Assessment Plan for Aluminum Alkoxides in Accordance with the USEPA High Production Volume Chemical Challenge Program

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TABLE OF CONTENTS

LIST OF TABLES

LIST OF APPENDICES

EXECUTIVE SUMMARY

The Aluminum Alkoxides Consortium (Consortium), a subgroup formed for this purpose under The Soap and Detergent Association (SDA), is sponsoring chemical substances best described as aluminum alkoxides in the US High Production Volume (HPV) Challenge program. These aluminum alkoxides are used predominantly as intermediates. The Consortium assembled and reviewed available public and private toxicological data, and developed an assessment plan for the sponsored chemicals.

Aluminum alkoxides hydrolyze rapidly to their constituent alcohols and alumina. Therefore the assessments have been made reviewing the available data on the relevant alcohols and alumina. The 2-propanol and the C6 to C22 (long chain) alcohols have been evaluated previously under the Organization for Economic Cooperation and Development (OECD) HPV program. The alcohols have low toxicity to human health. Aquatic toxicity varies depending on the carbon chain length. However, all of the alcohols will biodegrade and are not persistent. Monitoring data have shown that exposures are likely to be low. Given the predominant use pattern for these chemicals as manufacturing intermediates, significant environmental exposures are not expected. Alumina or aluminum oxide is present as a relatively low percentage of these products. It is a naturally occurring material and has low toxicity.

The potential for worker or environmental exposure during the manufacturing, processing, and distribution is limited through use of standard operating controls. No significant consumer exposure is expected because these materials are used predominantly as manufacturing intermediates.

Based on the availability of data and the limited exposure potential, the aluminum alkoxides covered in this assessment are considered to be of low concern and no further testing is necessary.

INTRODUCTION

The High Production Volume (HPV) Challenge Program is a voluntary initiative of the US chemical industry to complete hazard data profiles for approximately 2800 HPV chemicals as identified on the US Environmental Protection Agency's (USEPA) 1990 Toxic Substances Control Act (TSCA) Inventory Update Rule (IUR). In the US, HPV chemicals are those that are manufactured or imported in quantities greater than 1 million pounds per year. The hazard data to be provided in the program are those that meet the requirements of the Screening Information Data Set (SIDS) Program (OECD 1997). SIDS, which has been internationally agreed to by member countries of the Organization for Economic Cooperation and Development (OECD), provides the basic screening data needed for an initial assessment of the physical-chemical properties, environmental fate, and adverse human and environmental effects of chemicals. The information for completing the SIDS can come from existing data or may be generated as part of the HPV Challenge Program. Once the available studies are identified or conducted, "robust summaries" are prepared.

The USEPA, industry, and non-governmental organizations (NGOs) are unified in their commitment to minimize the numbers of animals tested in the HPV Challenge Program whenever it is scientifically justifiable (USEPA 1999a, 2000). Therefore, this assessment plan evaluates all of the existing reliable data for the sponsored chemicals in an effort to adequately characterize the human health and environmental hazard while reducing the number of animals required for testing.

The Aluminum Alkoxides Consortium (Consortium), a subgroup formed for this purpose under The Soap and Detergent Association (SDA), has agreed to assemble and review available public and private toxicological data, develop and provide an assessment plan for the sponsored chemicals and conduct additional research, including testing when necessary, for chemical substances best describe as aluminum alkoxides. The Consortium is comprised of the following member companies:

Chattem Chemicals
FedChem, LLC
Sasol North America Inc.

The aluminum alkoxides were originally a subcategory within the aliphatic alcohols (aka Long Chain Alcohols) category sponsored by SDA in the USEPA HPV challenge program. The alcohols category was then converted to the ICCA HPV program. During the review process (with the UK as sponsoring authority), that consortium decided to remove the aluminum alkoxides subcategory. The alkoxides-producing companies then formed the Aluminum Alkoxide Consortium and are re-sponsoring the aluminum alkoxides through the original HPV challenge program. Note that the aluminum alkoxides are also commonly referred to as the aluminum salt of the corresponding alcohol (e.g. 2-propanol aluminum salt).

This assessment plan is the result of the Consortium's efforts and provides a summary and analysis of the available data, and identifies any data gaps in the SIDS data profile. The first section of this assessment plan provides an identification of the sponsored chemicals, including

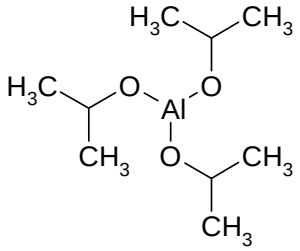
structure, production process, and use pattern. Following that are sections on the process used to collect the unpublished and published data and how those data were evaluated for quality and acceptability. This is followed by a discussion of the physical-chemical properties, environmental fate and transport, ecotoxicity and mammalian toxicity data as summarized in the accompanying robust summary document. Finally, conclusions regarding data availability and identification of data gaps in the SIDS profiles for the sponsored chemicals are presented.

IDENTIFICATION OF SPONSORED CHEMICALS

A. Chemical Structure

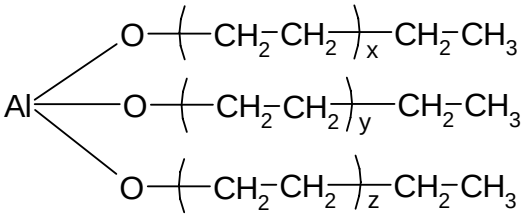
There are two chemical substances being sponsored comprising seventeen Chemical Abstracts Service (CAS) numbers. One is a discrete substance, 2-Propanol, Aluminum Salt (CAS No. 555-31-7). The other is a multi-component aluminum salts mixture that is described by the individual aluminum salts of which it is comprised. These individual salts are not produced as discrete chemicals; rather they exist only as constituents of the mixture. The separate compounds are included in this dossier and assessment plan because this is the way this mixture is designated for TSCA purposes. However, it must be emphasized that only the mixture is produced commercially.

The 2-Propanol, Aluminum Salt is a discrete short chain white solid substance with the following chemical structure:



Synonyms for the aluminum salt of 2-propanol include aluminum isopropoxide and aluminum isopropylate. The corresponding alcohol, 2-propanol, is also commonly known as isopropanol, isopropyl alcohol, and propan-2-ol.

The mixture C2-30, aluminum salts, CAS No. 68937-64-4, as well as each of the 15 individual salts that are constituents of the mixture (see Table 1), are better described as aluminum alkoxides. They are site-limited intermediates utilized in the Ziegler alcohol manufacturing process. The mixture is described by the following general structure:



where x, y and z are integers from 0 to 34 corresponding to a Poisson distribution.

These chemicals are comprised of an inorganic component and a linear alcohol component. As is discussed in more detail later in this assessment, upon contact with water, hydrolysis breaks down these aluminum salts into their component linear alcohols and alumina. Alumina is a very small component of these compounds on a molecular weight basis. The majority of the mixture (>90%) is composed of C6-C16 alkoxides.

Table 1. Sponsored Chemicals and Constituents

CAS Number	Chemical Name
555-31-7	**2-Propanol, Aluminum Salt**
68937-64-4	**A multi-component aluminum salts mixture comprised of the following constituents:**
555-75-9	Ethanol, Aluminum Salt
3085-30-1	1-Butanol, Aluminum Salt
3985-81-7	1-Octadecanol, Aluminum Salt
14624-13-6	1-Octanol, Aluminum Salt
14624-15-8	1-Dodecanol, Aluminum Salt
19141-82-3	1-Hexadecanol, Aluminum Salt
23275-26-5	1-Hexanol, Aluminum Salt
26303-54-8	1-Decanol, Aluminum Salt
67905-26-4	1-Triacontanol, Aluminum Salt
67905-27-5	1-Octacosanol, Aluminum Salt
67905-28-6	1-Hexacosanol, Aluminum Salt
67905-29-7	1-Tetracosanol, Aluminum Salt
67905-30-0	1-Docosanol, Aluminum Salt
67905-31-1	1-Eicosanol, Aluminum Salt
67905-32-2	1-Tetradecanol, Aluminum Salt

B. Production Process

A method for preparing 2-Propanol, Aluminum Salt was published in 1936 by Young, Hartung, and Crossley. Their procedure entails heating a mixture of aluminum, isopropyl alcohol, and mercuric chloride at reflux. The process occurs via the formation of an amalgam of the aluminum. Catalysis can sometimes be added to initiate the reaction.

The aluminum salt mixture is produced through a patented two-stage oxidation process of alcohols.

C. Use Patterns and Exposure Potential

The 2-Propanol, Aluminum Salt is used as an intermediate in the production of 2-propanol and pharmaceuticals. It is minimally used in finished products; it is used to make aluminum soaps, paints, and for waterproofing finishes of textiles and other chemicals. It is also used as a dehydrating agent, a viscosity adjustor for varnishes, an antitranspirant in cosmetics, and an inert ingredient used in pesticide formulations.

The aluminum salt mixture is a site-limited intermediate utilized in the Ziegler alcohol manufacturing process. Only the mixture is produced commercially. The individual salts are not produced as discrete chemicals.

The potential for worker exposure during the manufacturing, processing, and distribution is limited by standard operational controls. Normal engineering controls are in place to minimize worker exposure. Local exhaust ventilation is used to control exposure. Workers also wear standard personal protective equipment including safety goggles, chemical resistant protective gloves, protective clothing as necessary to minimize contact, and respiratory masks when necessary to minimize inhalation exposure.

Engineering controls are also in place to minimize releases to the environment. Waste disposal is to licensed facilities and controls are in place to avoid discharging into the sewer system. Spills are easily contained in placed in appropriate containers for disposal. Standard first aid measures are generally sufficient to address exposure.

As stated previously, the 2-Propanol, Aluminum Salt is used minimally in finished products. U.S. EPA determined that, taking into consideration the available information on 2-Propanol, Aluminum Salt, there is a reasonable certainty that no harm to any population subgroup will result from aggregate exposure when considering exposure through dietary exposure and all other non-occupational sources for which there is reliable information (USEPA 2006).

Because the aluminum salt mixture is used as process intermediates, there is no opportunity for consumer exposure.

COLLECTION OF UNPUBLISHED AND PUBLISHED DATA

Consortium member companies contributed any available in-house studies of physical-chemical properties, environmental fate and transport, ecotoxicity, and mammalian toxicity for the

sponsored alkoxide chemical and mixture. Much of the available data are derived from studies conducted on the corresponding alcohol rather than the aluminum salt itself. In addition, an extensive review of all data on the "long chain alcohols" (i.e., from C6 to approximately C22) has been performed by another SDA consortium. The SIDS Initial Assessment Report (SIAR) and dossiers for these data were approved by OECD at the SIDS Initial Assessment Meeting (SIAM) in April 2006. Therefore, the Aluminum Alkoxides Consortium has relied on the summaries prepared for the long chain alcohols where appropriate to support the current HPV Challenge submission.

