

## SCREENING-LEVEL HAZARD CHARACTERIZATION

### Lubricating Grease Thickeners Category (See Appendix for list of chemicals)

The High Production Volume (HPV) Challenge Program<sup>1</sup> was conceived as a voluntary initiative aimed at developing and making publicly available screening-level health and environmental effects information on chemicals manufactured in or imported into the United States in quantities greater than one million pounds per year. In the Challenge Program, producers and importers of HPV chemicals voluntarily sponsored chemicals; sponsorship entailed the identification and initial assessment of the adequacy of existing toxicity data/information, conducting new testing if adequate data did not exist, and making both new and existing data and information available to the public. Each complete data submission contains data on 18 internationally agreed to “SIDS” (Screening Information Data Set<sup>1,2</sup>) endpoints that are screening-level indicators of potential hazards (toxicity) for humans or the environment.

The Environmental Protection Agency’s Office of Pollution Prevention and Toxics (OPPT) is evaluating the data submitted in the HPV Challenge Program on approximately 1400 sponsored chemicals by developing hazard characterizations (HCs). These HCs consist of an evaluation of the quality and completeness of the data set provided in the Challenge Program submissions. They are not intended to be definitive statements regarding the possibility of unreasonable risk of injury to health or the environment.

The evaluation is performed according to established EPA guidance<sup>2,3</sup> and is based primarily on hazard data provided by sponsors; however, in preparing the hazard characterization, EPA considered its own comments and public comments on the original submission as well as the sponsor’s responses to comments and revisions made to the submission. In order to determine whether any new hazard information was developed since the time of the HPV submission, a search of the following databases was made from one year prior to the date of the HPV Challenge submission to the present: (ChemID to locate available data sources including Medline/PubMed, Toxline, HSDB, IRIS, NTP, ATSDR, IARC, EXTOXNET, EPA SRS, etc.), STN/CAS online databases (Registry file for locators, ChemAbs for toxicology data, RTECS, Merck, etc.) and Science Direct. OPPT’s focus on these specific sources is based on their being of high quality, highly relevant to hazard characterization, and publicly available.

OPPT does not develop HCs for those HPV chemicals which have already been assessed internationally through the HPV program of the Organization for Economic Cooperation and Development (OECD) and for which Screening Initial Data Set (SIDS) Initial Assessment Reports (SIAR) and SIDS Initial Assessment Profiles (SIAP) are available. These documents are presented in an international forum that involves review and endorsement by governmental authorities around the world. OPPT is an active participant in these meetings and accepts these documents as reliable screening-level hazard assessments.

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<sup>1</sup> U.S. EPA. High Production Volume (HPV) Challenge Program; <http://www.epa.gov/chemrtk/index.htm>.

<sup>2</sup> U.S. EPA. HPV Challenge Program – Information Sources; <http://www.epa.gov/chemrtk/pubs/general/guidocs.htm>.

<sup>3</sup> U.S. EPA. Risk Assessment Guidelines; <http://cfpub.epa.gov/ncea/raf/rafguid.cfm>.

These hazard characterizations are technical documents intended to inform subsequent decisions and actions by OPPT. Accordingly, the documents are not written with the goal of informing the general public. However, they do provide a vehicle for public access to a concise assessment of the raw technical data on HPV chemicals and provide information previously not readily available to the public.

<b>Chemical Abstract Service Registry Number (CASRN)</b>	<b>See Appendix</b>
<b>Chemical Abstract Index Name</b>	<b>See Appendix</b>
<b>Structural Formula</b>	<b>See Appendix</b>

### Summary

The lubricating grease thickeners category consists of calcium or lithium salts of fatty acids mostly ranging from C16 to C22. At ambient temperatures, lubricating grease thickeners are solids or waxy solids, with negligible to high water solubility and negligible vapor pressure. They are synthesized in an oil as insoluble fatty acid metal salts that gel the oil into a functional grease, and generally exist only in the grease matrix; under normal conditions they have limited bioavailability from the grease. These factors need to be taken into account when interpreting data developed on the isolated salts.

If considered as isolated substances, all the members of this category are expected to have low to moderate mobility in soil. The sponsored and supporting chemicals are salts that do not volatilize in the environment. The rate of hydrolysis is expected to be negligible. The rate of atmospheric photo-oxidation is considered moderate to rapid for members of the category; however, this is not expected to be an important environmental fate process for most category members, as they are not expected to exist in the vapor phase in the atmosphere. Ready biodegradability data plus the overall weight of experimental evidence and data from structurally similar compounds suggest that most of the components of these mixtures will have low persistence (P1) and low (B1) to high (B3) bioaccumulation potential.

### Human Health Hazard

The acute toxicity of the lubricating grease thickeners category via the oral and dermal routes in rats is low based on data with the supporting chemical, Lithium Complex Grease/Grease Starplex 2. A repeated-dose dietary toxicity study in rats with supporting chemical magnesium stearate showed mortality and hematological effects in males, and signs of liver toxicity in males and females at ~ 10000 mg/kg-bw/day; the NOAEL for systemic toxicity was ~5000 mg/kg-bw/day. A repeated-dose oral gavage toxicity study in rats with supporting chemical R960002575 showed no signs of adverse treatment-related effects at 1000 mg/kg/day, the highest dose tested; the NOAEL for systemic toxicity was 1000 mg/kg/day. A repeated-dose dermal toxicity study in rats with the supporting chemical R960002575 also showed no signs of adverse treatment-related effects at 2100 mg/kg/day, the highest dose tested; the NOAEL for systemic toxicity was 2100 mg/kg/day. A repeated-dose dermal toxicity study in rats with a non-commercial formulation, Generic Calcium Grease, showed no signs of adverse treatment-related effects at 2000 mg/kg/day, the highest dose tested; the NOAEL for systemic toxicity was 2000 mg/kg/day. A repeated-dose dermal toxicity study in rats with a non-commercial formulation, Mobilegrease

HP, showed no signs of adverse treatment-related effects at 2000 mg/kg/day, the highest dose tested; the NOAEL for systemic toxicity was 2000 mg/kg/day. A repeated-dose dermal toxicity study in rats with a non-commercial formulation, Mobilux EP-2, showed no signs of adverse treatment-related effects at 2000 mg/kg/day, the highest dose tested; the NOAEL for systemic toxicity was 2000 mg/kg/day. No standard one- or two-generation reproductive toxicity studies on the sponsored chemicals are available; however, data on reproductive organs in a repeated-dose oral toxicity study with supporting chemical magnesium stearate in rats did not show any effects on reproductive organs at doses as high as ~10000 mg/kg-bw/day. Likewise, repeated-dose dermal toxicity studies in rats with several non-commercial formulations did not report any effects on male/female reproductive organs or on sperm count and morphology at doses as high as 2000 mg/kg/day. No prenatal developmental toxicity studies on either the sponsored or supporting chemicals are available; however, a prenatal developmental toxicity study by the dermal route in rats with the non-commercial formulation, Lithium 12-Hydroxystearate – Generic Grease, showed decreases in body weight and body weight gain in the dams at 500 mg/kg/day, the lowest dose tested. No adverse treatment-related effects were reported in the fetuses; the NOAEL for developmental toxicity was 2000 mg/kg/day. No genetic toxicity studies for either the sponsored or supporting chemicals, or for any of the non-commercial formulations, are available. Magnesium stearate has been tested in the Ames test and was negative for mutagenicity. Likewise, overall evidence from several in vitro and in vivo studies with soluble lithium salts indicated no mutagenic activity, with a possible effect on chromosomes following an intraperitoneal dose of lithium at 2000 mg/kg. Supporting chemical Lithium Complex Grease/Grease Starplex 2 is moderately irritating to rabbit skin and eyes, while the supporting chemical R960002575 is not sensitizing to guinea pig skin. Supporting chemical PARL-3093-GR-81 showed no evidence of carcinogenicity when applied to mouse skin.

No data gaps have been identified under the HPV Challenge Program.

### **Hazard to the Environment**

The grease thickeners in this category are not commonly synthesized as pure compounds and exist only in the grease matrix. Furthermore, these insoluble metal salts thicken the oil into a functional grease that is highly resistant to water wash-out (“bleed-out”), which is an essential performance characteristic of these grease thickeners. EPA has considered these factors, and concluded that the ecotoxicity of the Grease Thickeners category members is expected to have “no effects at saturation”.

No data gaps have been identified under the HPV Challenge Program.

## **Introduction**

The sponsor, the American Petroleum Institute Petroleum HPV Testing Group, submitted a Test Plan and Robust Summaries to EPA for the Lubricating Grease Thickeners category on December 15, 2003. EPA posted the submission on the ChemRTK HPV Challenge website on March 3, 2004 (<http://www.epa.gov/chemrtk/pubs/summaries/lbgrease/c15019tc.htm>). EPA comments on the original submission were posted to the website on August 12, 2005. Public comments were also received and posted to the website. The sponsor submitted updated/revise documents on May 10, 2005. EPA received the Sponsor's category analysis on March 24, 2009 (posted June 8, 2009). See the Appendix for a list of the members of the lubricating grease thickeners category and their structures.

The ten category members are represented by eleven CASRNs. According to the 2003 Test Plan, two of the category members, calcium stearate (CASRN 1592-23-0) and calcium salts of tallow fatty acids (CASRN 64755-01-7), are considered adequately characterized for SIDS endpoints because EPA's preliminary review indicated that SIDS testing would not further the understanding of the properties of these chemicals in the HPV Challenge program.

A hazard characterization is being prepared for another sponsored chemical, hydrocarbon waxes, petroleum, oxidized, Me esters, calcium salts (CASRN 68603-11-2) as a member of the Petroleum Oxidates and Derivatives category which will be available at: [http://iaspub.epa.gov/opthpv/hpv\\_hc\\_characterization.get\\_report?doctype=2](http://iaspub.epa.gov/opthpv/hpv_hc_characterization.get_report?doctype=2).

In the 2003 Test Plan, the sponsor proposed to conduct a dermal reproductive/developmental toxicity study using a grease with a lithium fatty acid salt. No such study was included in the Robust Summaries. However, the sponsor did submit several pre-existing repeated-dose toxicity studies evaluating reproductive organs, as well as a prenatal developmental toxicity study, all via the dermal route, using non-commercial grease formulations with a lithium fatty acid salt (see discussion below under Justification for Supporting Chemicals).

In its comments on the Test Plan, EPA proposed that a study be conducted on the bioavailability of lithium salts from the grease matrix, as well as an *in vitro* study to help characterize the dermal absorption potential. On March 12, 2009, the Sponsor provided a robust summary of an existing *in vivo* dermal penetration study in rats with a non-commercial grease formulation, Mobilux EP-2. This study is discussed in this hazard characterization in the section *Additional Information*.

## **Category Justification**

The members of the Lubricating Grease Thickener category consist of lithium and calcium salts of long-chain (largely  $\geq C_{16}$ ) fatty acids formed *in situ* during the manufacture of certain types of lubricating greases from mineral or synthetic oil. The insoluble metal salt gels the oil into a functional grease that the Sponsor states is highly resistant to water wash-out ("bleed-out"), such resistance being an essential performance characteristic. Greases typically contain 1-14% thickener on a mass basis. The grease thickeners in this category are not commonly synthesized as pure compounds and exist only in the grease matrix. Within the grease matrix and under normal conditions, the long-chain fatty acid salts have limited bioavailability.

Although the starting fatty acids and esters used *in situ* to make the corresponding grease thickeners are structurally varied, with some having unspecified hydrocarbon chain lengths, they have similar physicochemical properties that include high log  $K_{ow}$  and low water solubility. EPA has agreed that the category is reasonable on the basis of structural similarity, physicochemical properties and anticipated resistance of the category members to migration from the grease matrix.

