine the time to completion of hydrolysis at pH 7 to clarify the reactivity of the entire mixture.

If "rapid" hydrolysis cannot be supported for all mixture components, the submitter may need to discuss whether an intermediate overall hydrolysis rate might present experimental difficulties for ecological testing owing to the formation of insoluble hydrolysis products over time. The hydrolysis of aluminum alkoxide mixtures such as the one considered in the test plan could be complicated by the formation of insoluble alcohols and of gels of aluminum hydroxide. An adequate technical discussion of all these issues is needed. Without better information on these points, EPA must reserve judgment on the need for ecological effects testing and the submitter's proposed use solely of data on the hydrolysis products.

Category Justification

The submitter bases the grouping on the similarity in structure and reactivity between the single chemical and the mixture components, all having an Al atom and three alcohol components. The submitter's justification for including the two sponsored substances in one submission is adequate.

Test Plan

Physical chemical properties (melting point, boiling point, vapor pressure, partition coefficient and water solubility)

The submitter's approach and the available data are in general adequate for the purposes of the HPV Challenge Program. However, available literature data for aluminum isopropoxide need to be provided in a robust summary. In addition, freshly precipitated $Al(OH)_3$ has different properties from $Al(OH)_3$ that has been dried or acid-treated, for example, to form alumina (Al_2O_3). The submitter needs to discuss the relationship among forms of aluminum hydroxide/oxide and distinguish among their properties where applicable. In the test plan, the submitter provides a table (Table 3B) outlining the physical chemical properties of aluminum oxide. No robust summaries were provided. Given that aluminum hydroxide is also present, the submitter should prepare robust summaries, with technical discussions where appropriate, to address the SIDS endpoints for alumina and aluminum hydroxide.

Environmental Fate (photodegradation, stability in water, biodegradation, fugacity)

The submitter's approach is in general adequate for the purposes of the HPV Challenge Program. A technical discussion of hydrolysis needs to be added in robust summary format. As noted above under Analog Justification, hydrolysis testing of the mixed alkoxides may be needed; such a study should be designed to determine the time to completion of hydrolysis at pH 7 and at temperatures of 20-30°C. For aluminum isopropoxide, the hydrolysis data mentioned above under Category Justification need to be included in robust summary format.

Health Effects (acute toxicity, repeated-dose toxicity, genetic toxicity, and reproductive/developmental toxicity)

Adequate data are available to address the SIDS health effects endpoints for the purposes of the HPV Challenge Program. Adequate analog data are available on the alcohol hydrolysis products to characterize the varying carbon chain lengths and to read across to those alcohols for which data are not available. The U.S. Department of Health and Human Services has recently published a toxicological profile for aluminum (http://www.atsdr.cdc.gov/toxprofiles/tp22.html) that addresses the hazards of

aluminum oxide and aluminum hydroxide. The submitter needs to prepare robust summaries, with technical discussions where appropriate, to address the SIDS endpoints for alumina and aluminum hydroxide. For the alcohols, published OECD hazard assessments (for all except CAS Nos. 593-50-0, 557-61-9, 506-52-5 and 506-51-4) and robust summaries (included in the submission) are available (http://www.chem.unep.ch/irptc/sids/OECDSIDS/sidspub.html). The submitter needs to describe in the test plan how the read-across approach is going to be used for the data gaps for the hydrolysis products lacking OECD hazard assessments.

Ecological Effects (fish, invertebrates, and algae)

EPA reserves judgment on these endpoints for the reasons described above.

Specific Comments on the Robust Summaries

Ecological Effects

Although only brief statements were provided on submitted WAF data (Nielsen 1993) for alumina (Dispal 23N4), the study was conducted above the water solubility limit. Therefore, the data are inadequate for determining hazard.

Followup Activity

EPA requests that the submitter advise the Agency within 60 days of any modifications to its submission and of a projected schedule for submission of a final package to the Challenge program.