The majority of data presented in the summary table for aluminum alkoxide salts are taken from the SIAR and accompanying IUCLID Robust Study Summaries for the corresponding alcohols (see Table 1 below for list of the corresponding alcohols of the aluminum alkoxide salts with their Chemical Abstracts Service Registry Number (CASRN)). All data for ethanol, 1-butanol, 1-hexanol, 1-octanol, 1-decanol, 1-tetradecanol, 1-hexadecanol, 1-eicosanol, and 1-docosanol were obtained from IUCLID Data Sets from OECD SIDS RSS documents that are publicly available. For 2-propanol aluminum salt, all data were obtained from the 2-propanol OECD SIDS, except for adsorption to soil which was calculated using EPI Suite v3.12 (Table 4A). For 1-dodecanol and 1-octadecanol, most data were taken from the respective Supporting Robust Study Summaries for those substances (Table 4A). Data for Photodegradation, volatization, distribution, and adsorption to soil for 1-dodecanol and 1-octadecanol were calculated using EPI Suite v3.12 (Table 4A).

Data for the very long chain alcohols (1-tetracosanol, 1-hexacosanol, 1-octacosanol, and 1-triacontanol were less available. However, it should be noted that the sum of the aluminum alkoxides above C22 in the mixture is less than 0.3 percent. Toxicity (section 5) data for these species were obtained from a supporting Robust Study Summary for long chain aliphatic alcohols (CASRN 123607-66-9). This supporting Robust Study Summary covers long-chain alcohols with even chain lengths of 24 – 36 carbons, and includes 1-tetracosonal, 1-hexacosanol, 1-octacosanol, and 1-triacontanol. Environmental Fate and Pathways and Ecotoxicity data for these substances were calculated using EPI Suite. Physical-Chemical Data were obtained from experimental values found in literature such as the *CRC Handbook of Chemistry and Physics* or databases such as Registry. If experimental data were not available, values calculated using EPI Suite were used. In addition some of the Physical-Chemical Data and Toxicity data for 1-triacontanol were obtained from BIBRA Information Services Ltd.

Table 2. List of Aluminum Alkoxide Salts and their Corresponding Alcohols

Aluminum Alkoxide Salt (CASRN)	**Corresponding Alcohol** (CASRN)
Ethanol, aluminum salt (555-75-9)	ethanol (64-17-5)
2-propanol, aluminum salt (555-31-7)	2-propanol (67-63-0)
1-butanol, aluminum salt (3085-30-1)	1-butanol (71-36-3)
1-hexanol, aluminum salt (23275-26-5)	1-hexanol (111-27-3)
1-octanol, aluminum salt (14624-15-8)	1-octanol (111-87-5)
1-decanol, aluminum salt (26303-54-8)	1-decanol (112-30-1)
1-dodecanol, aluminum salt (14624-15-8)	1-dodecanol (112-53-8)

1-tetradecanol, aluminum salt (67905-32-2)	1-tetradecanol (112-72-1)
1-hexadecanol, aluminum salt (19141-82-3)	1-hexadecanol (36653-82-4)
1-octadecanol, aluminum salt (3985-81-7)	1-octadecanol (112-92-5)
1-eicosanol, aluminum salt (67905-31-1)	1-eicosanol (629-96-9)
1-docosanol, aluminum salt (67905-30-0)	1-docosanol (661-19-8)
1-tetracosanol, aluminum salt (67905-29-7)	1-tetracosanol (506-51-4)
1-hexacosanol, aluminum salt (67905-28-6)	1-hexacosanol (506-52-5)
1-octacosanol, aluminum salt (67905-27-5)	1-octacosanol (557-61-9)
1-triacontanol, aluminum salt (67905-26-4)	1-triacontanol (593-50-0)

Few data were available for the corresponding aliphatic alcohols with chain lengths of 24-30 carbons, 1-tetracosanol (CASRN 506-51-4), 1-hexacosanol (CASRN 506-52-5), 1-octacosanol (CASRN 557-61-9), and 1-triacontanol (CASRN 593-50-0). Extensive searching was done on numerous databases for information on the substances including TOXNET (which includes the Hazardous Substance Database, CCRIS, DART, IRIS, ITER, ToxLine Special, LactMed, GENETOX, and TRI), Ecotox (which includes the former AQUIRE, PHYTOTOX, and TERRETOX), Syracuse Research Corporation (SRC) (which includes BIOLOG, BIODEG, CHEMFATE, DATALOG, and PhysProp), PUBMED, Chemical Toxicity Database, the US National Toxicology Program (NTP), the US Environmental Protection Agency High Production Volume program, IRIS, the Toxic Substances Control Acts Test Submissions, the Environmental Fate DataBase, the SIRI Material Safety Data Sheet database, and the Merck Index. No new or relevant data were found for the above chemicals from these sources. However, these chemicals are unlikely to be toxic due to their predicted insolubility.

To supplement these industry data, and to compile information on the alcohols with chain lengths not encompassed by the Long Chain Alcohols SIAR, literature searches were conducted of on-line databases (*e.g.*, Hazardous Substances Databank [HSDB], Registry of Toxic Effects of Chemical Substances [RTECS], and the USEPA's ECOTOX database), standard scientific data compendia (*e.g.*, *CRC Handbook of Chemistry and Physics* and *The Merck Index*), and other published sources (*e.g.*, International Uniform Chemical Information Database [IUCLID]).

EVALUATION OF DATA FOR QUALITY AND ACCEPTABILITY

The collected data were reviewed for quality and acceptability following the general USEPA and OECD SIDS guidance (USEPA 1999b; OECD 1997) and the systematic approach described by Klimisch et al. (1997). These methods include consideration of the reliability, relevance and adequacy of the data in evaluating their usefulness for hazard assessment purposes. The Klimisch et al. (1997) approach specifies four categories of reliability for describing data adequacy. These are:

1. **Reliable without Restriction:** Includes studies or data complying with Good Laboratory Practice (GLP) procedures, or with valid and/or internationally accepted testing guidelines, or in which the test parameters are documented and comparable to these guidelines.

2. **Reliable with Restrictions:** Includes studies or data in which test parameters are documented but vary slightly from testing guidelines.

3. **Not Reliable:** Includes studies or data in which there are interferences, or that use non-relevant organisms or exposure routes, or which were carried out using unacceptable methods, or where documentation is insufficient.

4. **Not Assignable:** Includes studies or data in which insufficient detail is reported to assign a rating, *e.g.*, listed in abstracts or secondary literature.

As noted above, much of the data were derived from the Long Chain Alcohols SIAR and dossiers for the corresponding alcohols as compiled by another SDA consortium. Because of the extensive evaluation that these data underwent, the Aluminum Alkoxides Consortium has relied on the Klimisch reliability scores as assigned and reported in the available dossiers. For studies compiled from other sources, only those studies which are deemed reliable for the current HPV Challenge Program purposes are included in the data set for this assessment plan. Reliable studies include both categories rated 1 (Reliable without restriction) and 2 (Reliable with restrictions). Studies rated 3 (Not reliable) were not used. Studies rated 4 (Not assignable) were used when professional judgment deemed it appropriate as part of a weight-of-evidence approach.

ROBUST SUMMARIES AND CONSTRUCTION OF DATA MATRIX

Robust summaries were prepared according to the formats recommended by the USEPA (1999c) and OECD (1997). All of the summaries are collected into a dossier comprising all the salient information from each of the reliable studies available for the discrete alkoxide compound's corresponding alcohol and the constituents of the alkoxide mixture and their corresponding alcohols. The dossier is attached as Appendix A and should be used in conjunction with this assessment plan.

Tables 3A through 6 of this assessment plan is a matrix of SIDS/HPV endpoints and the available data supporting each of the sponsored chemical and chemical mixture's corresponding alcohols and alumina. Data drawn from the robust summaries are shown in the table for each endpoint and chemical when available. The data presented for the corresponding aliphatic alcohols are derived from the dossiers developed for the ICCA HPV program as described above.

EVALUATION OF MATRIX DATA PATTERNS

Evaluation of "Read Across" Patterns

The following discussion reviews the "read across" patterns identified for each of the four major data areas: physical-chemical properties, environmental fate and transport, ecotoxicity, and mammalian toxicity.

Note that aluminum alkoxides break down into their component alcohols and alumina, so data for the corresponding alcohols have been incorporated into Tables 3A through 6. Data are listed for the alcohol with the alcohol CAS number and the CAS number for the corresponding aluminum salt is listed in parenthesis. For example, data listed for ethanol, CAS No. 64-17-5 is provided to support ethanol, aluminum salt (CAS No. 555-75-9).

Data for alumina are presented separately in the corresponding part B tables for clarity.

Physical-Chemical Properties

The primary patterns of interest with respect to the physical-chemical properties of chemicals in the Aluminum Alkoxide category are trends in the parameters that affect partitioning between air and water, and between water and organic phases (e.g., soil or biota). The most important of these parameters are vapor pressure, water solubility, and the octanol/water partition coefficient (K_{ow}). As noted above, the aluminum alkoxides rapidly hydrolyze into alumina and the corresponding alcohols. Therefore, the physical-chemical properties of the alcohols and alumina are representative of the aluminum alkoxides. Properties vary with carbon chain length in accordance with normal expectations.

The available data for the alcohols, even carbons from C2 through C30 and 2-propanal, are presented in Table 3A. Greater than 90% of the aluminum salt mixture consists of C6 to C16 alkoxides with the average chain length around C10. These data indicate a strong trend toward increasing values for melting point and boiling point with increasing chain length. Conversely, vapor pressure decreases with increasing carbon chain length, except in cases where tests conducted at elevated temperatures skew the results. In each of these cases, the results are because molecular weight and intermolecular forces become higher as carbon chain length increases. Melting and boiling point measurements ranged from -114 to 87°C and from 78 to 494°C, respectively, rising consistently from ethanol up through triacontanol. Vapor pressures decrease from around 60 hPa for ethanol to around 9.5×10^{-11} hPa for triacontanol. It should be noted that the minor iso-branching of the 2-propanol does not break from this strong trend associated with carbon chain length.

Dissociation constant pK_a data are not included in Table 3A since long chain aliphatic alcohols are extremely weak acids and only dissociate under strongly basic conditions (pH >16). In the range of pH usually considered relevant to the environment, i.e. pH 4-9, these substances will be non-ionized.

Similarly, the octanol-water partition coefficient ($\log K_{ow}$) data increase with increasing molecular weight (and carbon chain length) since each additional CH_2 group makes the octanol phase more preferable in terms of relative solvation energy. These values range from very low for ethanol ($\log K_{ow} = -0.31$) to very high for triacontanol ($\log K_{ow} = 13.6$). EPI Suite modeling software (USEPA 2007) was used to estimate the $\log K_{ow}$ of the C24 through C30 materials. Comparison of EPI Suite estimated data with data from the other sources for the chain lengths less then C24 show a close correlation, thereby confirming the structural activity relationship (SAR) of increasing K_{ow} with increasing carbon chain length.

Water solubility data indicate a clear pattern of decreasing values with increasing carbon chain length. This is expected as the free energy required for a molecule to dissolve becomes less favorable for larger molecules. The shortest carbon chain length compounds (C2 and C4) are miscible in water. Slightly longer carbon chain length chemicals like hexanol (C6) are still very water soluble (e.g., the water solubility of C6 is around 5000 mg/L). Solubility quickly decreases with increasing chain length. For example, chemicals with chain lengths of around C12 have solubilities around 1 mg/L or less. This trend continues as carbon chain lengths above C16 are insoluble. In addition, the values estimated with the EPI Suite software confirm the SAR pattern of decreasing water solubility with increasing carbon chain length. These values are consistent with the K_{ow} values, which expectedly show an inverse relationship with water solubility.