### **Justification for Supporting Chemicals**

No data were available for any HPV Challenge Program endpoints for any of the category members.

Studies with magnesium stearate (CASRN 557-04-0) were provided by the sponsor to address the repeated-dose toxicity endpoint for the calcium salt category members. The sponsor indicated that magnesium stearate was structurally similar to the category member calcium stearate (CASRN 1592-23-0), and should also serve as a supporting chemical for all the calcium salt category members. EPA agrees that magnesium stearate is acceptable as a supporting chemical for the calcium salts for read-across purposes. However, EPA considers the lithium salts to have a greater potential for producing adverse health effects than the calcium salts. This assumption is based on evidence cited in the sponsor's test plan for teratogenic effects in pregnant psychiatric patients treated with partially soluble lithium salts. Moreover, calcium is a normal component of blood and tissue, whereas lithium is not. Therefore, supporting chemical data appropriate for the calcium salts are not considered applicable to the lithium salts.

Studies with three grease matrix complexes containing lithium fatty acid salts (Lithium Complex Grease/Grease Starplex 2, R960002575, and PARL-3093-GR-2) were provided by the sponsor to fill the acute toxicity, repeated-dose toxicity, and reproductive toxicity endpoints for the lithium fatty acid salt category members. EPA agrees with the use of these supporting chemicals for the category.

Studies with several non-commercial formulations (Generic Calcium Complex Grease, Mobilegrease HP, Mobilux EP-2 Grease, and Lithium 12-Hydroxystearate – Generic Grease) were also provided by the sponsor to address the repeated-dose and reproductive/developmental toxicity endpoints for the lithium salt category members. The sponsor indicated that the additive concentrations in these non-commercial formulations were intentionally doubled for the purposes of testing the toxicity of a grease with exaggerated levels of additives. EPA agrees with the use of these additional supporting chemicals for the category.

Toxic effects of lithium are described elsewhere and therefore not summarized here. For further details, see (<http://toxnet.nlm.nih.gov/>) [search "lithium"].

Finally, the sponsor provided 90-day repeated-dose and reproductive toxicity studies for castor oil (CASRN 8001-79-4). Castor oil is 85-95% esterified ricinoleic acid, which is a structural analog of the fatty acid moiety of the proposed category members, lithium and calcium 12-hydroxystearate. However, EPA does not consider castor oil appropriate for addressing the reproductive toxicity of the lithium and calcium fatty acid salt category members because (1) it is

a triester (a triglyceride), not a salt, and (2) the lithium and calcium salts are considered to have a greater potential for producing adverse health effects than castor oil. Therefore, these studies were not included in the hazard characterization.

## 1. Chemical Identity

### 1.1 Identification and Purity

The following comes from the 2003 Test Plan:

The 10 substances (eleven CASRN) in this category are lithium and calcium salts of fatty acids having mostly 18-22 carbon atoms. These fatty acids are, or are similar to, edible fatty acids derived from animal fats and vegetable oils. They are synthesized by dissolving one or more fatty acids or esters in mineral or synthetic oil and then adding a base such as calcium or lithium hydroxide. These reactants form an insoluble metal salt of the fatty acid (or grease thickener) which gels the oil into a functional grease that the Sponsor states is highly resistant to water wash-out (“bleed-out”), such resistance being an essential performance characteristic. Such greases typically contain 1-14% thickener on a mass basis. The fatty acids/esters used as starting materials in this category are mostly monocarboxylic acids and include stearic acid (C18), 12-hydroxystearic acid, docosanoic acid (C22), hydrogenated castor oil (comprised of ricinoleic and similar C18 acids), and methyl esters of oxidized hydrocarbon waxes ( $C \geq 18$ ). One lithium salt of a dicarboxylic acid (dilithium azelate, CASRN 38900-29-7) is included in the category. [Note: the Sponsor states clearly that methyl esters are sometimes used in the synthesis and are converted to salts via hydrolysis to the acids. Thus, the names of category members that include both a methyl ester and a metal ion should be viewed skeptically. For example, the sponsor states that category members methyl 12-hydroxystearate, lithium salt, and lithium 12-hydroxystearate are the same substance, despite the “methyl” in the former name. This caveat also applies to castor oil, hydrogenated, lithium salt (CASRN 64754-95-6), which hydrolysis would convert mostly to lithium 12-hydroxystearate plus smaller amounts of other C18 acid salts. The structures in the Appendix reflect the salt, not the ester, forms.]

Greases are used for the lubrication of bearings and other moving parts in virtually every segment of the transportation industry. Grease thickeners are not commonly synthesized as pure compounds and generally exist only in the grease matrix. The function of these fatty acid salts is to maintain the oil in a gel-like state in contact with the surfaces being lubricated. [In its 2009 category analysis, the sponsor very briefly describes the grease matrix structure as a steel wool-like scaffold, formed by the fatty acid salts, whose spaces are filled by the oil components. Thus the term “oil matrix”, not completely abandoned by the sponsor, is misleading; this Hazard Characterization employs the term “grease matrix” exclusively.] These factors need to be considered when interpreting data developed on the isolated salts.

Chemical structures are provided in the Appendix.

### 1.2 Physical-Chemical Properties

The physical-chemical properties of the isolated sponsored substances and supporting chemicals in the lubricating grease thickeners category are summarized in Table 1.

<b>Property</b>	Octadecanoic acid, 12-hydroxy-, calcium salt (2:1)	Nonanedioic acid, lithium salt (1:2)	Octadecanoic acid, lithium salt (1:1)	Docosanoic acid, lithium salt (1:1)	Octadecanoic acid, 12-hydroxy-, methyl ester <sup>2</sup> , lithium salt (1:1)
CASRN	3159-62-4	38900-29-7	4485-12-5	4499-91-6	53422-16-5
Molecular Weight	639	200	290	347	320
Physical State	Solid or waxy solid	Solid or waxy solid	Solid or waxy solid	Solid or waxy solid	Solid or waxy solid
Melting Point	320°C (measured)	No data. >25°C (solid)	220–221.5°C (measured) <sup>3</sup>	192–196°C (measured) <sup>4</sup>	No data. >25°C (solid)
Boiling Point	>300°C (estimated) <sup>5</sup>	>300°C (estimated) <sup>5</sup>	>300°C (estimated) <sup>5</sup>	>300°C (estimated) <sup>5</sup>	>300°C (estimated) <sup>5</sup>
Vapor Pressure	<1×10 <sup>-10</sup> mm Hg at 25°C (estimated) <sup>5</sup>	<1×10 <sup>-10</sup> mm Hg at 25°C (estimated) <sup>5</sup>	<1×10 <sup>-10</sup> mm Hg at 25°C (estimated) <sup>5</sup>	<1×10 <sup>-10</sup> mm Hg at 25°C (estimated) <sup>5</sup>	<1×10 <sup>-10</sup> mm Hg at 25°C (estimated) <sup>5</sup>
Dissociation Constant (pK <sub>a</sub> )	Not applicable for salts (the corresponding carboxylic acids have pK <sub>a</sub> values of approximately 4.75)				
Henry's Law Constant	Not applicable <sup>6</sup>				
Water Solubility	9.7×10 <sup>-9</sup> mg/L at 25°C (estimated) <sup>5</sup>	1×10 <sup>6</sup> mg/L at 25°C (estimated) <sup>5</sup>	98 mg/L at 18°C (measured) <sup>7</sup> ; 4.1 mg/L at 25°C (estimated) <sup>5</sup>	4.0×10 <sup>-2</sup> mg/L at 25°C (estimated) <sup>5</sup>	2.7 mg/L at 25°C (estimated) <sup>5</sup>
Log K <sub>ow</sub>	11.67 (estimated) <sup>5</sup>	-3.56 (estimated) <sup>5</sup>	4.13(estimated) <sup>5</sup>	6.10 (estimated) <sup>5</sup>	4.14 (estimated) <sup>5</sup>

<sup>1</sup> Lubricating Grease Thickeners Consortium. 2009. Revised Robust Summary and Test Plan for Lubricating Grease Thickeners. Available online at <http://www.epa.gov/chemrtk/pubs/summaries/lbgrease/c15019tc.htm> as of April 26, 2011.

<sup>2</sup> Not an ester, according to sponsor – see text

<sup>3</sup> Jacobson, CA; Holmes, A. 1916. Solubility data for various salts of lauric, myristic, palmitic, and stearic acids. J Biol Chem 25:29–53.

<sup>4</sup> Meyer, H; Brod, L; Soyka, W. 1913. Uber die lignocerinsäure. Monatsh Chem 34:1113–1142.

<sup>5</sup> U.S. EPA. 2011. Estimation Programs Interface Suite™ for Microsoft® Windows, v4.00. U.S. Environmental Protection Agency, Washington, DC, USA. Available online at <http://www.epa.gov/opptintr/exposure/pubs/episuitedi.htm> as of May 2, 2011.

<sup>6</sup> Data are not applicable for this endpoint; salt will not volatilize into the environment.

<sup>7</sup> Partheil, A; Ferie, F. 1903. Zur kenntnis der fette. Arch Pharm. (Weinheim Ger.) 241(7):545–560.



<b>Property</b>	Castor oil, hydrogenated, lithium salt <sup>2</sup>	Fatty acids, C16 – 22, lithium salts	Octadecanoic acid, 12-hydroxy-, lithium salt (1:1)	Hydrocarbon waxes, petroleum, oxidized, Me esters <sup>2</sup> , calcium salts	Octadecanoic acid, calcium salt (2:1)] (Supporting Chemical)
CASRN	64754-95-6	68783-36-8	7620-77-1	68603-11-2	1592-23-0
Molecular Weight	>260	263–347	306	>600	607
Physical State	Solid or waxy solid	Solid or waxy solid	Solid or waxy solid	Solid or waxy solid	Solid or waxy solid
Melting Point	No data. >25°C (solid)	No data. >25°C (solid)	No data. >25°C (solid)	41.84°C (measured) <sup>3</sup>	179°C (measured)
Boiling Point	>300°C (estimated) <sup>4</sup>	>300°C (estimated) <sup>4</sup>	>300°C (estimated) <sup>4</sup>	192.8 to >648.9°C (measured) <sup>3</sup>	>300°C (estimated) <sup>4</sup>
Vapor Pressure	<1×10 <sup>-10</sup> mm Hg at 25°C (estimated) <sup>4</sup>	<1×10 <sup>-10</sup> mm Hg at 25°C (estimated) <sup>4</sup>	<1×10 <sup>-10</sup> mm Hg at 25°C (estimated) <sup>4</sup>	<1×10 <sup>-7</sup> to 0.70 mm Hg at 25°C (estimated) <sup>5</sup>	<1×10 <sup>-10</sup> mm Hg at 25°C (estimated) <sup>4</sup>
Dissociation Constant (pK <sub>a</sub> )	Not applicable for salts (the corresponding carboxylic acids have pK <sub>a</sub> values of approximately 4.75)				
Henry's Law Constant	Not applicable <sup>6</sup>				
Water Solubility	1.6×10 <sup>-15</sup> mg/L (estimated) <sup>4</sup>	0.04–41 mg/L at 25°C (estimated) <sup>4</sup>	222 mg/L at 25°C (estimated) <sup>4</sup>	1.29 mg/L at 25°C (measured) <sup>4</sup>	40 mg/L at 15°C (measured); 2 mg/L at 35°C (measured) <sup>7</sup>
Log K <sub>ow</sub>	17.18 (estimated) <sup>4</sup>	3.15–6.10 (estimated) <sup>4</sup>	2.60 (estimated) <sup>4</sup>	14.5–21.0 (estimated) <sup>4</sup>	14.34 (estimated) <sup>4</sup>

<sup>1</sup> Lubricating Grease Thickeners Consortium. 2009. Revised Robust Summary and Test Plan for Lubricating Grease Thickeners. Available online at <http://www.epa.gov/chemrtk/pubs/summaries/lbgrease/c15019tc.htm> as of April 26, 2011.