The available physical/chemical property data for alumina are summarized in Table 3B. Aluminum oxide is a white solid high melting point (2030^{o}C) essentially insoluble material with insignificant vapor pressure at 20^{o}C (1 mm hg at 2158^{o}C). It is naturally occurring in the environment and would be expected to be associated with soil or sediment.

In summary, the aluminum alkoxides, as represented by their corresponding short and long chain aliphatic alcohols, show a strongly predictable pattern of decreasing water solubility and increasing melting point, boiling point, and K_{ow} as carbon chain length increases. In addition, these materials are not particularly volatile. An important trend for interpretation of the toxicity data is the lack of water solubility at the higher chain lengths (especially C12 and above).

The 2-propanol, aluminum salt exists as a discreet chemical. The remaining alcohols, spanning C2 to C30 are components of the aluminum alkoxide mixture. Therefore, the mixture properties would reflect not the properties of any one alcohol, but that of the combined mixture, especially within the range C6 to C16, since those carbon chain lengths make up more than 90% of the mixture. Because of the rapid decomposition of these aluminum alkoxides, data for the alcohols and alumina are representative of the exposures these compounds would present to human health or the environment.

Based on the extensive analysis carried out by SDA's Long Chain Alcohols Consortium, the availability of the Long Chain Alcohol SIAR, the series of OECD SIDS documents, and data from other sources, the Consortium believes that the physical-chemical properties of the aluminum alkoxides as represented by the corresponding alcohols are adequately characterized for HPV Challenge purposes. Each of these data compilations and analyses is publicly available for review should more detailed information be desired. Therefore, no further testing for these properties is proposed.

Table 3A. Physical/Chemical Properties of Alcohol Fraction					
Description	**CAS Number Alcohol (Alkoxide)**	Melting Point	Boiling Point	Density	Vapour Pressure
Ethanol	**64-17-5 (555-75-9)**	-114°C	78.3°C at 1013.25 hPa	0.7864 at 25°C, 0.7892 - 0.7896 at 20°C	57.26 hPa at 19.6°C, 78.7 hPa at 25°C, 66.3 hPa at 21.2°C
2-Propanol	**67-63-0 (555-31-7)**	-90°C	ca. 82 to 83°C at 1012 hPa	ca. 0.785 - 0.786 at 20°C	43 hPa at 20°C
1-Butanol	**71-36-3 (3085-30-1)**	-89.9°C	117.6°C at 101.325 kPa	0.8097	0.56 hPa at 20°C, 0.82 kPa at 25°C
1-Hexanol	**111-27-3 (23275-26-5)**	-44 to -51°C, -51.6°C	158°C	0.82	1.22 hPa at 25°C, 2 hPa at 40°C
1-Octanol	**111-87-5 (14624-13-6)**	-15.5 to -17°C, -18°C	194 to 195°C	0.826	0.1 hPa at 25°C, 1.33 hPa at 54°C, 2.2 hPa at 60.1°C
1-Decanol	**112-30-1 (26303-54-8)**	6.4°C, -7°C	229°C at 1013 hPa	0.8297	0.0113 hPa at 25°C, 2.93 hPa at 9°C, 1.33 hPa at 69.5°C
1-Dodecanol	**112-53-8 (14624-15-8)**	22.6 to 24°C	255 to 269°C, 259°C at 1013 hPa	0.83	0.00113 hPa at 25°C, 0.0087 hPa at 20°C
1-Tetradecanol	**112-72-1 (67905-32-2)**	39.5°C, 35 to 38°C	289°C, 263.2°C at 1013 hPa	0.8236 at 38°C, 0.81- 0.82 at 40°C	1.4×10^{-4} hPa at 25°C, 0.0133 hPa at 20°C
1-Hexadecanol	**36653-82-4 (19141-82-3)**	50°C	334 to 344°C, 300 to 320°C	0.8176 at 50°C	1.4×10^{-5} hPa at 25°C, 1.33 hPa at 122.7°C
1-Octadecanol	**112-92-5 (3985-81-7)**	59.5°C, 58°C	210°C at 15 mmHg	0.812 at 59°C	3.3×10^{-6} hPa at 25°C, 1.33 hPa at 150.3°C
1-Eicosanol	**629-96-9 (67905-31-1)**	66°C, 64 to 68°C	309°C, 372°C	0.8405 at 20°C, 0.8 - 0.804 at 4°C	1.5×10^{-7} hPa at 25°C, < 1 hPa at 20°C
1-Docosanol	**661-19-8 (67905-30-0)**	72.5°C, 69 to 73°C	401.1°C, 180°C	0.805 - 0.809 at 4°C	8.2×10^{-8} at 25°C, < 1 hPa at 20°C
1-Tetracosanol	**506-51-4 (67905-29-7)**	74 to 76°C	230 to 235°C at 12 Torr	0.839	2.4×10^{-9} mm Hg [4]
1-Hexacosanol	**506-52-5 (67905-28-6)**	77 to 78°C	175°C at 0.012 Torr, 305°C at 20 Torr	0.84	2.16×10^{-9} mm Hg at 25°C [4]
1-Octacosanol	**557-61-9 (67905-27-5)**	80 to 82°C	470.70°C [4]	0.841	4.02×10^{-10} mm Hg at 25°C [4]
1-Triacontanol	**593-50-0 (67905-26-4)**	87°C	493.91°C [4]	0.841	7.1×10^{-11} mm Hg at 25°C [4]

Table 3A. Physical/Chemical Properties of Alcohol Fraction						
Description	**CAS Number Alcohol (Alkoxide)**	Octanol/ Water Partition Coefficient (log)	Water Solubility	Flash Point	Auto-flammability	Viscosity
Ethanol	**64-17-5 (555-75-9)**	-0.31 at 25°C	> 10000 mg/L at 25°C, Miscible	14°C, 13°C	--	1.22 mPa*s at 20°C
2-Propanol	**67-63-0 (555-31-7)**	0.05	Miscible	12°C	425°C	--
1-Butanol	**71-36-3 (3085-30-1)**	0.88 at 20°C	77,000 mg/L at 20°C	37°C, 29°C to 35°C	365°C	--
1-Hexanol	**111-27-3 (23275-26-5)**	2.03	5900 mg/L at 25°C, 4231 mg/L at 20°C, 6270 at mg/L at 25°C	ca. 65°C, 60°C, 62°C	--	--
1-Octanol	**111-87-5 (14624-13-6)**	3.15	551 mg/L, 495 - 596 mg/L at 25°C, 300 mg/L at 20°C	ca. 90°C, 81°C	--	--
1-Decanol	**112-30-1 (26303-54-8)**	4.57	39.5 mg/L, 7.97 mg/L at 20°C, 106 mg/L at 20°C	82°C, ca. 110°C	--	--
1-Dodecanol	**112-53-8 (14624-15-8)**	5.36	1.93 mg/L at 20°C, 1.7 - 2.9 mg/L, 4 mg/L at 25°C	--	--	--
1-Tetradecanol	**112-72-1 (67905-32-2)**	6.03	0.191 mg/L at 25°C, 0.35 mg/L at 25°C	140°C, 155°C	--	--
1-Hexadecanol	**36653-82-4 (19141-82-3)**	6.65	0.013 mg/L at 25°C, 0.03 mg/L, 0.12 mg/L at 25°C	135°C, 175°C	--	--
1-Octadecanol	**112-92-5 (3985-81-7)**	7.19	0.0011 mg/L at 25°C	170°C	--	--
1-Eicosanol	**629-96-9 (67905-31-1)**	7.75	0.0027 mg/L at 25°C, Not soluble	195°C	--	--
1-Docosanol	**661-19-8 (67905-30-0)**	7.75	0.0027 mg/L at 25°C	195°C, ca. 227°C	--	--
1-Tetracosanol	**506-51-4 (67905-29-7)**	10.66[4]	1.471×10^{-5} mg/L at 25°C [4]	141.7°C	--	--
1-Hexacosanol	**506-52-5 (67905-28-6)**	11.65[4]	1.438×10^{-6} mg/L at 25°C [4]	139.2°C	--	--
1-Octacosanol	**557-61-9 (67905-27-5)**	12.63[4]	1.398×10^{-7} mg/L at 25°C [4]	135.3°C	--	--
1-Triacontanol	**593-50-0 (67905-26-4)**	13.61[4]	1.35×10^{-8} mg/L at 25°C [4], Insoluble	130.1°C	--	--

[1] Estimations using EPI SUITE v.3.11 software, [2] Read-across, expert judgment to related chemicals, [3] Estimations using EPI SUITE v.3.10 software, [4] Estimations using EPI SUITE v.3.12 software.

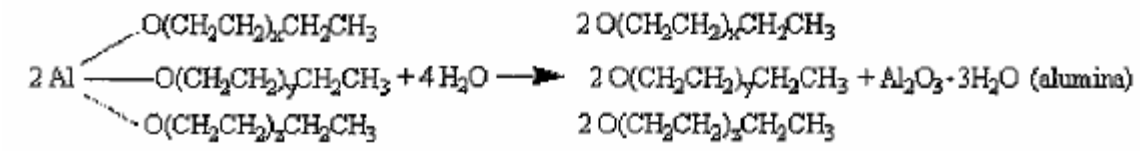
Table 3B. Physical/Chemical Properties of Alumina*	
Description	**Alumina (1344-28-1)**
Melting Point	2030°C
Boiling Point	2977°C
Density at 20ºC	4.0 g/cm^2
Vapor Pressure at 20ºC	Negligible (1 mm Hg at 2158°C)
Octenol/Water Partition Coefficient (log)	Not available
Water Solubility	Insoluble
Flash Point	Not flammable
Autoflamibility	N/A
Viscosity at 20ºC	solid

* Material Safety Data Sheet (Fisher Scientific 2007)

Environmental Fate and Transport

Environmental fate data are important for demonstrating the primary mechanism or mechanisms of degradation and how a material's properties affect its transport in the environment. For organic chemicals in general, fate is generally a function of the breakdown of compounds into smaller constituents by biological degradation. Other breakdown mechanisms that may be important are photolysis and hydrolysis. These breakdown mechanisms are necessarily dependent on what environmental compartment (air, water, soil, sediment) to which the chemicals are distributed. Fugacity modeling can be used to estimate the relative percentage of chemicals that will partition to various compartments at steady state. The results of the Level I fugacity modeling using EPI Suite using its standard estimated input parameters for the alcohol portion are shown in Table 4A. Information for alumina is shown in Table 4B. EPI Suite utilizes input values for relevant physicochemical parameters from its resident database, which has undergone extensive peer review and is accessed by input of the CAS number.