<sup>2</sup> Not an ester, according to sponsor – see text

<sup>3</sup> Lubrizol Corporation. 2006. Revised Robust Summary and Test Plan for Petroleum Oxidates and Derivatives Thereof Category. Available online at <http://www.epa.gov/chemrtk/pubs/summaries/petroxid/c14068tc.htm> as of April 21, 2011.

<sup>4</sup> U.S. EPA. 2011. Estimation Programs Interface Suite™ for Microsoft® Windows, v4.00. U.S. Environmental Protection Agency, Washington, DC, USA. Available online at <http://www.epa.gov/opptintr/exposure/pubs/episuitedi.htm> as of May 2, 2011.

<sup>5</sup> NOMO5. 1987. Programs to Enhance PC-Gems Estimates of Physical Properties for Organic Compounds. The Mitre Corp.

<sup>6</sup> Data are not applicable for this endpoint; salt will not volatilize into the environment.

<sup>7</sup> SRC. The Physical Properties Database (PHYSPROP). Syracuse, NY: Syracuse Research Corporation. Available online at <http://www.syrres.com/esc/physprop.htm> as of March 21, 2011.

<b>Property</b>	Fatty acids, tallow, calcium salts (Supporting Chemical)	Octadecanoic acid, magnesium salt (2:1) (Supporting Chemical)	Lithium Complex Grease (Not Supporting Chemical) <sup>2</sup>
CASRN	64755-01-7	557-04-0	Unavailable
Molecular Weight	>490	591	200–639 (average molecular weight for other category members)
Physical State	Solid or waxy solid	Solid or waxy solid	Solid or waxy solid
Melting Point	No data. >25°C (solid)	132 °C (measured) <sup>3</sup>	No data. >25°C (solid)
Boiling Point	>300°C (estimated) <sup>4</sup>	>300°C (estimated) <sup>4</sup>	>300°C (estimated) <sup>4</sup>
Vapor Pressure	<1×10 <sup>-10</sup> mm Hg at 25°C (estimated) <sup>4</sup>	<1×10 <sup>-10</sup> mm Hg at 25°C (estimated) <sup>4</sup>	<1×10 <sup>-10</sup> mm Hg at 25°C (estimated) <sup>4</sup>
Dissociation Constant (pK <sub>a</sub> )	Not applicable for salts (the corresponding carboxylic acids have pK <sub>a</sub> values of approximately 4.75)		
Henry's Law Constant	Not applicable <sup>5</sup>		
Water Solubility	2.0×10 <sup>-10</sup> mg/L at 25°C (estimated) <sup>4</sup>	1.0×10 <sup>-10</sup> mg/L at 25°C (estimated) <sup>4</sup>	2.7 - 1×10 <sup>6</sup> mg/L at 25°C (estimated) <sup>3</sup>
Log K <sub>ow</sub>	13.91 (estimated) <sup>4</sup>	14.34 (estimated) <sup>4</sup>	-3.56 – 4.14 (estimated) <sup>3</sup>

<sup>1</sup> Lubricating Grease Thickeners Consortium. Revised Robust Summary and Test Plan for Lubricating Grease Thickeners. March 24, 2009. Available at: <http://www.epa.gov/chemrtk/pubs/summaries/lbgrease/c15019tc.htm> as of April 26, 2011.

<sup>2</sup> Lithium Complex Grease is a complex mixture containing 65% base oil, 13.1% octadecanoic acid, 12-hydroxy-, methyl ester, lithium salt (1:1) and octadecanoic acid, 12-hydroxy-, lithium salt (1:1) [CASRN 53422-16-5 and 7620-77-1] and 2.6% Nonanedioic acid, lithium salt (1:2) [CASRN 38900-29-7]

<sup>3</sup> Shekhtur YN., Bogjanova TI., Teterina LN., Fuks IG., Zaslavskaya IR. 1976. Polarity and Functional Properties of Stearic Acid. Chem. Technol. Of Fuels and Oils 11: 734-737

<sup>4</sup> U.S. EPA. 2011. Estimation Programs Interface Suite™ for Microsoft® Windows, v4.00. U.S. Environmental Protection Agency, Washington, DC, USA. Available online at <http://www.epa.gov/opptintr/exposure/pubs/episuitedi.htm> as of May 2, 2011.

<sup>5</sup> Data are not applicable for this endpoint; salt will not volatilize into the environment.

## **2. General Information on Exposure**

### **2.1 Production Volume and Use Pattern**

The Lubricating Grease Thickeners category chemicals had an aggregated production and/or import volume in the United States between 12.5 million pounds and 64.5 million pounds during calendar year 2005.

- |                    |                                      |
|--------------------|--------------------------------------|
| • CASRN 3159-62-4  | 500,000 pounds to <1 million pounds; |
| • CASRN 38900-29-7 | 1 million to <10 million pounds;     |
| • CASRN 4485-12-5  | 500,000 pounds to <1 million pounds; |
| • CASRN 4499-91-6  | < 500,000 pounds;                    |
| • CASRN 64754-95-6 | < 500,000 pounds;                    |
| • CASRN 68783-36-8 | < 500,000 pounds;                    |
| • CASRN 7620-77-1  | 10 million to <50 million pounds;    |
| • CASRN 68603-11-2 | 500,000 pounds to <1 million pounds; |

CASRN 53422-16-5 was not reported in the 2006 IUR.

CASRN 3159-62-4, 38900-29-7 and 64754-95-6:

Non-confidential information in the IUR indicated that the industrial processing and uses for the chemicals include petroleum and petroleum products merchant wholesalers (except bulk stations and terminals) and other direct selling establishments as lubricants. Non-confidential commercial and consumer uses of these chemicals include lubricants, greases and fuel additives.

CASRN 4485-12-5 and 68783-36-8:

Industrial processing and uses, and commercial and consumer uses of these chemicals are claimed confidential.

CASRN 4499-91-6:

No industrial processing and uses, and commercial and consumer uses were reported for this chemical.

CASRN 7620-77-1

Non-confidential information in the IUR indicated that the industrial processing and uses for the chemicals include automotive mechanical and electrical repair and maintenance; commercial and industrial machinery and equipment (except automotive and electronic repair and maintenance); oil and gas extraction; other direct selling establishments; other gasoline stations; other petroleum and coal products manufacturing; petroleum refineries; and petroleum and petroleum products merchant wholesalers (except bulk stations and terminals) as lubricants. Non-confidential commercial and consumer uses of these chemicals include lubricants, greases and fuel additives.

CASRN 68603-11-2

Non-confidential information in the IUR indicated that the industrial processing and uses for the chemicals include all other chemical product and preparation manufacturing as lubricants. Non-confidential commercial and consumer uses of these chemicals include lubricants, greases and fuel additives.

## 2.2 Environmental Exposure and Fate

The substances in the lubricating grease thickeners category, when considered as isolated chemicals, are expected to have low to moderate mobility in soil. Biodegradation data exist for three substances in this category. Octadecanoic acid, calcium salt (2:1) (CASRN 1592-23-05) was degraded 55–99% after 28 days using several modified Sturm tests (OECD 301B) using various combinations of dispersion and/or agitation. The same substance was also degraded 91 and 93% after 28 days in two MITI I tests (OECD 301C); it is therefore considered readily biodegradable. Octadecanoic acid, calcium salt (2:1) (CASRN 3159-62-4) degraded 61.5 and 67.6% after 28 days in several shake flask tests (EPA 560/6-82-003) and is considered readily biodegradable. 12-Hydroxyoctadecanoic acid, lithium salt (1:1) (CASRN 7620-77-1) was degraded 74.7% after 28 days using a shake flask test (EPA 560/6-82-003) and is considered readily biodegradable. The sponsored and supporting chemicals are salts, which do not volatilize in the environment. The rate of hydrolysis is expected to be negligible since the substances in this category do not have water-reactive functional groups. The overall weight of experimental evidence and data from structurally similar compounds suggest that the members of this category will have low persistence (P1). The members of this category are expected to have low (B1) to high (B3) bioaccumulation potential. The environmental fate properties are provided in Table 2.

<b>Property</b>	Octadecanoic acid, 12-hydroxy-, calcium salt (2:1)	Nonanedioic acid, lithium salt (1:2)	Octadecanoic acid, lithium salt (1:1)	Docosanoic acid, lithium salt (1:1)	Octadecanoic acid, 12-hydroxy-, methyl ester <sup>2</sup> , lithium salt (1:1)
CASRN	3159-62-4	38900-29-7	4485-12-5	4499-91-6	53422-16-5
Photodegradation Half-life	2.1 hours (estimated) <sup>3</sup>	17 hours (estimated) <sup>3</sup>	6.0 hours (estimated) <sup>3</sup>	4.7 hours (estimated) <sup>3</sup>	3.4 hours (estimated) <sup>3</sup>
Hydrolysis Half-life	Stable	Stable	Stable	Stable	7.3 years at pH 7; 270 days at pH 8 (estimated) <sup>3</sup>
Biodegradation	61.5 and 67.6% in 28 days (readily biodegradable)	No data	No data	No data	No data
Bioaccumulation Factor	BAF = 20 (estimated) <sup>3</sup>	BAF = 3.0 (estimated) <sup>3</sup>	BAF = 8.1×10 <sup>3</sup> (estimated) <sup>3</sup>	BAF = 3.2×10 <sup>3</sup> (estimated) <sup>3</sup>	BAF = 94 (estimated) <sup>3</sup>
Log K <sub>oc</sub>	5.7 (estimated) <sup>3</sup>	2.2 (estimated) <sup>3</sup>	4.1 (estimated) <sup>3</sup>	5.1 (estimated) <sup>3</sup>	3.6 (estimated) <sup>3</sup>
Fugacity (Level III Model) <sup>2</sup>					
Air (%)	0.1	<0.1	<0.1	0.2	<0.1
Water (%)	16.3	19.7	14.9	10.7	15.9
Soil (%)	83.5	80.1	79.9	56.6	82.3
Sediment (%)	<0.1	0.1	5.2	32.5	1.8
Persistence <sup>4</sup>	P1 (low)	P1 (low)	P1 (low)	P1 (low)	P1 (low)
Bioaccumulation <sup>4</sup>	B1 (low)	B1 (low)	B3 (high)	B2 (moderate)	B1 (low)

<sup>1</sup> The Petroleum HPV Testing Group. 2004. Revised Test Plan and Robust Summary for Lubricating Oil Basestock Category. Available online at <http://www.epa.gov/chemrtk/pubs/summaries/lubolbse/c14364tc.htm> as of May 2, 2011.

<sup>2</sup> Not an ester, according to sponsor – see text

<sup>3</sup> U.S. EPA. 2011. Estimation Programs Interface Suite™ for Microsoft® Windows, v4.00. U.S. Environmental Protection Agency, Washington, DC, USA. Available online at <http://www.epa.gov/opptintr/exposure/pubs/episuitedl.htm> as of May 2, 2011.

<sup>4</sup> Federal Register. 1999. Category for Persistent, Bioaccumulative, and Toxic New Chemical Substances. *Federal Register* 64, Number 213 (November 4, 1999) pp. 60194–60204.

<b>Property</b>	Castor oil, hydrogenated, lithium salt <sup>2</sup>	Fatty acids, C16 – 22, lithium salts	Octadecanoic acid, 12-hydroxy-, lithium salt (1:1)	Hydrocarbon waxes, petroleum, oxidized, Me esters <sup>2</sup> , calcium salts	Octadecanoic acid, calcium salt (2:1) (Supporting chemical)
CASRN	64754-95-6	68783-36-8	7620-77-1	68603-11-2	1592-23-0
Photodegradation Half-life	1.2 hours (estimated) <sup>3</sup>	4.7–6.9 hours (estimated) <sup>3,4</sup>	4.2 hours (estimated) <sup>3</sup>	2.2–2.9 hours (estimated) <sup>3,4</sup>	3.0 hours (estimated) <sup>3</sup>
Hydrolysis Half-life	1.5 years at pH 7; 55 days at pH 8 (estimated) <sup>2</sup>	Stable	Stable	Stable	Stable
Biodegradation	No data	No data	74.7% in 28 days (readily biodegradable)	No data	55–99% in 28 days; 91 and 93% in 28 days (readily biodegradable)
Bioaccumulation Factor	BAF = 0.89 (estimated) <sup>3</sup>	BAF = $3.2 \times 10^3$ to $3.8 \times 10^3$ (estimated) <sup>3,4</sup>	BAF = 341 (estimated) <sup>3</sup>	BAF = 0.9–7.9 (estimated) <sup>3,4</sup>	BAF = 9.1 (estimated) <sup>3</sup>
Log K <sub>oc</sub>	12.2 (estimated) <sup>3</sup>	3.5–5.1 (estimated) <sup>3,4</sup>	3.0 (estimated) <sup>3</sup>	7.9–11.4 (estimated) <sup>3,4</sup>	7.9 (estimated) <sup>3</sup>
Fugacity (Level III Model) <sup>3,4</sup>					
Air (%)	0.2	<0.1–0.2	<0.1	0.2–0.6	0.2
Water (%)	23.4	10.7–15.7	18.4	16.1–39.3	15.9
Soil (%)	76.4	56.6–82.5	81.2	60.0–83.7	83.9
Sediment (%)	<0.1	1.74–32.5	0.42	<0.1	<0.1
Persistence <sup>5</sup>	P1 (low)	P1 (low)	P1 (low)	P1 (low)	P1 (low)
Bioaccumulation <sup>5</sup>	B1 (low)	B2 (moderate)	B1 (low)	B1 (low)	B1 (low)

<sup>1</sup>The Petroleum HPV Testing Group. 2004. Revised Test Plan and Robust Summary for Lubricating Oil Basestock Category. Available online at <http://www.epa.gov/chemrtk/pubs/summaries/lubolbse/c14364tc.htm> as of May 2, 2011.

<sup>2</sup>Not an ester, according to sponsor – see text

<sup>3</sup>U.S. EPA. 2011. Estimation Programs Interface Suite™ for Microsoft® Windows, v4.00. U.S. Environmental Protection Agency, Washington, DC, USA. Available online at <http://www.epa.gov/opptintr/exposure/pubs/episuitedi.htm> as of May 2, 2011.

<sup>4</sup>Data range is based upon the representative structures; see Appendix for detailed information on the structures.

<sup>5</sup>Federal Register. 1999. Category for Persistent, Bioaccumulative, and Toxic New Chemical Substances. *Federal Register* 64, Number 213 (November 4, 1999) pp. 60194–60204.

<b>Property</b>	Fatty acids, tallow, calcium salts (Supporting chemical)	Octadecanoic acid, magnesium salt (2:1) (Supporting chemical)	Lithium Complex Grease (Supporting chemical)
CASRN	64755-01-7	557-04-0	No CASRN
Photodegradation Half-life	0.8 hours (estimated) <sup>2</sup>	3.0 hours (estimated) <sup>2</sup>	3.4 – 17 hours (estimated) <sup>2</sup>
Hydrolysis Half-life	Stable		
Biodegradation	No data	No data	No data
Bioaccumulation Factor	BAF = 29 (estimated) <sup>2</sup>	BAF = 9.7 (estimated) <sup>2</sup>	BAF = 3 – 341 (estimated) <sup>2,3</sup>
Log K <sub>oc</sub>	7.9 (estimated) <sup>2</sup>	7.9 (estimated) <sup>2</sup>	2.2 -3.6 (estimated) <sup>2,3</sup>
Fugacity (Level III Model) <sup>2</sup>			
Air (%)	<0.1	0.2	<0.1
Water (%)	17.5	15.9	15.9 – 19.7
Soil (%)	82.4	83.9	80.1 – 82.3
Sediment (%)	<0.1	<0.1	0.1 – 1.8
Persistence <sup>4</sup>	P1 (low)	P1 (low)	P1 (low)
Bioaccumulation <sup>4</sup>	B1 (low)	B1 (low)	B1 (low)

<sup>1</sup> The Petroleum HPV Testing Group. 2004. Revised Test Plan and Robust Summary for Lubricating Oil Basestock Category. Available online at <http://www.epa.gov/chemrtk/pubs/summaries/lubolbse/c14364tc.htm> as of May 2, 2011.

<sup>2</sup> U.S. EPA. 2011. Estimation Programs Interface Suite™ for Microsoft® Windows, v4.00. U.S. Environmental Protection Agency, Washington, DC, USA. Available online at <http://www.epa.gov/opptintr/exposure/pubs/episutedl.htm> as of May 2, 2011.

<sup>3</sup> Lithium Complex Grease is a complex mixture containing 65% base oil, 13.1% octadecanoic acid, 12-hydroxy-, methyl ester, lithium salt (1:1) and octadecanoic acid, 12-hydroxy-, lithium salt (1:1) [CASRN 53422-16-5 and 7620-77-1] and 2.6% Nonanedioic acid, lithium salt (1:2) [CASRN 38900-29-7]

<sup>4</sup> Federal Register. 1999. Category for Persistent, Bioaccumulative, and Toxic New Chemical Substances. *Federal Register* 64, Number 213 (November 4, 1999) pp. 60194–60204.

**Conclusion:** The lubricating grease thickeners category consists of calcium or lithium salts of fatty acids with carbon numbers mostly ranging from C16 to C22. At ambient temperatures, lubricating grease thickeners are solids or waxy solids, with negligible to high water solubility and negligible vapor pressure. As isolated substances, all the members of this category are expected to have low to moderate mobility in soil. The sponsored and supporting chemicals are salts that do not volatilize in the environment. The rate of hydrolysis is expected to be negligible. The rate of atmospheric photooxidation is considered moderate to rapid for members of the category; however, this is not expected to be an important environmental fate process for most category members, since these are not expected to exist in the vapor phase in the atmosphere. Three substances in this category are readily biodegradable. While it is not possible to conclude from these data that all substances in this category are readily biodegradable, the overall weight of experimental evidence and data from structurally similar compounds suggest that most of the category members or their components are expected to have low persistence (P1) and low (B1) to high (B3) bioaccumulation potential. The lubricating grease thickeners, made in mineral oil, form insoluble fatty acid metal salts that gel the oil into a functional grease and generally exist only in the grease matrix. Under normal conditions there is limited bioavailability from the grease for these calcium or lithium salts. EPA takes these factors into account when interpreting data developed on the isolated salts.

### 3. Human Health Hazard

A summary of health effects data submitted for SIDS endpoints is provided in Table 3.

#### *Acute Oral Toxicity*

***Lithium Complex Grease (no CASRN, supporting chemical; 65% base oil, 13.1% Li 12-hydroxy stearate and 2.6% dilithium azelate)***

Sprague-Dawley rats (5/sex/dose) were administered Grease Starplex 2 via gavage at 5000 mg/kg-bw and observed for 14 days following dosing. No mortalities were observed.

**LD<sub>50</sub> > 5000 mg/kg-bw**

***Hydrocarbon waxes (petroleum), oxidized, Me esters, Ca salts (CASRN 68603-11-2, supporting chemical)***

Sprague-Dawley rats (5/sex/dose) were administered hydrocarbon waxes (petroleum), oxidized, Me esters, Ca salts via gavage at 5, 10 or 15 mL/kg and observed for 14 days. No mortalities were observed.

**LD<sub>50</sub> > 15 mL/kg**

#### *Acute Dermal Toxicity*

***Lithium Complex Grease (no CASRN, supporting chemical; 65% base oil, 13.1% Li 12-hydroxy stearate and 2.6% dilithium azelate)***

New Zealand White rabbits (5/sex/dose) were administered Grease Starplex 2 via the dermal route at 3000 mg/kg-bw under occluded conditions for 24 hours and observed for 14 days. No mortalities were observed.

**LD<sub>50</sub> > 3000 mg/kg-bw**



### ***Repeated-Dose Toxicity***

#### ***Magnesium stearate (CASRN 557-04-0, supporting chemical)***

Wistar rats (20/sex/dose) were administered magnesium stearate via the diet at 0, 5, 10 and 20% for 3 months. The Robust Summary for this study indicates that the carbohydrates of the diet were substituted by magnesium stearate and estimated the 5% magnesium stearate in the diet to correspond to ~ 2500 mg/kg-bw/day. By extension, the 10 and 20% magnesium stearate in the diet should correspond to ~ 5000 and 10000 mg/kg-bw/day. Mortality was observed in four high-dose males due to stone formation in the lower urinary pathways. Four other high-dose males and one high-dose female also showed stone formation in the renal pelvis and the lower urinary pathway at necropsy. Clinical signs observed included decreases in body weight gain, and increases in quietness, incontinence and unsteady movements in all high-dose males. Hematology effects included statistically significant reductions in packed cell volume in high-dose males. Increases in iron in the liver in high-dose males and females and decreases in liver glycogen in high-dose males were also reported. Statistically significant ( $p < 0.001$ ) dose-related decreases in relative liver weights were observed in low-, mid- and high-dose males; and statistically significant ( $p < 0.05$ ) decreases relative kidney weights were observed in mid-dose males. Statistically significant ( $p < 0.001$ ) dose-related decreases in kidney weights were observed in low-, mid-, and high-dose females; and statistically significant ( $p < 0.05$ ) decreases in relative liver weights were observed in high-dose females. Severe nephrocalcinosis (excess calcium in the kidneys) was observed in 20/20 females and 12/20 males in the control group, and only slight to moderate nephrocalcinosis was observed 19/20 high-dose females and 7/20 high-dose males. The study authors suggested that the increased magnesium content of the diet could explain the reduction of nephrocalcinosis in the high-dose animals when compared with controls. They report that the occurrence of nephrocalcinosis is a common finding in animals fed semi-synthetic diets and also note that a high magnesium content of the diet has been previously shown to be associated with a greater incidence of stone formation in the lower part of the urinary track. No effects were reported for male/female reproductive organ weights or histology.

**LOAEL = 20% (~10000 mg/kg-bw/day)** (based on mortality and hematological effects in males; and possible signs of liver toxicity in males and females)

**NOAEL = 10% (~ 5000 mg/kg-bw/day)**

#### ***R960002575 (no CASRN, supporting chemical; 80% base oil, 8.8% Li 12-hydroxy stearate and 1.8% dilithium azelate)***

(1) Sprague-Dawley rats (10/sex/dose) were administered R960002575 via gavage at 0, 250, 500 or 1000 mg/kg/day for 90 days. Detailed hematology, clinical chemistry, and histological examinations were conducted. Food intake was increased in the mid- and high-dose groups. Increases in prothrombin time in mid- and high-dose males and increases in partial thromboplastin time in low- and high-dose animals were observed. These effects were considered to be within normal ranges of historical controls and therefore not considered related to treatment. No mortalities were reported at any dose level. Likewise, no effects were noted for ophthalmoscopic examinations, clinical signs of toxicity, body weight, clinical chemistry, necropsy, or organ weight and histology, including male/female reproductive organs.