For the aluminum alkoxides, there is a two-step process of degradation. The first step is the hydrolysis of the aluminum alkoxides to their constituent linear alcohols and alumina. The chemical equation for the hydrolysis of aluminum salts is:



The reaction mechanism is described in depth in Brinker and Scherer (1990), who indicate that under neutral, acid or base conditions it is expected that the hydrolysis and condensation reactions would be quite rapid. While no rates of hydrolysis for aluminum alkoxides are available in the literature, data for silicone alkoxide show rapid hydrolysis (log K_{spont}) in aqueous systems. Log K_{spont} values within the pH range 4 to 10 vary from approximately -4 at neutral pH

to -2 at both acid and base pH. Since this reaction is acid catalyzed, the rate at pH 1 is anticipated to extend even further upward from the "acidic portion" of the curve. Based on reaction dynamics, aluminum alkoxide would be expected to be even faster than silicone alkoxide under both environmental and physiological conditions (Brinker and Scherer 1990). Under neutral conditions, it is expected that both hydrolysis and condensation of aluminum alkoxides occur by nucleophilic addition, followed by proton transfer and elimination of either water or alcohol in a manner analogous to transition metal alkoxides. Likewise, both of these reactions are catalyzed by addition of either acid or base. Acids protonate OR or OH ligands creating good leaving groups and eliminating the requirements for proton transfer in the intermediate. Bases deprotonate water or OH ligands, creating strong nucleophiles. Although the hydrolysis kinetics are not well documented, since aluminum alkoxides may be coordinatively unsaturated, kinetic pathways of nucleophilic reactions should be quite facile. Consequently, the rates of hydrolysis (and condensation) are greater than for silicon alkoxides which are coordinatively saturated and normally exhibit only one stable coordination number (Brinker and Scherer 1990).

The second step of the degradation process follows the predominant biodegradation mechanisms of the resultant alcohols. Thus, the environmental fate characteristics of the resultant alcohols are summarized below and discussed in depth in the Long Chain Alcohols SIAR are reflective of the aluminum salts.

Detailed results are provided in the Long Chain Alcohols SIAR (C6 to C22) and the individual IUCLID data sets (C2 to C4 plus 2-propanol) and in the robust summaries attached to the current document. Data consist of both actual studies and (Q)SAR methods, with the measured data confirming the validity of the modeled results. Category members do not possess any particularly unusual features, which provide confidence in the prediction of physical-chemical and environmental fate properties. The data show that mammalian biotransformation of aliphatic alcohols involves an oxidation step of the alcohol function to the corresponding aliphatic carboxylic acid, with the aldehyde being a transient intermediate. These carboxylic acids (i.e. fatty acids) are subsequently broken down by stepwise removal of one or several C-2 units from the aliphatic carbon chain through the β-oxidation process. The stepwise breakdown of aliphatic alcohols results in common intermediate metabolites with shorter chain lengths. Aliphatic alcohols are, in general, highly efficiently metabolized and there is limited potential for retention or bioaccumulation for the parent alcohols and their biotransformation products.

Aliphatic alcohols have been extensively studied and reported. Measured biodegradation data are available for most of the compounds in this category. For some members, e.g., the very long carbon length alcohols (C24 to C30) EPI Suite modeling was used to estimate biodegradation. These data show that aliphatic alcohols up to about C18 are readily biodegradable. Carbon chain lengths ≤C14 generally reached the pass levels for ready biodegradation with the 10-day window. Chain lengths of C16 to C18 achieved ready test pass levels, but not within the 10-day window. Carbon chain lengths >C18 biodegraded more slowly.

As noted above, aluminum alkoxides are not stable in environmental systems. The 2-propanol portion of the aluminum alkoxide is readily biodegradable, as are the alcohol portions of the mixture, >90% of which are C6 to C16.

The atmospheric oxidation potential of the aliphatic alcohols is available across the range of carbon chain lengths. Most of the data were estimated using the EPI Suite software. This estimation suggests that photodegradation may be a significant mechanism for the breakdown of aliphatic alcohols in the atmosphere. Based on the model estimates, the hydroxyl radical reaction half-lives ranged from about 3 to about 30 hours. In respect to abiotic degradation in water, aliphatic alcohols are expected to be stable. Photooxidation in aqueous systems is not significant. In addition, aliphatic alcohols would be expected to be stable in water because alcohols have no hydrolysable groups and are therefore not susceptible to hydrolysis (Lyman et al. 1990).

The Long Chain Alcohols SIAR indicates that no reliable guideline standard measured bioconcentration data are available. Based on the fact that log K_{ow} values for carbon chain lengths of about C11 and above are greater than 4.5, these materials could be potentially bioaccumulative. However, the rapid biodegradation and evidence of rapid metabolism in mammalian studies suggests that it would actually be unlikely that bioaccumulation would be seen under environmental conditions. Estimated BCF data are provided in Table 4A for completeness, but the data set should not be considered definitive for this endpoint.

The remaining question has to do with the environmental fate of the resulting alumina component. The environmental fate characteristics of aluminum and its many complexes are well understood (Research Triangle Institute 1997). In addition, alumina is a naturally occurring material and is ubiquitous in the environment. Therefore, it is not necessary to conduct additional testing for the HPV Challenge program.

In conclusion, results of the environmental fate and transport studies demonstrate that aliphatic alcohols are readily biodegradable up to about C18 and are not expected to bioaccumulate. Longer chain alcohols will biodegrade at a slower rate, but also are not expected to bioaccumulate. Based on the availability of high quality biodegradation data and other estimated values for the full range of carbon chain lengths, no further testing of environmental fate endpoints is proposed.

Table 4A. Environmental Fate and Pathways of Alcohol Fractions							
Description	**CAS Number**	**Photodegradation**	**Volatization from Water**	**Distribution**	**Adsorption: Soil-Water Partition Coefficient**	**Biodegradation**	**Bioconcentration Factor**
Ethanol	**64-17-5 (555-75-9)**	15.4 hours	Stable	13.0% to Air 42.1% to Soil 44.8% to Water 0.039% to Sediment	Koc =1 [1]	74% degradation after 5 days, 75% degradation after 20 days, 37% degradation after 1 day, 91% degradation after 30 days, 96.8% degradation after 15 days	3.16 [1]
2-Propanol	**67-63-0 (555-31-7)**	18 - 25 hours	Stable	22.3% to Air 0.0% to Soil 77.7% to Water 0.0% to Sediment[1]	Koc = 1.06 [4]	49% degradation after 5 days at 20°C	1.0[1]
1-Butanol	**71-36-3 (3085-30-1)**	30 hours, 37 hours	39.51 days (river) 434.1 days (lake) [3]	40.2% to Air 44.1% to Soil 15.7% to Water >0.1% to Sediment[3]	Koc = 2.44 L/kg [3]	82% degradation after 20 days	3.162 L/kg [3]
1-Hexanol	**111-27-3 (23275-26-5)**	30.8 hours	Stable	28% to Air 6.23% to Soil 65.6% to Water 0.14% to Sediment	Koc = 56 Koc = 118 Koc = 19.6 Koc = 8.3[1]	77 to 61% degradation after 30 days, 58% degradation after 31 days, 77% degradation after 30 days	11[1]
1-Octanol	**111-87-5 (14624-13-6)**	26.7 hours	Stable	17.3% to Air 45.4% to Soil 36.3% to Water 1.01% to Sediment	Koc = 448 Koc = 455.0 Koc = 53.5 Koc = 28.3[1]	92% degradation after 28 days, 60% degradation after 30 days, 59% degradation after 29 days	95[1]
1-Decanol	**112-30-1 (26303-54-8)**	25.1 hours[1]	Stable[2]	2.57% to Air 92.5% to Soil 2.81% to Water 2.06% to Sediment	Koc = 6330 Koc = 2490 Koc = 190 Koc = 96[1]	88% degradation after 30 days, 77% degradation after 30 days, 54% degradation after 31 days, 29% degradation after 29 days	1530[1]
1-Dodecanol	**112-53-8 (14624-15-8)**	7.054 hours [4]	1.558 days (river) 21.77 days (lake) [4]	0.989% to Air 58.2% to Soil 16.3% to Water 24.5% to Sediment [4]	Koc = 327.1 [4]	79% degradation after 28 days, 100% degradation after 28 days, 71% degradation after 28 days, 50% degradation after 28 days	3801
1-Tetradecanol	**112-72-1 (67905-32-2)**	18.3 hours[1]	Stable[2]	0.33 % to Air 97.3% to Soil 0.10% to Water 2.16% to Sediment[1]	Koc = 50830, Koc = 96500 Koc = 14300 Koc = 710 Koc = 1110[1]	92% degradation after 28 days, 57% degradation after 31 days, 28% degradation after 28 days, 55 - 66% degradation after 28 days	33900

Table 4A. Environmental Fate and Pathways of Alcohol Fractions

Description	CAS Number	Photodegradation	Volatization from Water	Distribution	Adsorption: Soil-Water Partition Coefficient	Biodegradation	Bioconcentration Factor
1-Hexadecanol	**36653-82-4 (19141-82-3)**	16.2 hours[1]	Stable[2]	0.13% to Air 97.6% to Soil 0.03% to Water 2.17% to Sediment	Koc = 307000 Koc = 30100 Koc = 1240 Koc = 3790[1]	62% degradation after 28 days, 76% degradation after 28 days, 97% degradation after 28 days, 90.1% degradation after 28 days	45300
1-Octadecanol	**112-92-5 (3985-81-7)**	4.812 hours [4]	0.1176 days (river) 7.029 days (lake) [4]	0.317% to Air 28.8% to Soil 3.79% to Water 67.1% to Sediment [4]	Koc = 12880 [4]	38 - 69% degradation after 29 days, 67% degradation after 28 days, 67% degradation after 31 days, 43% degradation after 28 days	100000[1]
1-Eicosanol	**629-96-9 (67905-31-1)**	13.1 hours[1]	Stable[2]	1.61×10^{-3}% to Air 97.8% to Soil 1.96×10^{-3}% to Water 2.17% to Sediment[1]	Koc = 2390000 Koc = 112000 Koc = 3330 Koc = 43800[1]	Biodegradable[2]	31800
1-Docosanol	**661-19-8 (67905-30-0)**	11.9 hours[1]	Stable	1.05×10^{-3}% to Air 97.8% to Soil 1.96×10^{-3}% to Water 2.17% to Sediment	Koc = 2390000 Koc = 112000 Koc = 3330 Koc = 149000[1]	37% degradation after 28 days	31800
1-Tetracosanol	**506-51-4 (67905-29-7)**	3.651 hours [4]	0.09597 days (river) 7.627 days (lake) [4]	0.188% to Air 31.2% to Soil 3.57% to Water 65.1% to Sediment[4]	Koc = 5.07×10^{5} [4]	Primary - Days - weeks Ultimate - Weeks [4]	3.162 [4]
1-Hexacosanol	**506-52-5 (67905-28-6)**	3.380 hours [4]	0.09256 days (river) 7.845 days (lake) [4]	0.179% to Air 31% to Soil 3.58% to Water 65.3% to Sediment [4]	Koc = 1.724×10^{6} [4]	Primary - Days - weeks Ultimate - Weeks [4]	3.162 [4]
1-Octacosanol	**557-61-9 (67905-27-5)**	3.146 hours [4]	0.09169 (river) 8.081 (lake) [4]	0.0676% to Air 30.9% to Soil 1.82% to Water 67.2% to Sediment [4]	Koc = 5.866×10^{6} [4]	Primary - Days - weeks Ultimate - Weeks - months[4]	3.162 [4]
1-Triacontanol	**593-50-0 (67905-26-4)**	2.942 hours [4]	0.0923 (river) 8.326 (lake) [4]	0.0643% to Air 30.8% to Soil 1.83% to Water 67.3% to Sediment [4]	Koc = 1.995×10^{7} [4]	Primary - Days - Weeks Ultimate - Weeks - months [4]	3.162 [4]

[1] Estimations using EPI SUITE v.3.11 software, [2] Read-across, expert judgment to related chemicals, [3] Estimations using EPI SUITE v.3.10 software, [4] Estimations using EPI SUITE v.3.12 software.