**NOAEL = 1000 mg/kg/day** (based on no treatment-related adverse effects at the highest dose tested)

(2) Sprague-Dawley rats (10/sex/dose) were administered R960002575 via the dermal route at 0, 525, 1050 or 2100 mg/kg/day under occluded conditions 6 hours/day, 5 days/week for 13 weeks. No treatment-related effects were noted for mortality, ophthalmoscopic examinations, clinical signs of toxicity, food intake, hematology, clinical chemistry, necropsy, or organ weight and histology, including male/female reproductive organs. Although details were not provided, the robust summary states that mid-dose males had slightly lower body weights than controls; however, since this effect was not observed in high-dose animals, it was not considered treatment-related.

**NOAEL = 2100 mg/kg/day** (based on no adverse treatment-related effects at the highest dose tested)

***Generic Calcium Complex Grease (no CASRN, non-commercial formulation; 3.5 % calcium acetate 3.5 % calcium salts of coco fatty acids, 1.4% calcium salts of C6-C12 fatty acids, 1.2% calcium salts of tallow fatty acids, hydrogenated, and the remainder as performance additives and base oil)***

Sprague-Dawley rats (10/sex/dose) were administered generic calcium grease via the dermal route at 0, 500, or 2000 mg/kg/day under non-occluded conditions for 5 days/week for 13 weeks. An additional group received 2000 mg/kg/day of the specific mineral oil that comprised the majority of the grease formulation. Clinical signs, body weight, urinalysis, hematology, and serum chemistry parameters were assessed. All animals were necropsied and organs weighed. Histological examination of selected organs, including male/female reproductive organs, was conducted in control and high-dose animals only. Sperm morphology was evaluated. Minimal dermal irritation was reported at the site of dosing. No treatment-related effects were reported in body weights, clinical signs, serum chemistry, urinalysis, gross appearance at necropsy, including microscopic examination. No differences were seen in sperm morphology. A statistically significant increase in platelets in the additional group receiving mineral oil alone was reported. Statistically significant increases in absolute and relative liver and kidney weight were noted in males at 500 and 2000 mg/kg/day, and in females at 2000 mg/kg/day; however, these organ weight changes occurred in the absence of abnormal histopathology or biochemical parameters. Similarly, these organ weight changes were also reported in the mineral oil group, possibly suggesting that they were related to treatment with that oil and not the test compound. Therefore, the changes in organ weights were not considered to be adverse treatment-related effects.

**NOAEL = 2000 mg/kg/day** (based on no adverse treatment-related effects at highest dose tested)

***Mobilgrease HP (no CASRN, non-commercial formulation; 7.9% lithium hydroxystearate, 0.9% lithium salts of C16-C22 fatty acids, 10.8% performance additives, and the remainder base oil)***

Sprague-Dawley rats (10/sex/dose) were administered Mobilgrease HP via the dermal route at 0, 500, or 2000 mg/kg/day under non-occluded conditions for 5 days/week for 13 weeks. Clinical signs, body weight, urinalysis, hematology, and serum chemistry parameters were assessed. All animals were necropsied and organs weighed. Histological examination of selected organs, including male/female reproductive organs, was conducted in control and high-dose animals only. Sperm count and morphology were evaluated. Minimal skin irritation was noted at the treatment area. No clinical signs were reported. Statistically significant changes were reported in hemoglobin, hematocrit, and platelets at 500 and 2000 mg/kg/day dose groups in males; however, these changes were considered comparable to historical controls (i.e., between the 10<sup>th</sup>

and 90<sup>th</sup> percentiles of historical controls) and therefore not likely to be biologically meaningful. Statistically significant differences were reported for several serum chemistry and urinalysis parameters in males and females. These included creatinine, total protein, phosphorus, and sodium in males; sorbital dehydrogenase, phosphorus, and potassium in females. Again, these values were reported as being within the 10<sup>th</sup> and 90<sup>th</sup> percentiles for historical controls, although dose-response information and the magnitude of these differences were not given. No treatment-related effects were reported at necropsy. Absolute and relative liver weights were statistically significantly increased at both doses in males, and at 2000 mg/kg/day in females. Relative kidney weights were increased in males at 2000 mg/kg/day. No histological changes were reported in any organs. No differences were noted in any of the reproductive parameters in males.

**NOAEL = 2000 mg/kg/day** (based on no adverse treatment-related effects at the highest dose tested)

***Mobilux EP-2 (no CASRN, non-commercial formulation; 5.6% lithium hydroxystearate, 0.7% lithium salts of C16-C22 fatty acids, 7% performance additives, and the remainder base oil)***

Sprague-Dawley rats (10/sex/dose) were administered Mobilux EP-2 via the dermal route at 0, 300, 1200, or 2000 mg/kg/day under non-occluded conditions for 5 days/week for 13 weeks. An additional group received 1200 mg/kg/day of the specific mineral oil that comprised the majority of the grease formulation. Clinical signs, body weight, urinalysis, hematology, and serum chemistry parameters were assessed. All animals were necropsied and organs weighed. Histological examination of selected organs, including male/female reproductive organs, was conducted in control and high-dose animals only. Sperm count and morphology were evaluated. Minimal dermal irritation was reported at the site of dosing. No significant differences were reported in treated animals compared with controls for clinical signs, body weight, serum chemistry and urinalysis parameters, gross appearance at necropsy, organ weights, and histological examination, or in any of the sperm parameters. Slight, but statistically significant decreases in the number of red blood cells, hemoglobin, and hematocrit were observed in males at  $\geq 300$  mg/kg/day and in females at 2000 mg/kg/day. These changes were also reported in the mineral oil group, possibly suggesting that they were related to treatment with that oil and not the test compound. Therefore, the hematological changes were not considered to be adverse treatment-related effects.

**NOAEL = 2000 mg/kg/day** (based on no adverse treatment-related effects at the highest dose tested)

***Reproductive Toxicity***

No one- or two-generation reproductive toxicity studies on the sponsored chemicals are available for either the calcium or lithium fatty acid salt category members. A repeated-dose dietary toxicity study with supporting chemical, magnesium stearate described above, did not report any effects on male/female reproductive organs at doses as high as  $\sim 10000$  mg/kg-bw/day.

Likewise, no effects on reproductive organs or on sperm parameters were observed at doses as high as 2000 mg/kg/day in several repeated-dose toxicity studies via the dermal route with the non-commercial formulations, Generic Calcium Complex Grease, Mobilgrease HP, and Mobilux EP-2, described above.

### ***Developmental Toxicity***

No adequate prenatal developmental toxicity studies on either the sponsored or supporting chemicals were available. However, a prenatal developmental toxicity study was available for one of the non-commercial formulations.

#### ***Lithium 12-Hydroxystearate – Generic Grease (no CASRN, non-commercial formulation; 8.1% lithium hydroxystearate, 0.9% lithium salts of C16-C22 fatty acids, 18.4% performance additives, and the remainder base oil)***

Pregnant Sprague-Dawley rats (15/dose) were administered generic grease via the dermal route at 0, 500, or 2000 mg/kg/day under non-occluded conditions on gestation days (GD) 0-19. Each dam was observed daily for clinical signs of toxicity. Body weights and food consumption were recorded at intervals during gestation. Females were sacrificed on GD 20. Serum chemistry parameters were assessed. Organs were weighed and examined microscopically, including the ovaries and gravid uterine weight. The number of corpora lutea per ovary, number and location of implantations, early and late resorptions, and live and dead fetuses were recorded. Each fetus was weighed and examined grossly and subjected to visceral and skeletal evaluations. A dose-related increase in the incidence in dermal irritation at the site of dosing was observed in the dams. Dose-related decreases in mean maternal body weight and body weight gains were observed, with statistical significance at the highest dose group. No changes in food consumption were reported. Dose-related decreases in serum calcium levels were observed, with statistical significance at the highest dose group. The biological significance of this effect is unclear. No other effects were reported in the dams. No effects were reported in the fetuses on any parameters.

**LOAEL (maternal toxicity) = 500 mg/kg/day** (based on decreases in maternal body weight and body weight gain)

**NOAEL (maternal toxicity) = Not established**

**NOAEL (developmental toxicity) = 2000 mg/kg/day** (based on no adverse treatment-related effects at the highest dose tested)

### ***Genetic Toxicity***

No adequate data were available for gene mutation or chromosomal aberration endpoints. However, according to the 2003 Test Plan, magnesium stearate has been tested in the Ames test and was negative for mutagenicity. Likewise, the overall evidence from several in vitro and in vivo studies with soluble lithium salts indicated no mutagenic activity, with a possible effect on chromosomes following an intraperitoneal dose of lithium at 2000 mg/kg.

### ***Additional Information***

#### ***Eye Irritation***

#### ***Lithium Complex Grease/Grease Starplex 2 (no CASRN, supporting chemical; 65% base oil, 13.1% Li 12-hydroxy stearate and 2.6% dilithium azelate)***

Undiluted Grease Starplex 2 (0.1 mL) was instilled onto the conjunctival sac of the right eye of six female New Zealand White rabbits. Eyes were examined at 1, 24, 48 and 72 hours and 7 days post application. Conjunctival redness was observed in all animals 1 hour after application and in three animals at 24 hours. Iritis and corneal opacity were observed in one animal at 24 hours. All eyes were normal after 7 days.

**Lithium Complex Grease was moderately irritating to rabbit eyes in this study.**

### ***Skin Irritation***

#### ***Lithium Complex Grease/Grease Starplex 2 (no CASRN, supporting chemical; 65% base oil, 13.1% Li 12-hydroxy stearate and 2.6% dilithium azelate)***

New Zealand White rabbits (3/sex/dose) were administered Grease Starplex 2 (0.5 mL) on shaved, intact and abraded skin (one abraded site and two intact sites) under semi-occlusive conditions. One intact site was covered for 4 hours, while the other intact and abraded sites were covered for 24 hours. Residual test material was removed from the skin using gauze and mineral oil. No clinical signs of toxicity or effects on body weight gain were observed. Slight irritation was noted in animals treated with the 4-hour exposure, while animals treated for 24 hours experienced moderate to severe erythema and well-defined to severe edema. Skin responses were resolved by day 6. The primary irritation indices were 0.38 for the 4-hour exposure and 4.92 for the 24-hour exposure.

**Lithium Complex Grease was moderately irritating to rabbit skin in this study.**

### ***Sensitization***

#### ***R960002575 (no CASRN, supporting chemical; 80% base oil, 8.8% Li 12-hydroxy stearate and 1.8% dilithium azelate)***

Guinea pigs (10/sex) were treated with R960002575 under an occlusive dressing to shaved skin for 6 hours. After application, residual test material was removed using a gauze and mineral oil. Animals received one application every week for 3 weeks. Two weeks following the third application, a challenge dose was applied in the same manner as the previous doses, but on a naïve site. Positive and negative groups were included. No dermal irritation or sensitization was noted in any animal.

**R960002575 was not a sensitizer to guinea pig skin in this study.**

### ***Carcinogenicity***

#### ***PARL-3093-GR-81 (no CASRN, supporting chemical; 80% base oil, 7.5% Li-12-hydroxystearate)***

C3H mice (50/sex) were administered 50 mg undiluted PARL-3093-GR-81 via the dermal route to shaved skin 2 times/week for 104 weeks. There were three other groups in the study: untreated controls, positive controls (BaP in toluene), and toluene vehicle controls. For the grease group, one female had a malignant tumor and two males had benign tumors (the same total tumors seen in the untreated control group). This study was a study of skin carcinogenicity only.