Table 4B. Environmental Fate and Pathways of Alumina	
CAS Number	**1344-28-1**
Photodegradation	None
Volatization from Water	Stable
Distribution	Soil or sediment
Biodegradation	N/A
Bioconcentration Factor	N/A

Ecotoxicity

The primary pattern to look for in ecotoxicity of organic compounds is whether the toxicity to aquatic organisms changes as carbon chain length increases. In addition, it is important to determine whether the physical-chemical properties of the chemicals affect their bioavailability, and subsequently, their aquatic toxicity. Aliphatic alcohols fit into the neutral organics class of compounds and generally exert toxicity through a non-polar narcosis mode of action (Lipnick et al. 1985). As chain length increases, hydrophobicity increases and water solubility decreases, resulting in greater toxicity. However, at a critical point (the cut-off), the decreased water solubility limits the bioavailability of the alcohol. At this point, a toxic concentration can not be achieved.

The aquatic toxicity of aliphatic alcohols has been extensively studied (Long Chain Alcohols SIAR 2006). Acute fish toxicity data are available for most of the corresponding individual carbon chain length alcohols that make up the alkoxide mixture. The data indicate very low toxicity for the shorter (<C8) carbon chain length alcohols (e.g., ethanol 96-hr LC_{50} = 13,000 mg/L). Then, there is a clear pattern of increasing toxicity (i.e., decreasing LC_{50} values) with increasing chain length until approximately C14. Beyond this cut-off, no toxicity is observed. As discussed above, the water solubility of aliphatic alcohols decreases as chain length increases. This results in the higher carbon chain length chemicals reaching saturation at very low concentrations in water. Thus, saturation occurs below the concentration that is toxic to fish and these compounds are neither bioavailable nor toxic.

The 2-propanol portion of the aluminum alkoxide has low aquatic toxicity. The mixture in which >90% of the compounds are C6 to C16 would be expected to have an aquatic toxicity relative to the varying toxicities of the mixture components, however, the exposure potential would be expected to be very low, since it is a site limited intermediate.

Acute toxicity data for invertebrates (such as *Daphnia*) and algae demonstrate the same limitation in water solubility and lack of toxicity seen for fish. Toxicity of aliphatic alcohols to *Daphnia* and algae increases until approximately C14, after which low water solubility limits how much of the chemical is bioavailable.

Similarly, chronic effects for the aliphatic alcohols are also shown by the available data to again indicate that effects of the individual alcohols are anticipated up to around C14. For alcohols with carbon numbers higher than this there are significant experimental difficulties in producing, maintaining and quantifying exposures of the test substance. Even so, it is unlikely that they would exhibit chronic toxicity because of limited bioavailability due to their low water solubility.

The relationship between carbon number and chronic toxicity, established from the test results that are available, suggests that the solubility of the alcohol would limit the bioavailable dissolved fraction to sub-toxic concentrations.

In addition, the majority of the aliphatic alcohols in this category biodegrade rapidly. This would limit the concentration to which organisms would be exposed to over time. The increased toxicity observed with some of the chain length alcohols would be balanced by their rapid degradation.

The aquatic toxicity of alumina has been studied using *Daphnia magna*, fathead minnows and rainbow trout (Nielsen 1993). No mortality was observed at a 100% water soluble fraction (WSF) concentration for all three species. In a second set of tests, the measured 96-hour LC_{50} values for a colloidal suspension of alumina (Dispal 23N4) were >2,100 mg/L and >10,000 mg/L for rainbow trout and fathead minnow, respectively, indicating very low toxicity. The 48-hour LC_{50} to daphnia of the Dispal 23N4 suspension was >10,000 mg/L. Based on these results, no aquatic concern is warranted from the alumina component of the aluminum alkoxide salts.

In summary, as shown in Tables 5A, the toxicity to aquatic organisms increases with increasing carbon chain length until approximately C14, after which low water solubility limits how much of the chemical is bioavailable and no additional toxicity is observed. No additional ecotoxicity testing is necessary to support the HPV Challenge program.

Table 5A. Ecotoxicity of Alcohol Fractions					
Description	**CAS Number Alcohol (Alkoxide)**	**Acute/Prolonged Toxicity to Fish**	**Acute Toxicity to Daphnia**	**Toxicity to Aquatic Plants (e.g., algae)**	**Chronic Toxicity to Daphnia**
Ethanol	**64-17-5 (555-75-9)**	96-hr LC_{50} = 13000 mg/L, 96-hr LC_{50} = 13480 mg/L, 96-hr LC_{50} = 14.2 g/L	48-hr LC_{50} = 12340 mg/L, 18-hr EC_{50} = 12.1 g/L	96-hr EC_{50} = 1000 mg/L, 96-hr EC_{50} = 10000 mg/L	NOEC = 9.6 mg/L
2-Propanol	**67-63-0 (555-31-7)**	96-hr LC_{50} = 9640 mg/L	24-hr EC_{50} > 10,000 mg/L, 48-hr LC_{50} = 1400 mg/L	TT = 1800 mg/L	NOEC = 141 mg/L NOEC = 30 mg/L
1-Butanol	**71-36-3 (3085-30-1)**	96-hr LC_{50} = 1376 mg/L, 96-hr LC_{50} = 1400 mg/L, 96-hr LC_{50} = 1730 mg/L	48-hr EC_{50} = 1328 mg/L, 48-hr EC_{50} = 2337 mg/L 48-hr EC_{50} = 1983 mg/L	96-hr EC_{50} = 225 mg/L, 96-hr EC_{50} > 500 mg/L	LC_{50} = 21mg/L [3]
1-Hexanol	**111-27-3 (23275-26-5)**	96-hr LC_{50} = 97.2 - 97.5 mg/L	24-hr EC_{50} = 201 mg/L	72-hr $EC_{50}ErC_{50}$ = 79.7 mg/L	NOEC = 6.8 - 13 mg/L
1-Octanol	**111-87-5 (14624-13-6)**	96-hr LC_{50} = 13.3 - 13.5 mg/L,	24-hr EC_{50} = 20 mg/L	48-hr $EC_{50}ErC_{50}$ = 6.5 - 14 mg/L	NOEC = 1 mg/L
1-Decanol	**112-30-1 (26303-54-8)**	96-hr LC_{50} 2.3 mg/L,	48-hr EC_{50} = 2.9 mg/L,	EC_{50} = ca. 1 - 10 mg/L [2]	LOEC = NOEC = 110370 µg/L
1-Dodecanol	**112-53-8 (14624-15-8)**	96-hr LC_{50} = 1.01 mg/L,	48-hr EC_{50} = 0.765 mg/L,	72-hr EbC_{50} =0.62 mg/L, 72-hr ErC_{50} = 2.6 mg/L,	NOEC = 14 µg/L,
1-Tetradecanol	**112-72-1 (67905-32-2)**	96-hr LC_{50} > 1 mg/L, (>LOS)	EC_{50} = 4 mg/L (>LOS)	96-hr $ErLC_{50}$ > 10 mg/L (>LOS)	NOEC = 1.6 µg/L
1-Hexadecanol	**36653-82-4 (19141-82-3)**	96-hr LC_{50} > 0.4 mg/L, (>LOS)	EC_{50} > 100 mg/L [1] (>LOS)	96-hr $ErI_{50}ErL_{50}$ > 980 mg/L, 96-hr EC_{50} = 690EbL_{50} = 680 mg/L (>LOS)	No chronic effects [2]

Table 5A. Ecotoxicity of Alcohol Fractions					
Description	**CAS Number Alcohol (Alkoxide)**	**Acute/Prolonged Toxicity to Fish**	**Acute Toxicity to Daphnia**	**Toxicity to Aquatic Plants (e.g., algae)**	**Chronic Toxicity to Daphnia**
1-Octadecanol	**112-92-5 (3985-81-7)**	96-hr LC_{50} > 0.4 mg/L, (>LOS)	48-hr EC_{50} = 1700 mg/L (>LOS)	96-hr EC_{50} = 250 mg/L (>LOS)	NOEC = 0.98 mg/L (>LOS)
1-Eicosanol	**629-96-9 (67905-31-1)**	LC_{50} > 100 mg/L[1] (>LOS)	EC_{50} > 100 mg/L[1] (>LOS)	EC_{50} > 100 mg/L[2] (>LOS)	No chronic effects[2]
1-Docosanol	**661-19-8 (67905-30-0)**	96-hr LL_{50} > 1000 mg/L, (>LOS)	EC_{50} > 100 mg/L[1] (>LOS)	EC_{50} > 100 mg/L[2] (>LOS)	No chronic effects[2]
1-Tetracosanol	**506-51-4 (67905-29-7)**	96-hr LC_{50} = 1.9 x 10^{-6} mg/Lppm [4] (>LOS)	48-hr LC_{50} = 3.71 x 10^{-6} ppm[4]mg/L[4] (>LOS)	96-hr EC_{50} = 3.82 x 10^{-6} ppm[4]mg/L[4] (>LOS)	16-day EC_{50} = 8.41 x 10^{-6} [4]mg/L[4] (>LOS)
1-Hexacosanol	**506-52-5 (67905-28-6)**	96-hr LC_{50} = 2.41 x 10^{-7} ppm[4]mg/L[4] (>LOS)	48-hr LC_{50} = 5.03 x 10^{-7} ppm[4] mg/L[4] (>LOS)	96-hr EC_{50} = 5.48 x 10^{-7} ppm[4]mg/L[4] (>LOS)	16-day EC_{50} = 1.76 x 10^{-6} [4]mg/L[4] (>LOS)
1-Octacosanol	**557-61-9 (67905-27-5)**	96-hr LC_{50} = 3.1 x 10^{-8} mg/L[4] (>LOS)	48-hr LC_{50} = 6.92 x 10^{-8} mg/L[4] (>LOS)	96-hr EC_{50} = 7.98 x 10^{-8} mg/L[4] (>LOS)	16-day EC_{50} = 3.72 x 10^{-7} [4]mg/L[4] (>LOS)
1-Triacontanol	**593-50-0 (67905-26-4)**	96-hr LC_{50} = 3.97 x 10^{-9} mg/L[4] (>LOS)	48-hr LC_{50} = 9.49 x 10^{-9} mg/L[4] (>LOS)	96-hr EC_{50} = 1.16 x 10^{-8} mg/L[4] (>LOS)	16-day EC_{50} = 7.82 x 10^{-8} [4]mg/L[4] (>LOS)

[1] Estimations using ECOSAR v.0.99g in EPI SUITE v.3.11 software, [2] Read-across, expert judgment to related chemicals, [3] Estimations using ECOSAR v.0.99g in EPI SUITE v.3.10 software, [4] Estimations using ECOSAR v.0.99g in EPI SUITE v.3.12 software., LOS = Limit of Solubility

Table 5B. Ecotoxicity of Alumina	
Description	**Alumina**
Acute/Prolonged Toxicity to Fish	>100% WSF rainbow trout and fathead minnow
Acute Toxicity to Daphnia	>10,000 mg/L
Toxicity to Aquatic Plants (e.g., algae)	Not available
Chronic Toxicity to Daphnia	Not available

Mammalian Toxicity

Acute toxicity

Toxicity to mammalian test animals is an important surrogate for estimating potential effects on humans. Again, patterns related to carbon chain length are evaluated to determine if data endpoints without values can be predicted from the data that are available. Several aspects of mammalian toxicity are evaluated. Acute testing provides information on gross effects, such as mortality, from exposure to high doses. Repeated dose testing provides information on toxicity associated with multiple doses over time. Genetic testing is conducted to evaluate the potential for mutagenic effects by using bacterial systems (e.g., the Ames test), non-bacterial systems (e.g., chromosomal aberrations), and *in vivo* (i.e., live animal) systems. Reproductive and developmental/teratogenic testing provides information on the potential effects in developing embryos and young animals. It is important to note that the lack of significant exposure may obviate the need to fill apparent data gaps with mammalian testing, especially in light of animal welfare concerns.