**PARL-3093-GR-81 was not a skin carcinogen in this study.**

### ***In Vivo Dermal Penetration***

#### ***Mobilux EP-2 (no CASRN, non-commercial formulation; 5.6% lithium hydroxystearate, 0.7% lithium salts of C16-C22 fatty acids, 7% performance additives, and the remainder base oil)***

Sprague-Dawley rats (5/sex/dose) were administered Mobilux EP-2 via the dermal route with 2000 mg/kg/day Mobilux EP-2 under non-occluded conditions for 5 days/week for 13 weeks, followed by 4 days of the grease fortified with <sup>14</sup>C-dotriacontane. The goal of this study was limited to the measurement of in vivo dermal penetration of radiolabelled dotriacontane that had

been added to the applied grease as a surrogate for the chemical components in the grease. This was not a pharmacokinetic study and no metabolites were measured. This study was ancillary to the 13-week dermal toxicity study on Mobilux EP-2. Extra groups of untreated controls and animals receiving 2000 mg/kg/day were included in the dosing regimen of that study (described above). Exposure sites were not covered; the animals wore cardboard “Elizabethan” collars to minimize ingestion of the test material. Following treatment, animals were sacrificed and the skin removed. Radioactivity in the urine and fecal samples and in the whole body at the time of sacrifice was measured by liquid scintillation. The mean bioavailability of <sup>14</sup>C-dotriacontane in dermally applied Mobilux EP-2 grease was less than 0.1% among the untreated controls and ≤ 0.9% among animals previously treated with Mobilux EP-2 for 13 weeks. The study authors concluded that since dotriacontane represented the relatively more soluble components in the oil phase of the grease matrix, the dermal penetration of the physically larger and less mobile grease thickeners would be expected to be significantly much less.

**Conclusion:** The acute toxicity of the lubricating grease thickeners category via the oral and dermal routes in rats is low based on data with the supporting chemical, Lithium Complex Grease/Grease Starplex 2. A repeated-dose dietary toxicity study in rats with supporting chemical magnesium stearate showed mortality and hematological effects in males, and signs of liver toxicity in males and females at ~ 10000 mg/kg-bw/day; the NOAEL for systemic toxicity was ~5000 mg/kg-bw/day. A repeated-dose oral gavage toxicity study in rats with supporting chemical R960002575 showed no signs of adverse treatment-related effects at 1000 mg/kg/day, the highest dose tested; the NOAEL for systemic toxicity was 1000 mg/kg/day. A repeated-dose dermal toxicity study in rats with the supporting chemical R960002575 also showed no signs of adverse treatment-related effects at 2100 mg/kg/day, the highest dose tested; the NOAEL for systemic toxicity was 2100 mg/kg/day. A repeated-dose dermal toxicity study in rats with a non-commercial formulation, Generic Calcium Grease, showed no signs of adverse treatment-related effects at 2000 mg/kg/day, the highest dose tested; the NOAEL for systemic toxicity was 2000 mg/kg/day. A repeated-dose dermal toxicity study in rats with a non-commercial formulation, Mobilegrease HP, showed no signs of adverse treatment-related effects at 2000 mg/kg/day, the highest dose tested; the NOAEL for systemic toxicity was 2000 mg/kg/day. A repeated-dose dermal toxicity study in rats with a non-commercial formulation, Mobilux EP-2, showed no signs of adverse treatment-related effects at 2000 mg/kg/day, the highest dose tested; the NOAEL for systemic toxicity was 2000 mg/kg/day. No standard one- or two-generation reproductive toxicity studies on the sponsored chemicals are available; however, data on reproductive organs in a repeated-dose oral toxicity study with supporting chemical magnesium stearate in rats did not show any effects on reproductive organs at doses as high as ~10000 mg/kg-bw/day. Likewise, repeated-dose dermal toxicity studies in rats with several non-commercial formulations did not report any effects on male/female reproductive organs or on sperm count and morphology at doses as high as 2000 mg/kg/day. No prenatal developmental toxicity studies on either the sponsored or supporting chemicals are available; however, a prenatal developmental toxicity study by the dermal route in rats with the non-commercial formulation, Lithium 12-Hydroxystearate – Generic Grease, showed decreases in body weight and body weight gain in the dams at 500 mg/kg/day, the lowest dose tested. No adverse treatment-related effects were reported in the fetuses; the NOAEL for developmental toxicity was 2000 mg/kg/day. No genetic toxicity studies for either the sponsored or supporting chemicals, or for any of the non-commercial formulations, are available. Magnesium stearate has been tested in the Ames test and was negative for mutagenicity. Likewise, overall evidence

from several in vitro and in vivo studies with soluble lithium salts indicated no mutagenic activity, with a possible effect on chromosomes following an intraperitoneal dose of lithium at 2000 mg/kg. Supporting chemical, Lithium Complex Grease/Grease Starplex 2, is moderately irritating to rabbit skin and eyes, while the supporting chemical, R960002575, is not sensitizing to guinea pig skin. Supporting chemical, PARL-3093-GR-81, showed no evidence of carcinogenicity when applied to mouse skin.

<b>Table 3. Summary Table of the Screening Information Data Set as Submitted under the U.S. HPV Challenge Program – Human Health Data</b>					
<b>Endpoints</b>	<b>Lithium stearate</b>	<b>Lithium docosanoate</b>	<b>Methyl 12-hydroxystearate, lithium salt<sup>b</sup></b>	<b>Lithium 12-hydroxystearate</b>	<b>Dilithium azelate</b>
<b>CASRN</b>	<b>(4485-12-5)</b>	<b>(4499-91-6)</b>	<b>(53422-16-5)</b>	<b>(7620-77-1)</b>	<b>(38900-29-7)</b>
<b>Acute Oral Toxicity LD<sub>50</sub> (mg/kg-bw)</b>	No Data >5000 (RA)	No Data >5000 (RA)	No Data >5000 (RA)	No Data >5000 (RA)	No Data >5000 (RA)
<b>Acute Dermal Toxicity LD<sub>50</sub> (mg/kg-bw)</b>	No Data >3000 (RA)	No Data >3000 (RA)	No Data >3000 (RA)	No Data >3000 (RA)	No Data >3000 (RA)
<b>Repeated-Dose Toxicity NOAEL/LOAEL Oral (mg/kg-bw/day)</b>	No Data NOAEL = 1000 LOAEL = not established (RA)	No Data NOAEL = 1000 LOAEL = not established (RA)	No Data NOAEL = 1000 LOAEL = not established (RA)	No Data NOAEL = 1000 LOAEL = not established (RA)	No Data NOAEL = 1000 LOAEL = not established (RA)
<b>Repeated-Dose Toxicity NOAEL/LOAEL Dermal (mg/kg-bw/day)</b>	No Data NOAEL = 2000 LOAEL = not established (RA)	No Data NOAEL = 2000 LOAEL = not established (RA)	No Data NOAEL = 2000 LOAEL = not established (RA)	No Data NOAEL = 2000 LOAEL = not established (RA)	No Data NOAEL = 2000 LOAEL = not established (RA)
<b>Reproductive Toxicity NOAEL/LOAEL Oral (mg/kg-bw/day)</b>	No Data	No Data.	No Data	No Data	No Data
<b>Developmental Toxicity NOAEL/LOAEL Oral (mg/kg-bw/day)</b>	No Data	No Data	No Data	No Data	No Data
<b>Developmental Toxicity Maternal NOAEL/LOAEL</b>	No Data NOAEL - Not established LOAEL = 500	No Data NOAEL - Not established LOAEL = 500	No Data NOAEL - Not established LOAEL = 500	No Data NOAEL - Not established LOAEL = 500	No Data NOAEL - Not established LOAEL = 500
<b>Developmental NOAEL/LOAEL Dermal (mg/kg-bw/day)</b>	NOAEL = 2000 LOAEL = not established (RA)	NOAEL = 2000 LOAEL = not established (RA)	NOAEL = 2000 LOAEL = not established (RA)	NOAEL = 2000 LOAEL = not established (RA)	NOAEL = 2000 LOAEL = not established (RA)



Table 3 cont'd. Summary Table of the Screening Information Data Set as Submitted under the U.S. HPV Challenge Program – Human Health Data					
Endpoints	Lithium stearate	Lithium docosanoate	Methyl 12-hydroxystearate, lithium salt <sup>b</sup>	Lithium 12-hydroxystearate	Dilithium azelate
CASRN	(4485-12-5)	(4499-91-6)	(53422-16-5)	(7620-77-1)	(38900-29-7)
Genetic Toxicity – Gene Mutation <i>In vitro</i>	No Data	No Data	No Data	No Data	No Data
Genetic Toxicity – Chromosomal Aberrations <i>In vitro</i>	No Data	No Data	No Data	No Data	No Data
Additional Information	No Data	No Data	No Data	No Data	No Data
Skin Irritation	Moderately irritating	Moderately irritating	Moderately irritating	Moderately irritating	Moderately irritating
Eye Irritation	Moderately irritating	Moderately irritating	Moderately irritating	Moderately irritating	Moderately irritating
Sensitization	Not sensitizing (RA)	Not sensitizing (RA)	Not sensitizing (RA)	Not sensitizing (RA)	Not sensitizing (RA)
Carcinogenicity	-	-	-	-	-

<b>Table 3 Cont'd. Summary Table of the Screening Information Data Set as Submitted under the U.S. HPV Challenge Program – Human Health Data</b>			
<b>Endpoints</b>	<b>Castor oil, hydrogenated, lithium salt<sup>b</sup></b>	<b>Fatty acids, C<sub>16-22</sub>, lithium salts</b>	<b>Hydrocarbon waxes, petroleum, oxidized, Me esters, calcium salts<sup>b</sup></b>
<b>CASRN</b>	<b>(64754-95-6)</b>	<b>(68783-36-8)</b>	<b>(68603-11-2)</b>
<b>Acute Oral Toxicity LD<sub>50</sub> (mg/kg-bw)</b>	No Data >5000 (RA)	No Data >5000 (RA)	See link under Introduction
<b>Acute Dermal Toxicity LD<sub>50</sub> (mg/kg-bw)</b>	No Data >3000 (RA)	No Data >3000 (RA)	See link under Introduction
<b>Repeated-Dose Toxicity NOAEL/LOAEL Oral (mg/kg-bw/day)</b>	No Data NOAEL = 1000 LOAEL = not established (RA)	No Data NOAEL = 1000 LOAEL = not established (RA)	See link under Introduction
<b>Repeated-Dose Toxicity NOAEL/LOAEL Dermal (mg/kg-bw/day)</b>	No Data NOAEL = 2000 LOAEL = not established (RA)	No Data NOAEL = 2000 LOAEL = not established (RA)	See link under Introduction
<b>Reproductive Toxicity NOAEL/LOAEL Oral (mg/kg-bw/day)</b>	No Data	No Data	See link under Introduction
<b>Developmental Toxicity NOAEL/LOAEL Oral (mg/kg-bw/day)</b>	No Data	No Data	See link under Introduction
<b>Developmental Toxicity Maternal NOAEL/LOAEL</b>	No Data NOAEL - Not established LOAEL = 500	No Data NOAEL - Not established LOAEL = 500	See link under Introduction
<b>Developmental NOAEL/LOAEL Dermal (mg/kg-bw/day)</b>	NOAEL = 2000 LOAEL = not established (RA)	NOAEL = 2000 LOAEL = not established (RA)	

<b>Table 3 Cont'd. Summary Table of the Screening Information Data Set as Submitted under the U.S. HPV Challenge Program – Human Health Data</b>			
<b>Endpoints</b>	<b>Castor oil, hydrogenated, lithium salt<sup>b</sup></b>	<b>Fatty acids, C<sub>16-22</sub>, lithium salts</b>	<b>Hydrocarbon waxes, petroleum, oxidized, Me esters, calcium salts<sup>b</sup></b>
<b>CASRN</b>	<b>(64754-95-6)</b>	<b>(68783-36-8)</b>	<b>(68603-11-2)</b>
<b>Genetic Toxicity – Gene Mutation <i>In vitro</i></b>	No Data	No Data	See link under Introduction
<b>Genetic Toxicity – Chromosomal Aberrations <i>In vitro</i></b>	No Data	No Data	See link under Introduction
<b>Additional Information</b>	No Data No data	No Data	See link under Introduction
<b>Skin Irritation</b>	Moderately irritating	Moderately irritating	
<b>Eye Irritation</b>	Moderately irritating	Moderately irritating	
<b>Sensitization</b>	Not sensitizing	Not sensitizing	
<b>Carcinogenicity</b>	–	–	

Table 3 Cont'd. Summary Table of the Screening Information Data Set as Submitted under the U.S. HPV Challenge Program – Human Health Data					
Endpoints CASRN	Calcium 12-hydroxystearate (3159-62-4)	Magnesium stearate (557-04-0, supporting chemical) <sup>a</sup>	Lithium Complex Grease/Grease Starplex 2 (no CASRN, supporting chemical)	R960002575 (no CASRN, supporting chemical)	PARL-3093-GR-82 (no CASRN, supporting chemical)
Acute Oral Toxicity LD <sub>50</sub> (mg/kg-bw)	No Data >5000 (RA)	–	> 5000	–	–
Acute Dermal Toxicity LD <sub>50</sub> (mg/kg-bw)	No Data >3000 (RA)	–	> 3000	–	–
Repeated-Dose Toxicity NOAEL/LOAEL Oral (mg/kg- bw/day)	No Data LOAEL = 10000 NOAEL = 5000 (RA)	<b>LOAEL = 10000 NOAEL = 5000</b>	–	<b>NOAEL = 1000 LOAEL = Not established</b>	–
Repeated-Dose Toxicity NOAEL/LOAEL Dermal (mg/kg- bw/day)	No Data NOAEL = 2000 LOAEL = Not established (RA)	–		<b>NOAEL = 2100 LOAEL = Not established</b>	–
Reproductive Toxicity NOAEL/LOAEL Oral (mg/kg- bw/day)	No Data	–	–	–	–
Developmental Toxicity NOAEL/LOAEL Oral (mg/kg- bw/day)	No Data	–	–	–	–
Developmental Toxicity NOAEL/LOAEL Dermal (mg/kg- bw/day)	No Data	–	–	–	–

<b>Table 3 Cont'd. Summary Table of the Screening Information Data Set</b> <b>Table 3 Cont'd. Summary Table of the Screening Information Data Set</b> <b>as Submitted under the U.S. HPV Challenge Program –</b> <b>Human Health Data</b>					
<b>Endpoints</b> <b>CASRN</b>	<b>Calcium</b> <b>12-hydroxystearate</b> <b>(3159-62-4)</b>	<b>Magnesium stearate</b> <b>(557-04-0, supporting</b> <b>chemical)<sup>a</sup></b>	<b>Lithium Complex</b> <b>Grease/Grease</b> <b>Starplex 2</b> <b>(no CASRN,</b> <b>supporting chemical)</b>	<b>R960002575</b> <b>(no CASRN,</b> <b>supporting chemical)</b>	<b>PARL-3093-GR-82</b> <b>(no CASRN,</b> <b>supporting chemical)</b>
<b>Genetic Toxicity</b> <b>– Gene Mutation</b> <i>In vitro</i>	No Data	–	–	–	–
<b>Genetic Toxicity</b> <b>– Chromosomal</b> <b>Aberrations</b> <i>In vitro</i>	No Data	–	–	–	–
<b>Additional</b> <b>Information</b> <b>Skin Irritation</b> <b>Eye Irritation</b> <b>Sensitization</b> <b>Carcinogenicity</b>	No Data Moderately irritating Moderately irritating Not sensitizing (RA) -	–	Moderately irritating Moderately irritating – –	– – <b>Not sensitizing</b> –	– – – <b>Not carcinogenic</b>

Table 3 Cont'd. Summary Table of the Screening Information Data Set as Submitted under the U.S. HPV Challenge Program – Human Health Data				
Endpoints CASRN	Generic Calcium Complex Grease (no CASRN, non- commercial formulation)	Mobilgrease HP (no CASRN, non-commercial formulation)	Mobilux EP-2 (no CASRN, non-commercial formulation)	Lithium 12- Hydroxystearate – Generic Grease (no CASRN, non- commercial formulation)
Acute Oral Toxicity LD <sub>50</sub> (mg/kg-bw)	–	–	–	–
Acute Dermal Toxicity LD <sub>50</sub> (mg/kg-bw)	–	–	–	–
Repeated-Dose Toxicity NOAEL/LOAEL Oral (mg/kg-bw/day)	–	–	–	–
Repeated-Dose Toxicity NOAEL/LOAEL Dermal (mg/kg-bw/day)	<b>NOAEL = 2000 LOAEL = not established</b>	<b>NOAEL = 2000 LOAEL = not established</b>	<b>NOAEL = 2000 LOAEL = not established</b>	–
Reproductive Toxicity NOAEL/LOAEL Oral (mg/kg-bw/day)	–	–	–	–
Developmental Toxicity NOAEL/LOAEL Oral (mg/kg-bw/day)	–	–	–	–
Developmental Toxicity Maternal NOAEL/LOAEL  Developmental NOAEL/LOAEL Dermal (mg/kg/day)	–	–	–	<b>NOAEL - Not established LOAEL = 500</b>  <b>NOAEL = 2000 LOAEL = not established</b>
Genetic Toxicity – Gene Mutation <i>In vitro</i>	–	–	–	–
Genetic Toxicity – Chromosomal Aberrations <i>In vitro</i>	–	–	–	–
Additional Information Skin Irritation Eye Irritation Sensitization Carcinogenicity	– – – –	– – – –	– – – –	– – – –

Measured data in bold text; (RA) = Read Across; – indicates that endpoint was not evaluated for this substance

<sup>a</sup>Magnesium stearate was used to support the category in lieu of calcium stearate (CASRN 1592-23-0), which is also considered to be an adequate sponsored chemical by EPA. No data were provided by the sponsor for calcium stearate. <sup>b</sup> Contains no ester function (see text)

#### **4. Hazard to the Environment**

The members of the Lubricating Grease Thickener category consist of lithium and calcium salts of long-chain (largely  $\geq C_{16}$ ) fatty acids formed *in situ* during the manufacture of certain types of lubricating greases from mineral or synthetic oil. The insoluble metal salt gels the oil into a functional grease that the Sponsor states is highly resistant to water wash-out (“bleed-out”), such resistance being an essential performance characteristic. Greases typically contain 1-14% thickener on a mass basis. The grease thickeners in this category are not commonly synthesized as pure compounds and exist only in the grease matrix. Within the grease matrix and under normal conditions, the long-chain fatty acid salts have limited bioavailability.

EPA is not making use of the submitted data because (1) the studies were conducted on substances that contained grease matrices and performance additives of unknown identity and composition, and (2) the data provided on lithium hydroxystearate is not considered, because for this category, EPA is assessing the fatty acid formed *in situ* in the grease matrix.

#### **Conclusion:**

The grease thickeners in this category are not commonly synthesized as pure compounds and exist only in the grease matrix. Furthermore, these insoluble metal salts thicken the oil into a functional grease that is highly resistant to water wash-out (“bleed-out”), which is an essential performance characteristic of these grease thickeners. EPA has considered these factors, and concluded that the ecotoxicity of the Grease Thickeners category members is expected to have “no effects at saturation”.

## Appendix

The materials in this category are calcium or lithium salts of fatty acids with carbon numbers mostly ranging from C16 to C22. The salts are synthesized *in situ* in an oil and exist only as part of a grease matrix, forming a mesh framework around the oil components. Greases typically contain from 1 to 14% thickener on a mass basis.

The fatty acid precursors are mostly monocarboxylic acids or their esters. One lithium salt of a dicarboxylic acid, commonly used in lithium complex greases, is included in the category. Those entries named as esters actually contain no ester function.

### Sponsored Chemicals

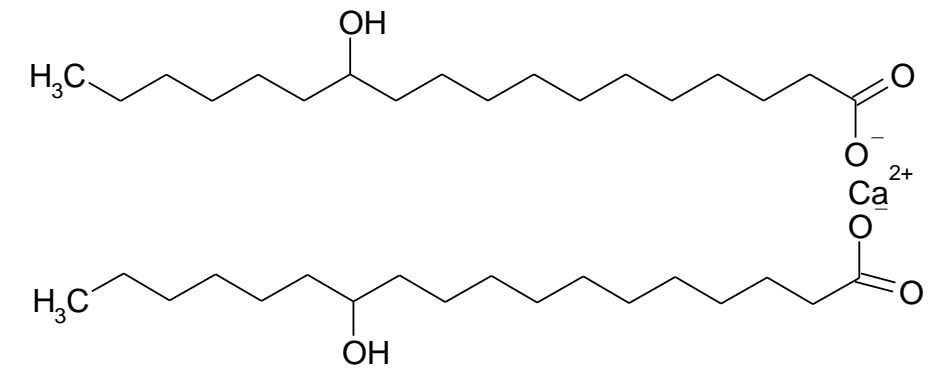
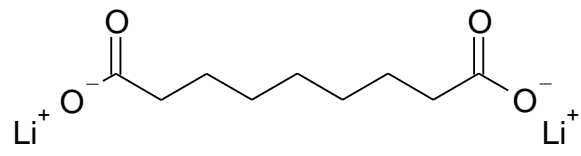
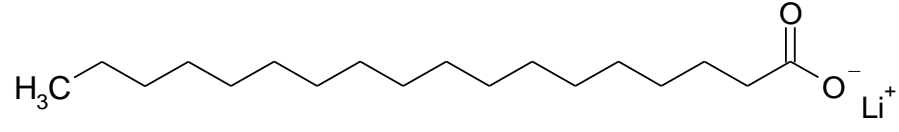
Calcium 12-hydroxystearate [CA name: octadecanoic acid, 12-hydroxy-, calcium salt (2:1)]	CASRN 3159-62-4
Dilithium azelate [CA name: nonanedioic acid, dilithium salt]	CASRN 38900-29-7
Lithium stearate [CA name: octadecanoic acid, lithium salt]	CASRN 4485-12-5
Lithium docosanoate [CA name: docosanoic acid, lithium salt]	CASRN 4499-91-6
Methyl 12-hydroxystearate, lithium salt* [CA name: octadecanoic acid, 12-hydroxy-, methyl ester, lithium salt]	CASRN 53422-16-5
Castor oil, hydrogenated, lithium salt [CA name: castor oil, hydrogenated, lithium salt]	CASRN 64754-95-6
Fatty acids, C <sub>16-22</sub> , lithium salts [CA name: fatty acids, C <sub>16-22</sub> , lithium salts]	CASRN 68783-36-8
Lithium 12-hydroxystearate* [CA name: octadecanoic acid, 12-hydroxy-, monolithium salt]	CASRN 7620-77-1
Hydrocarbon waxes, petroleum, oxidized, Me esters, calcium salts [CA name: hydrocarbon waxes, petroleum, oxidized, Me esters, calcium salts]	CASRN 68603-11-2
Calcium stearate [CA name: octadecanoic acid, calcium salt]	CASRN 1592-23-0
Fatty acids, tallow, calcium salts [CA name: fatty acids, tallow, calcium salts]	CASRN 64755-01-7

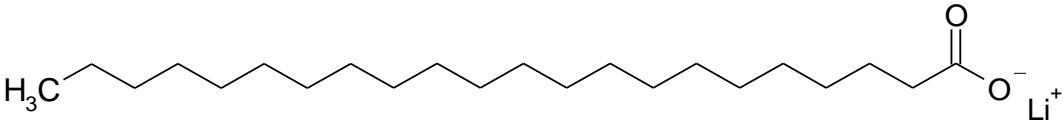
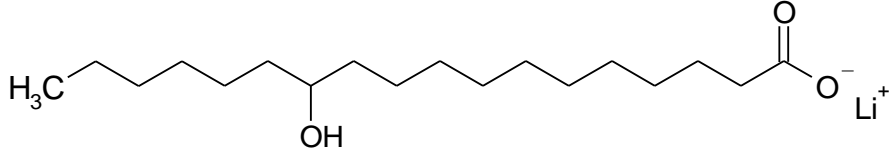
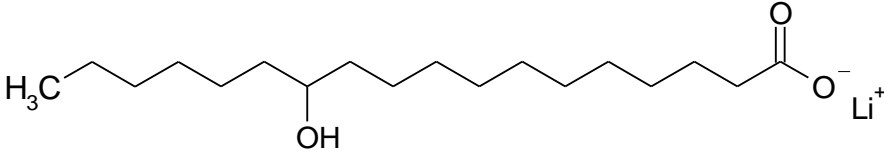
\*These entries represent the same substance—see text.