There are three primary routes of exposure used in the evaluation of acute toxicity: 1) oral, where the test substance is introduced in food or directly into the test animal by gavage; 2) inhalation, where the substance is introduced into the lungs as a vapor; and 3) dermal, where the substance is applied directly to the skin. The choice of exposure route depends on the physical-chemical characteristics of the test substance and the likely route by which animals or humans would be exposed. Data for all three routes of exposure are usually not necessary to understand the acute toxicity of a particular chemical substance.

For the Long Chain Alcohols category, acute oral toxicity data are available for virtually all of the discrete alcohols (as representatives of exposure to the aluminum salts). The data indicate generally low toxicity, with most of the LD50 values greater than the highest dose tested (e.g., LD50 values ranging from >3210 mg/kg bw to >30,000 mg/kg bw). Acute inhalation tests are available for the even carbon chains C2 through C16 and C20, as well as for 2-propanol. Only slight pulmonary irritation at relatively high doses was observed. Furthermore, the generally low volatility of aliphatic alcohols suggests that inhalation would not be a significant route of exposure as LC50 values exceed the saturated vapor pressure. Acute dermal toxicity data are available for the even carbon chains C2 through C16, C20 and C30, as well as for 2-propanol. These data indicate a generally low toxicity. Therefore, it is reasonable to predict that the values for the remaining compounds in the category will be similar to the pattern observed in the available data. Overall, the acute toxicity of aliphatic alcohols via the oral, inhalation and dermal exposure routes is exceptionally well characterized by the available data and, therefore, the production of additional hazard data is not warranted.

The acute oral toxicity of alumina has been studied in rats (Kuhn 1990). No mortality was observed at 5,050 mg/kg bw following oral intubation of 40% w/v aluminum monohydrate (Catapal D). Slight piloerection in males and females and slight diarrhea in males was observed in the first 0.5 to 3 hours, but had returned to normal in all animals by 6 hours. No other signs

were observed and no abnormalities were found in the gross necropsy. While specific acute inhalation and dermal data were not identified, it is reasonable to expect that exposure via these routes would result in a similar lack of acute toxicity. Therefore, toxicity to mammals from the alumina component of the aluminum salts subcategory is not a significant concern and production of additional hazard data is not warranted.

Repeated dose toxicity

Repeated dose data are available for C2, C4, C6, C12, C16, C18 (Long Chain Alcohols SIAR 2006). This carbon range accounts for ~98% of the material in the mixture. No effects on rat survival were observed after oral C2 exposures up to 1.2 g/kg bw/day or oral C4 exposures up to 500 mg/kg bw/day. Clinical signs of toxicity, including ataxia, tremors, and anesthesia, were observed for C6 in dogs at only the high dose of 1000 mg/kg/day. No effects were seen in rats exposed to 6.0% (60,000 mg/kg) C6 in the diet. The no observed adverse effect level (NOAEL) in rats exposed to C12 continuously through the diet for 37 days was 100 mg/kg bw/day. However, this NOAEL was based on a small effect on white blood cells and some effects on biochemical parameters only. No significant effects on body weight indices, or developmental or reproductive endpoints were observed at dietary doses of C12 up to 2000 mg/kg bw/day. Similarly, no significant dose responsive effects were observed in dogs or rats exposed orally to C16 at 1000 mg/kg/day or up to 10.0% w/w, respectively. No significant effects were observed in rats after exposure to 1000 mg/kg C18 given by oral gavage 5 days/week for 28 days. Data for 2-propanol are summarized in the OECD SIDS report. It has been tested both by the oral and inhalation routes with the only effects seen to the kidneys at some dose levels. The inhalation NOEL was reported to be 500 ppm and the oral NOEL was 1%. These data clearly demonstrate that toxicity to various mammalian species is very limited and no further repeated dose testing is necessary.

Alumina is generally non-toxic to aquatic and mammalian test animals, and is listed by the US Food and Drug Administration (FDA) under 21 CFR §176.180 as being cleared for limited food contact use. The trihydrated form, aluminum hydroxide, is listed as "Generally Recognized as Safe" (GRAS) under 21 CFR §182.90. Therefore, alumina (the non-hydrated form) would be expected to be considered GRAS as well.

Genetic toxicity

Bacterial *in vitro* data (Ames test) are available for C2, C4, C6, C8, C12, C16, C18, C22 and for 2-propanol. The results of all these studies were negative for mutagenicity. Based on the consistency of these results across the various chain lengths for which data are available, additional bacterial *in vitro* testing is not warranted.

Non-bacterial *in vitro* studies are available for C2, C4, C20, C22, C30 and for 2-propnol. Ethanol gave both negative and positive results. C4, C20, C22 and 2-propanol tests were negative while the C30 test was positive. However, aliphatic alcohols contain no structurally active group that would be expected to be mutagenic. Overall, the lack of concern is demonstrated by the universal lack of mutagenicity observed in a suite of bacterial in vitro tests conducted across nearly the full range of alcohols present in the category (and in the *in vivo* tests described in the next paragraph). Therefore, no non-bacterial *in vitro* studies are

recommended.

Mouse micronucleus *in vivo* data have been reported in the C12 and C18 dossiers prepared under the OECD SIDS program. For both alcohols, the results were negative. Furthermore, because of animal rights concerns, current U.S. Environmental Protection Agency guidance for the HPV Challenge Program strongly discourages conducting *in vivo* studies unless absolutely necessary (USEPA 1999a; USEPA 1999b). Therefore, no additional *in vivo* testing is recommended.

Results of a bacterial *in vitro* test on aluminum were negative (Marzin and Phi 1985), suggesting that the alumina component of the aluminum salts is not a significant concern with regard to genotoxicity.

Reproductive toxicity

Data on reproductive endpoints are available for C2, C4, C6, C8, C12, and C18 (Long Chain Alcohols SIAR 2006). No reproductive effects were seen in rats exposed via inhalation to concentrations of C2, C4, C6 or C8 up to 38,000 mg/m^3 administered on gestation days 1-19. Some signs of maternal toxicity (e.g., reduced feeding and narcosis) were observed at 18,000 mg/m^3 and above. No effects on reproductive endpoints were observed in rats given 10 consecutive daily doses (oral gavage) of C6 at 1000 mg/kg bw/day, although clinical signs and decreased body weight suggested maternal toxicity at this dose. These nonreproductive effects were not observed at 200 mg/kg bw/day. No effects on reproductive parameters (pregnancy rates, lengths of gestation periods, number of pups per litter) were seen in rats given C12 dietary exposures up to 2000 mg/kg bw/day for 14 days. In addition, no effects on maternal body weight, weight gain, food consumption or on the weight, sex ratio, or mortality rate of the young. Similarly, no effects on reproductive, hematological or pathological parameters were observed after rats were exposed to up to 2000 mg/kg bw/day C18 in the diet for 14 days. Reproduction testing by oral gavage on 2-propanol resulted in NOELs of ≤500 mg/kg/day for parental, F1 offspring and F2 offspring based on reduced mating index in the F1 males and reduced postnatal survival of F1 and F2 offspring. Based on the lack or very low incidence of reproductive toxicity across a wide range of carbon chain lengths, no further reproduction toxicity testing is necessary to characterize the category.

Developmental toxicity

Developmental/teratogenic toxicity data are available for C2 (inhalation), C4 (inhalation), C6 (oral and inhalation) C8 (oral and inhalation), C10 (inhalation), C12 (oral), C18 (oral) and 2-propanol (oral). No maternal toxicity, but some decrease in fetal weight gain, was observed in rats exposed to C2 at very high concentrations. It should be noted that the concentrations tested in the inhalation studies were the highest that could be generated as a vapor at average daily temperatures. These obtainable concentrations decreased as the carbon chain length increased. (19,000 mg/m^3). For C4, the NOAEL for both maternal and fetal developmental toxicity in rats was 10,500 mg/m^3. Teratogenic effects (primarily rudimentary cervical ribs) were observed at 24,000 mg/m^3 after exposure to C4 by inhalation. No treatment-related maternal or fetal effects were observed at the highest doses tested for all carbon chain lengths greater than C4. Aliphatic

alcohols longer than butanol (C4) did not show an increased incidence of developmental toxicity. These longer chain length chemicals may not generate vapors at sufficiently high concentrations to induce observable maternal toxicity in rats by inhalation, the main route of industrial exposure. 2-propanol produced developmental effects in rats, but not in rabbits. The toxicity occurred only at maternally toxic does and was confined to lower fetal weights with no evidence of teratogenicity. The NOAEL was 400 mg/kg/day. Based on the low volatility of these aliphatic alcohols and associated very low developmental/teratogenic toxicity above C4, no further developmental tests are necessary.

Overview of Health Effects

Toxicity data are summarized in Table 6. A review of the toxicological database for the category of the aliphatic alcohols demonstrates that these materials are of a low order of toxicity upon single or repeated exposure. Overall, the data show an inverse relationship between chain length and toxicity. The shorter chain alcohols tend to induce more pronounced effects when compared to materials with a longer chain length. This is illustrated most clearly by the degree of local irritation in studies involving single or repeat administration. Aliphatic alcohols have no skin sensitization potential, are not mutagenic and have not shown any adverse effects on fertility, development and reproduction. On the basis that a clear relationship exists between chain length and toxicological properties, substances with chain lengths exceeding the upper range tested can be expected to possess toxicological properties similar to those tested. Few data were available for the corresponding aliphatic alcohols with chain lengths of 24-30 carbons, 1-tetracosanol (CASRN 506-51-4), 1-hexacosanol (CASRN 506-52-5), 1-octacosanol (CASRN 557-61-9), and 1-triacontanol (CASRN 593-50-0). The few toxicity studies that have been done show low toxicity (e.g. LD_{50} >5000 mg/kg bw). Long-chain aliphatic alcohols occur naturally in plants. According to the US EPA (EPA 1983), "1-triacontanol is found to be ubiquitous in all plant life and insect waxes. Thus animals that consume vegetation, including humans naturally ingest this compound as a diet constituent." Octacosanol has been investigated as a diet supplement for increasing endurance (Kim 2003), and may have cholesterol-lowering effects (Menendez 2005). Treatment with hexacosanol can aid in the regeneration of damaged nerve fibers (Azzouz 1996). In light of these studies, it seems unlikely the small amounts of long-chain aliphatic alcohols released by aluminum alkoxide salts relative to the amount of the substances found naturally in the environment would be problematic.