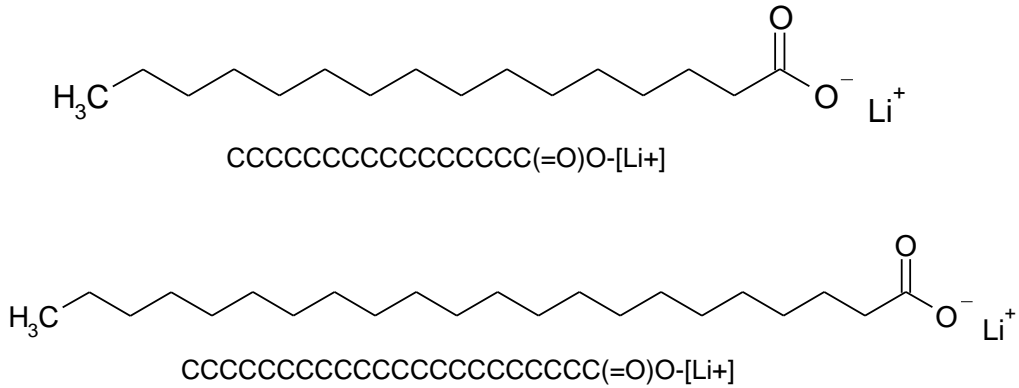
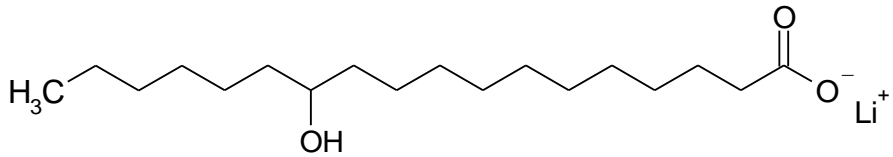
### Supporting Chemicals

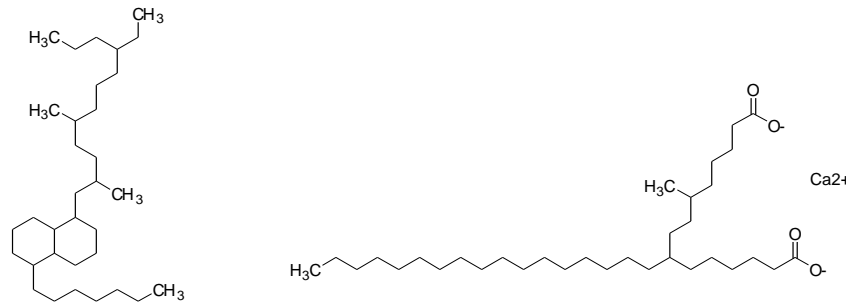
Magnesium stearate [CA name: octadecanoic acid, magnesium salt]	CASRN 557-04-0
Lithium Complex Grease	No CASRN
R960002575	No CASRN
PARL-3093-GR-82	No CASRN

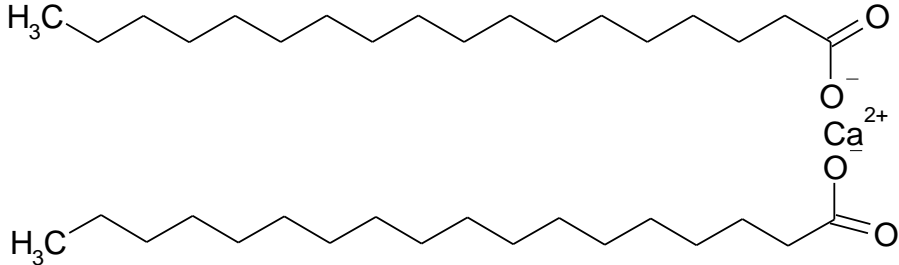
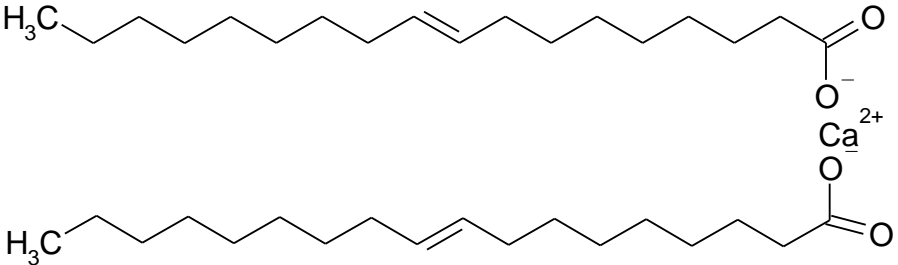


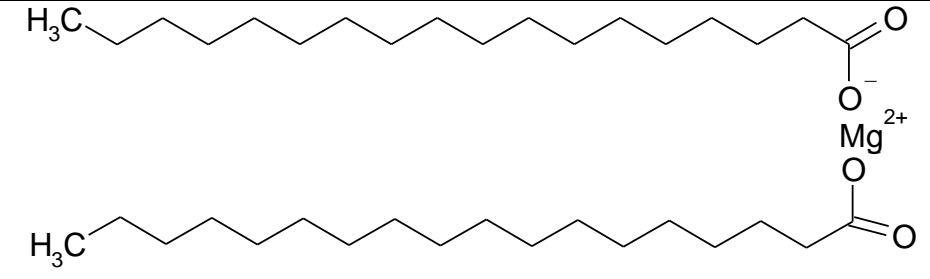
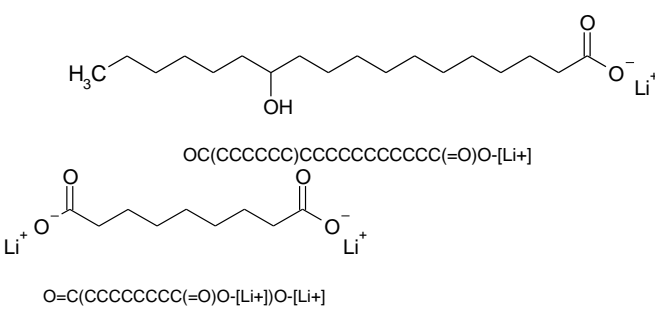
Chemical Name	CASRN	Structure
<p><b>Sponsored Chemicals</b></p> <p>Octadecanoic acid, 12-hydroxy-, calcium salt (2:1)</p>	<p>3159-62-4</p>	 <p><chem>OC(CCCCCC)CCCCCCCCCCC(=O)[O-].[Ca+2].OC(CCCCCC)CCCCCCCCCCC(=O)[O-]</chem></p>
<p>Nonanedioic acid, lithium salt (1:2)</p>	<p>38900-29-7</p>	 <p><chem>O=C(CCCCCCCC(=O)O-[Li+])O-[Li+]</chem></p>
<p>Octadecanoic acid, lithium salt (1:1)</p>	<p>4485-12-5</p>	 <p><chem>CCCCCCCCCCCCCCCC(=O)O-[Li+]</chem></p>

Chemical Name	CASRN	Structure
Docosanoic acid, lithium salt (1:1)	4499-91-6	 <chem>CCCCCCCCCCCCCCCCCCCC(=O)O.[Li+]</chem>
Octadecanoic acid, 12-hydroxy-, methyl ester, lithium salt (1:1)	53422-16-5	 <chem>OC(CCCCC)CCCCCCCC(=O)O.[Li+]</chem>
Castor oil, hydrogenated, lithium salt	64754-95-6	 <chem>OC(CCCCC)CCCCCCCC(=O)O.[Li+]</chem> <p data-bbox="898 1068 1346 1099">Includes small amounts of other C18 acids</p>

Chemical Name	CASRN	Structure
Fatty acids, C16 – 22, lithium salts	68783-36-8	 <p style="text-align: center;">CCCCCCCCCCCCCCCC(=O)O-[Li+]</p> <p style="text-align: center;">CCCCCCCCCCCCCCCCCCCCCCCC(=O)O-[Li+]</p> <p style="text-align: center;">Mixture consists of fatty acids having carbon numbers in the range of C16 to C22.</p>
Octadecanoic acid, 12-hydroxy-, lithium salt (1:1)	7620-77-1	 <p style="text-align: center;">OC(CCCCCC)CCCCCCCCCCCC(=O)O-[Li+]</p>

Chemical Name	CASRN	Structure
Hydrocarbon waxes, petroleum, oxidized, Me esters, calcium salts	68603-11-2	 <p> <chem>CC(CCC(CCCCC(CCC)CC)C)CC2CCCC1C(CCCCCC)CCCC12</chem> </p> <p> <chem>CCCCCCCCCCCCCCCCCC(CCC(C)CCCC([O-])=O)CCCCC([O-])=O</chem> </p> <p> <chem>CCCCCCCCCCCCCCCCCC(CCC(C)CCCC)CCCCC(OC)=O</chem> </p> <p> <chem>CC(CCCCCC(C)CCCCCCCCC)CCCCC(C)C(C)CCCC(C)CCCC</chem> </p> <p> <chem>CCCCCCCCCCCCCCCCCC(CCCC)=O</chem> </p> <p> <chem>CC(CCCCCC(C)CCCCCCC([H])=O)CCCCC(C)C(C)CCCC(C)CCCC</chem> </p> <p><b>Plus monocarboxylic acids and oxyacids</b></p>

Chemical Name	CASRN	Structure
Octadecanoic acid, calcium salt (2:1)	1592-23-0	 <chem>CCCCCCCCCCCCCCCCCC(=O)[O-].[Ca+2].CCCCCCCCCCCCCCCCCC(=O)[O-]</chem>
Fatty acids, tallow, calcium salts	64755-01-7	 <chem>CCCCCCCC=CCCCCCCCCC(=O)[O-].[Ca+2].CCCCCCCC=CCCCCCCCCC(=O)[O-]</chem> <p style="text-align: center;">Representative Structure</p>

Chemical Name	CASRN	Structure
<p><b>Supporting Chemicals</b></p> <p>Octadecanoic acid, magnesium salt (2:1)</p>	<p>557-04-0</p>	 <p>CCCCCCCCCCCCCCCC(=O)[O-].[Mg+2].CCCCCCCCCCCCCCCC(=O)[O-]</p>
<p>Lithium Complex Grease/Grease Starplex 2</p>	<p>No CASRN</p>	 <p>OC(CCCCC)CCCCCCCC(=O)O-[Li+]</p> <p>O=C(CCCCCC(=O)O-[Li+])O-[Li+]</p> <p>O=C(CCCCCC(=O)O-[Li+])O-[Li+]</p> <p>Lithium Complex Grease is a complex mixture containing 65% base oil, 13.1% octadecanoic acid, 12-hydroxy-, methyl ester, lithium salt (1:1) and octadecanoic acid, 12-hydroxy-, lithium salt (1:1) [CASRN 53422-16-5 and 7620-77-1] and 2.6% nonanedioic acid, lithium salt (1:2) [CASRN 38900-29-7]</p>