The acute oral toxicity of alumina has been studied in rats. No mortality was observed at 5050 mg/kg bw following oral intubation. While specific acute inhalation and dermal data were not identified, it is reasonable to expect that exposure via these routes would result in a similar lack of acute toxicity. Therefore, toxicity to mammals from the alumina component of the aluminum salts is not a significant concern and production of additional hazard data is not warranted.

In summary, there is generally low toxicity of aliphatic alcohols and 2-propanol to mammals. Acute toxicity data generally indicate LD_{50} and LC_{50} values greater than the highest doses examined. Similarly, the available repeated dose, developmental and teratogenic data indicate a low degree of toxicity, with the lowest toxicities observed at the medium and longer carbon chain lengths. All of the available adequate genetic toxicity studies have negative results. Due to the low overall toxicity and the slight trend toward lesser toxicity at the higher carbon chain

lengths, no further mammalian testing is necessary to characterize the toxicity of the aliphatic alcohols.

Table 6. Mammalian Toxicity Data of Alcohol Fractions				
Description	**CAS Number Alcohol (Alkoxide)**	Acute Oral Toxicity	Acute Inhalation Toxicity	Acute Dermal Toxicity
Ethanol	**64-17-5 (555-75-9)**	LD_{50} (mouse) = 9.8 - 11.6 ml/kg bw, LD_{50} (rat) = 15010 mg/kg bw, LD_{50} (rat) = 7000 - 11000 mg/kg bw	LC_{50} (mouse) > 6000 ppm	Ldlo (rabbit) = 20000 mg/kg bw
2-Propanol	**67-63-0 (555-31-7)**	LD_{50} (rat) = 4710 -5840 mg/kg, LD_{50} (mouse) = 4475 mg/kg, LD_{50} (rabbit) =5030 mg/kg, LD_{50} (dog) = 4830 mg/kg	4-hr LC_{50} (rat) = 72.6 mg/L, 8-hr LC_{50} (rat) = 51 mg/L, 2-hr LC_{50} (mouse) = 53 mg/L	LD_{50} (rabbit) = 12,870 mg/kg
1-Butanol	**71-36-3 (3085-30-1)**	LD_{50} (rat) = 4.36 g/kg, LD_{50} (rat) =2290 mg/kg, LD_{50} (rat) = 2.51 g/kg	LC_{50} (rat) > saturated vapour concentration, LC_{50} (rat) > 8000 ppm	LD_{50} (rabbit) = 3402 mg/kg
1-Hexanol	**111-27-3 (23275-26-5)**	LD_{50} (rat) =3210 mg/kg bw, LD_{50} = 4420 mg/kg bw, LD_{50} (mouse) =1950 mg/kg bw	LC_{50} (rat) > 21 mg/L, LC_{50} (mouse, rat, guinea pig) > 1060 ppm	LD_{50} (rat) =2330 mg/kg bw, LD_{50} (rabbit) = 1500-2000 mg/kg bw
1-Octanol	**111-87-5 (14624-13-6)**	LD_{50} (rat) = 18240 mg/kg bw, LD_{50} (rat) > 5000 mg/kg bw	LC_{50} (rat) > 5600 mg/m^3	LD_{50} (rabbit) = 2000 - 4000 mg/kg bw, LD_{50} (rabbit) > 5000 mg/kg bw
1-Decanol	**112-30-1 (26303-54-8)**	LD_{50} (rat) = 19500 mg/kg bw, LD_{50} (rat) > 26410 mg/kg bw, LD_{50} (rat) > 5000 mg/kg bw	LC_{50} (rat) > 71 mg/L, LC_{50} (mouse) = 4 mg/L	LD_{50} (rabbit) = 2000 - 4000 mg/kg bw, LD_{50} (rabbit) > 1000 mg/kg bw, LD_{50} (rabbit) = 18.8 mL/kg bw
1-Dodecanol	**112-53-8 (14624-15-8)**	LD_{50} (rat) > 26430 mg/kg bw, LD_{50} (rat) > 5000 mg/kg bw, LD_{50} (rat) > 10000 mg/kg bw	LC_{50} (rat) > 1.05 mg/L, 4-hr eq. > 1.5 mg/L	LD_{50} (rabbit) > 8000 -12000 mg/kg bw, LD_{50} (rabbit) = 1500 - 2000 mg/kg bw
1-Tetradecanol	**112-72-1 (67905-32-2)**	LD_{50} (rat) > 20000 mg/kg bw, LD_{50} (rat) = 32500 mL/kg bw	LC_{50} (rat) > 1.5 mg/L, LC_{50} (rat) > saturated vapour concentration	LD_{50} (rabbit) = 8000 mg/kg bw, LD_{50} (rabbit) = 7.13 mL/kg bw
1-Hexadecanol	**36653-82-4 (19141-82-3)**	LD_{50} (rat) > 2000 mg/kg bw, LD_{50} (rat) > 5000 mg/kg bw, LD_{50} (rat) > 7960 mg/kg bw	LC_{50} (rat) = 0.41 - 2.22 mg/L	LD_{50} (rabbit) > 5000 mg/kg
1-Octadecanol	**112-92-5 (3985-81-7)**	LD_{50} (rat) > 5000 mg/kg bw, LD_{50} (rat) > 7960 mg/kg bw, LD_{50} > 2000 mg/kg bw	LC_{50} > saturated vapour concentration [2]	LD_{50} > 2000 mg/kg [2]
1-Eicosanol	**629-96-9 (67905-31-1)**	LD_{50} (rat) > 10000 mg/kg bw, LD_{50} (rat) > 64 mg/kg bw	LC_{50} (rat) > saturated vapour concentration	LD_{50} (rabbit) > 20 mL/kg bw
1-Docosanol	**661-19-8 (67905-30-0)**	LD_{50} (rat) > 2000 mg/kg bw, LD_{50} (rat) > 10000 mg/kg bw, LD_{50} (mouse) > 1000 mg/kg bw	LC_{50} > saturated vapour concentration [2]	LD_{50} > 2000 mg/kg [2]

Table 6. Mammalian Toxicity Data of Alcohol Fractions				
Description	**CAS Number Alcohol (Alkoxide)**	Acute Oral Toxicity	Acute Inhalation Toxicity	Acute Dermal Toxicity
1-Tetracosanol	**506-51-4 (67905-29-7)**	LD_{50} (rat) > 5000 mg/kg bw	--	--
1-Hexacosanol	**506-52-5 (67905-28-6)**	LD_{50} (rat) > 5000 mg/kg bw	--	--
1-Octacosanol	**557-61-9 (67905-27-5)**	LD_{50} (rat) > 5000 mg/kg bw	--	--
1-Triacontanol	**593-50-0 (67905-26-4)**	LD_{50} (rat) > 5000 mg/kg bw	--	LD_{50} (rabbit) > 2000 mg/kg bw

Table 6. Mammalian Toxicity Data of Alcohol Fractions							
Description	**CAS Number Alcohol (Alkoxide)**	Skin Irritation	Eye Irritaion	Sensitization	Genetic Toxicity in-vitro (Bacterial test)	Genetic Toxicity in-vitro (Non-bacterial test)	Genetic Toxicity in-vivo
Ethanol	**64-17-5 (555-75-9)**	Not irritating, Slightly irritating	Moderately irritating	Not sensitizing	Negative, Positive	Negative, Positive	Negative, Positive
2-Propanol	**67-63-0 (555-31-7)**	Not irritating	Irritating	Not sensitizing	Negative	Negative	Negative
1-Butanol	**71-36-3 (3085-30-1)**	No irritation	Severely irritating, Not irritating	--	Negative	Negative	Negative
1-Hexanol	**111-27-3 (23275-26-5)**	Irritating, Moderately irritating, Slightly irritating, Highly irritating	Irritating	Not sensitizing	Negative	--	Negative[2]
1-Octanol	**111-87-5 (14624-13-6)**	Slightly irritating, Moderately irriatating	Irritating	Not sensitizing	Negative	--	Negative[2]
1-Decanol	**112-30-1 (26303-54-8)**	Irritating, Moderately irritating, Slightly irritating	Moderately irritating	Slightly sensitizing, Not sensitizing	Negative	--	Negative[2]
1-Dodecanol	**112-53-8 (14624-15-8)**	Mildy irritating, Not irritating	Not irritating	Not sensitizing	Negative	--	Negative
1-Tetradecanol	**112-72-1 (67905-32-2)**	Irritating, Not irritating	Moderately irritating, Not irritating	Not sensitizing	Negative	--	Negative[2]
1-Hexadecanol	**36653-82-4 (19141-82-3)**	Not irritating, Slightly irritating	Not irritating	Not sensitizing	Negative	--	Negative[2]
1-Octadecanol	**112-92-5 (3985-81-7)**	Not irritating	Not irritating	Not sensitizing	Negative	--	Negative

Table 6. Mammalian Toxicity Data of Alcohol Fractions							
Description	**CAS Number Alcohol (Alkoxide)**	Skin Irritation	Eye Irritaion	Sensitization	Genetic Toxicity in-vitro (Bacterial test)	Genetic Toxicity in-vitro (Non-bacterial test)	Genetic Toxicity in-vivo
1-Eicosanol	**629-96-9 (67905-31-1)**	Slightly irritating Not irritating	Slightly irritating	Not sensitizing[2]	Negative[2]	Negative[2]	Negative[2]
1-Docosanol	**661-19-8 (67905-30-0)**	Not irritating, Slightly irritating	Slightly irritating	Not sensitizing[2]	Negative	Negative	Negative
1-Tetracosanol	**506-51-4 (67905-29-7)**	--	--	--	--	--	Negative
1-Hexacosanol	**506-52-5 (67905-28-6)**	--	--	--	--	--	Negative
1-Octacosanol	**557-61-9 (67905-27-5)**	--	--	--	--	--	Negative
1-Triacontanol	**593-50-0 (67905-26-4)**	Not irritating	Severe irritation	--	Negative	Positive	Negative

Table 6. Mammalian Toxicity Data of Alcohol Fractions				
Description	**CAS Number**	**Repeated Dose Toxicity**	**Toxicity to Reproduction**	**Developmental Toxicity/Teratogenicity**
Ethanol	**64-17-5 (555-75-9)**	NOAEL (rat) = 2% LOAEL (rat) = 3% (oral), NOAEL (mouse) = 5% LOAEL (mouse) > 5 % (oral), NOAEL (rat) > 5% (oral)	NOAEL (parental) = 15% NOAEL (F1 offspring) = 10% NOAEL (F2 offspring) < 15% (mouse) (oral)	NOAEL (maternal) = 16000 ppm NOAEL (teratogenic) > 20000 ppm LOAEL (maternal) = 20000 ppm LOAEL (teratogenic) >= 20000 ppm (rat) (inhalation)
2-Propanol	**67-63-0 (555-31-7)**	NOEL (rat) = 500 ppm LOEL (rat) = 1500 ppm (inhalation), NOEL (rat) = 870 mg/kg/day LOEL (rat) = 1280 mg/kg/day (oral)	NOEL (parental) =< 500 mg/kg/day NOEL (F1 offspring) =< 500 mg/kg/day NOEL (F2 offspring) =< 500 mg/kg/day	NOEL (maternal) = 400 mg/kg/day NOEL (developmental) = 400 mg/kg/day (rat), NOEL (maternal) = 240 mg/kg/day NOEL (developmental) = 480 mg/kg/day (rabbit)
1-Butanol	**71-36-3 (3085-30-1)**	NOAEL (rat) = 125 mg/kg/day LOAEL (rat) = 500 mg/kg/day (oral), LD_{100} (rabbit) = 34020 mg/kg LD_0 (rabbit) = 16200 mg/kg	NOAEL (paternal) = 533 mg/kg/day LOAEL (paternal) > 533 mg/kg/day	NOAEL (maternal) = 3500 ppm NOAEL (teratogenic) = 3500 ppm (rat) (inhalation)
1-Hexanol	**111-27-3 (23275-26-5)**	NOAEL = 1127-1243 mg/kg/day (oral), NOAEL = 370 - 435 mg/kg bw LOAEL = 1000 mg/kg bw (oral)	NOAEL (parental) = 1127-1243 mg/kg bw, NOAEL (parental) = 370 mg/kg bw	NOAEL (maternal) = 3.5 mg/L NOAEL (teratogenic) = 3.5 mg/L, NOAEL (maternal) = 200 mg/kg bw NOAEL (teratogenic) = 1000 mg/kg bw
1-Octanol	**111-87-5 (14624-13-6)**	--	Negative[2]	NOAEL (maternal) = 130 mg/kg bw NOAEL (teratogenic) = 1300 mg/kg bw, NOAEL (maternal) > 0.4 mg/L NOAEL (teratogenic) > 0.4 mg/L
1-Decanol	**112-30-1 (26303-54-8)**	LOAEL (rat) = 180 mg/m^3 (inhalation), LOAEL (rabbit) = 200 mg/m^3 (inhalation) LOAEL (rat)= 58 mg/m^3 (inhalation)	Negative[2]	NOAEL (maternal) > 0.1 mg/L NOAEL (teratogenic) > 0.1 mg/L
1-Dodecanol	**112-53-8 (14624-15-8)**	NOAEL (rat) = 2000 mg/kg bw (oral)	NOAEL (parental) (rat) = 2000 mg/kg bw (oral), NOAEL (offspring) (rat) = 2000 mg/kg bw (oral)	NOAEL (maternal) (rat) = 2000 mg/kg bw NOAEL (teratogenic) = 2000 mg/kg bw (oral)
1-Tetradecanol	**112-72-1 (67905-32-2)**	NOAEL > 100 mg/kg (oral) [2]	Negative[2]	Negative[2]
1-Hexadecanol	**36653-82-4 (19141-82-3)**	NOAEL (rat) > 1000 mg/kg bw (oral), NOAEL (rat) = 723 mg/kg bw (oral), NOAEL (dog) > 1054 mg/kg bw (oral)	NOAEL (parental) (rat) = 1822 mg/kg bw, NOAEL (parental) (dog) > 1054 mg/kg bw	Negative[2]

Table 6. Mammalian Toxicity Data of Alcohol Fractions				
Description	**CAS Number**	**Repeated Dose Toxicity**	**Toxicity to Reproduction**	**Developmental Toxicity/Teratogenicity**
1-Octadecanol	**112-92-5 (3985-81-7)**	NOAEL (rat) > 1000 mg/kg bw (oral), NOAEL (rat) = 2000 mg/kg bw (oral)	NOAEL (parental) (rat) = 2000 mg/kg bw NOAEL (offspring) = 2000 mg/kg bw, NOAEL (rat) (parental) = 1000 mg/kg	NOAEL (rat) (maternal) = 2000 mg/kg bw NOAEL (teratogenic) = 2000 mg/kg bw (oral)
1-Eicosanol	**629-96-9 (67905-31-1)**	NOAEL >100 mg/kg [2]	Negative[2]	Negative[2]
1-Docosanol	**661-19-8 (67905-30-0)**	NOAEL (rat) = 1000 mg/kg bw (oral), NOAEL (dog) > 2000 mg/kg bw (oral)	NOAEL (parental) (rat) = 1000 mg/kg bw NOAEL (offspring) (rat) = 1000 mg/kg	NOAEL (maternal) (rat) = 1000 mg/kg bw, NOAEL (teratogenic) = 1000 mg/kg bw, NOAEL (maternal) (rabbit) > 2000 mg/kg bw NOAEL (teratogenic) > 2000 mg/kg bw
1-Tetracosanol	**506-51-4 (67905-29-7)**	NOAEL (dog) = 250 mg/kg bw (oral), NOAEL (rat) > 5000 mg/kg/day (gavage), NOAEL (rat) > 625 mg/kg bw, NOAEL (rat) > 1000 mg/kg bw (gavage)	NOAEL (parental) = 250 mg/kg bw (dog)	NOAEL (maternal) = 1000 mg/kg bw NOAEL (teratogenic) = 1000 mg/kg bw (rat), NOAEL (maternal) > 1000 mg/kg bw NOAEL (teratogenic) > 1000 mg/kg bw (rabbit)
1-Hexacosanol	**506-52-5 (67905-28-6)**	NOAEL (dog) = 250 mg/kg bw (oral), NOAEL (rat) > 5000 mg/kg/day (gavage), NOAEL (rat) > 625 mg/kg bw, NOAEL (rat) > 1000 mg/kg bw (gavage)	NOAEL (parental) = 250 mg/kg bw (dog)	NOAEL (maternal) = 1000 mg/kg bw NOAEL (teratogenic) = 1000 mg/kg bw (rat), NOAEL (maternal) > 1000 mg/kg bw NOAEL (teratogenic) > 1000 mg/kg bw (rabbit)
1-Octacosanol	**557-61-9 (67905-27-5)**	NOAEL (dog) = 250 mg/kg bw (oral), NOAEL (rat) > 5000 mg/kg/day (gavage), NOAEL (rat) > 625 mg/kg bw, NOAEL (rat) > 1000 mg/kg bw (gavage)	NOAEL (parental) = 250 mg/kg bw (dog)	NOAEL (maternal) = 1000 mg/kg bw NOAEL (teratogenic) = 1000 mg/kg bw (rat), NOAEL (maternal) > 1000 mg/kg bw NOAEL (teratogenic) > 1000 mg/kg bw (rabbit)
1-Triacontanol	**593-50-0 (67905-26-4)**	NOAEL (dog) = 250 mg/kg bw (oral), NOAEL (rat) > 5000 mg/kg/day (gavage), NOAEL (rat) > 625 mg/kg bw, NOAEL (rat) > 1000 mg/kg bw (gavage)	NOAEL (parental) = 250 mg/kg bw (dog)	NOAEL (maternal) = 1000 mg/kg bw NOAEL (teratogenic) = 1000 mg/kg bw (rat), NOAEL (maternal) > 1000 mg/kg bw NOAEL (teratogenic) > 1000 mg/kg bw (rabbit)

SUMMARY OF ALUMINUM ALKOXIDE PROPERTIES

Data for the sponsored individual aluminum salt and the mixture are represented by data derived from their corresponding alcohols. All of the salts undergo rapid hydrolysis into their component alcohols and alumina. The patterns of toxicity for the series of alcohols have been established and clearly indicate that higher carbon chain lengths are not toxic. Similarly, the discussion has established that alumina is not significantly toxic to aquatic or mammalian organisms. Furthermore, the C2-30, aluminum salt is a site-limited intermediate and not likely to be released into the environment in significant quantities. The individual aluminum salts exist only as a reporting function under TSCA and are, in fact, not ever produced individually. Therefore, no further testing of aluminum salts is necessary.

Table 7 shows the availability of data and assessment plan status for Aluminum Alkoxides.

Table 7. Data Availability and Status for Aluminum Alkoxides

	Data Available	Data Acceptable	Testing Required
Physical-Chemical Properties			
Melting Point	Y *	Y	N
Boiling Point	Y *	Y	N
Vapor Pressure	Y *	Y	N
Octanol/Water Partition Coefficient	Y *	Y	N
Water Solubility	Y	Y	N
pH Value, pK_a Value	N	-	N
Environmental Fate and Pathways			
Photodegradation	Y *	Y	N
Stability in Water	Y	Y	N
Biodegradation	Y *	Y	N
Bioaccumulation	Y *	Y	N
Ecotoxicity			
Acute/Prolonged Toxicity to Fish	Y	Y	N
Acute Toxicity to *Daphnia*	Y	Y	N
Toxicity to Aquatic Plants (algae)	Y	Y	N
Chronic Toxicity to Fish	Y **	Y	N
Chronic Toxicity to Aquatic Invertebrates	Y **	Y	N
Toxicity			
Acute Oral Toxicity	Y	Y	N
Acute Inhalation Toxicity	N	-	N
Acute Dermal Toxicity	N	-	N
Skin Irritation	Y	Y	N
Eye Irritation	Y	Y	N
Skin Sensitization	Y	Y	N
Repeated Dose Toxicity	Y	Y	N
Genetic Toxicity in vitro (Bacterial test)	Y	Y	N
Genetic Toxicity in vitro (Non-bacterial test)	Y	Y	N
Genetic Toxicity in vivo	Y***	Y	N
Carcinogenicity	Y***	Y	N
Toxicity to Reproduction	Y	Y	N
Developmental Toxicity	Y	Y	N

* Some endpoints estimated using EPI Suite v.3.10, 3.11 or 3.12
** Some endpoints estimated using ECOSAR v.0.99g
***Limited data

CONCLUSIONS

Aluminum alkoxides hydrolyze rapidly to their constituent alcohols and alumina. Therefore the assessments have relied on the substantial data available for the relevant alcohols and alumina. The 2-propanol and the C6 to C22 (long chain) alcohols have been evaluated previously under the OECD HPV program and have been found to be low priority for further work. The alcohols have low toxicity to human health. All of the alcohols will biodegrade and are not persistent. Monitoring data have shown that exposures are likely to be low. Given the use pattern for these chemicals as manufacturing intermediates, environmental exposures are not expected. Alumina or aluminum oxide is present as a relatively low percentage of these products. It is a naturally occurring material and has low toxicity.

The potential for worker exposure during the manufacturing, processing, and distribution is limited by standard operational controls. Engineering controls are also in place to minimize releases to the environment. No consumer exposure is expected because these materials are only used as manufacturing intermediates.

Based on the availability of data and the limited exposure potential, the aluminum alkoxides covered in this assessment are considered to be of low concern and no further testing is necessary.

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