Response to EPA's Hazard Characterization of the Lubricating Oil Basestocks Category
The American Petroleum Institute Petroleum HPV Testing Group
June 17, 2013

The following comments are in response to EPA's Hazard Characterization (HC) for the Lubricating Oil Basestocks Category (U.S. EPA, 2011). This Category was sponsored by the American Petroleum Institute (API) Petroleum HPV Testing Group (Testing Group) as part of EPA's HPV Chemical Challenge Program (www.petroleumhpv.org).

Below is EPA's generic table of content for all the HPV Hazard Characterizations they have prepared, including Lubricating Oil Basestocks. The Testing Group's comments are found on the page numbers indicated below.

Summary

1. The EPA hazard characterization for several Petroleum HPV Categories including Lubricating Oil Basestocks, refers to the category members as complex mixtures when in fact they are Class 2 UVCB substances. (HC page 3, 6, 8, 26, Appendix B)

Substances on the US TSCA Inventory are divided into two classes for ease of identification (EPA 1995). Class 1 substances are those single compounds composed of molecules with particular atoms arranged in a definite, known structure. However, many commercial substances that are subject to TSCA are not Class 1 substances, because they have unknown or variable compositions or are composed of a complex combination of different molecules. These are designated Class 2 substances. Class 2 includes substances that have no definite molecular formula representation and either partial structural diagrams or no structural diagrams. These are the "UVCB" substances (Unknown or Variable compositions, Complex reaction products and Biological materials). An example of this kind of substance is given below.

CAS Number: 64742-65-0
CAS Name: Distillates (petroleum), solvent-dewaxed heavy paraffinic
CAS Definition: A complex combination of hydrocarbons obtained by removal of normal paraffins from a petroleum fraction by solvent crystallization. It consists predominantly of hydrocarbons having carbon numbers predominantly in the range of C_{20} through C_{50} and produces a finished oil with a viscosity not less than 100 SUS at 100°F (19cSt at 40°C).

Petroleum substances are subject to nomenclature rules developed jointly by the U.S. EPA and the American Petroleum Institute (EPA, 1995b). In that guidance document, EPA adopts the definitions of petroleum process stream terms provided in API's published reference document Petroleum Stream Terms Included in the Chemical Substance Inventory under TSCA (1983, reprinted in 1985). The Stream Terms definitions include the CAS definition and registry number, the source of the substance and process (i.e., last refining step), short name, indication of carbon number, and indication of distillation range (or other appropriate characteristic). Therefore all members of the Lubricating Oil Basestocks Category are UVCB substances, not mixtures, under EPA's nomenclature guidance.

Category Justification

The key reason for the data "gaps" identified by EPA for this Category is the organization of the 36 substances into subcategories. The Testing Group's final Category Assessment Document or CAD (April 2011) included subcategories that were different from the original HPV Test Plan (2004). The Testing Group also proposed the use of modeling to predict certain health hazard endpoints of untested substances. EPA did not find the rationale for the re-categorization or the modeling approach to be justified and continued to use the original subcategories in their assessment of data "gaps". The Testing Group believes the subcategory approach used in our 2011 CAD reflects what was learned about the role of polycyclic aromatic compounds (PAC) in causing the mammalian toxicity of high-boiling point petroleum substances including lubricating oil basestocks. The Testing Group now believes there is no need for subcategories based on the origin or type of the lubricating oil basestock substance (i.e., residual oils, re-refined oils) because the mammalian hazards are related to PAC content of the sample and the environmental hazards are related to the carbon range. The three subcategories used in the

April 2011 CAD (Raw or mildly refined oils, Other oils, and White mineral oil) are sufficient to read-across to untested members and no additional testing is necessary.

1. Substances in the subcategory "Raw or mildly refined oils" are expected to contain enough PAC to be carcinogenic, mutagenic, and cause PAC related toxicity to several target organs and fetal development/viability. No further testing is needed.
2. Substances in the subcategory "Other oils" have been processed to meet performance specifications. Depending on the process parameters used at the refinery (feed stock, space-velocity, catalyst, solvent, solvent-ratio, temperature, pressure, etc.) the resulting oils can be essentially non-toxic. Each manufacturer must determine if their process conditions reduce PAC to an acceptable level by conducting analytical and/or biological tests on their finished product. The identity of the substance (CAS Number, CAS Name, and CAS Definition) does not sufficiently inform the hazard characterization of the substance. No further testing on these "Other oils" is necessary for the HPV Challenge.
3. Substances in the subcategory "White mineral oil" meets FDA requirements for oils and waxes use in food preparation, cosmetics, and medicinal applications. The FDA requirements insure that the PAC content is extremely low (U.S. FDA, 2002). No further testing is needed.

EPA did not acknowledge the utility of the statistical models developed by the Testing Group to evaluate untested samples of Lubricating Oil Basestocks and other high-boiling petroleum substances. In the original Test Plan for this category, a relationship between mammalian toxicity and the polycyclic aromatic compound (PAC) content of the substances in that category was asserted or implied. To study this relationship, toxicology studies and analytical reports on high-boiling petroleum substances (HBPS) like Lubricating Oil Basestocks were collected from the Testing Group's member companies and analyzed in order to address two key questions: 1) Are there quantitative relationships between PAC content of petroleum substances and their critical effects as identified in repeat-dose, developmental, bacterial genotoxicity, and reproductive toxicity studies, and 2) can the critical effects/levels of untested petroleum substances be predicted from their PAC content?

The assessment by the Testing Group showed (a) that the toxicological effects of high boiling petroleum-derived substances (i.e., final boiling points > 650 ^{o}F) were associated with PAC content, (b) that subchronic effects associated with PAC content included liver enlargement, thymic weight reductions, reduced hematological parameters, and developmental effects including reduced live-births and birth-weight, and (c) that the effects of these high boiling petroleum-derived substances could be predicted from PAC contents using predictive statistical models for several repeat-dose, mutagenic, and developmental toxicity endpoints. The models used the weight percent of each of the aromatic ring classes (the "PAC profile") as the independent variable. The effects found to be associated with the PAC profile are consistent with those reported for a number of individual PAHs and PAC-containing materials. A predictive model for bacterial mutagenesis was also developed. The Testing Group had the results of its model building exercise reviewed through an expert peer consultation process (TERA, 2008). The Testing Group has followed up the peer consultation with additional testing and analysis and has prepared several detailed manuscripts for publication (Murray et al., 2013; Nicolich et al., 2013; Roth et al., 2013; McKee et al., 2013). The statistical models can be one of several techniques used to evaluate the hazard of the Lubricating Oil Basestocks Category (along with ASTM E1687, FDA CFR Title 21, Section 172.878, IP 346, etc.).

3. Human Health Hazard

EPA concludes that Draize scores of less than 5/110 for CAS 64741-50-0 and 64742-53-6 makes them eye irritants. (HC page 38). The Testing Group believes that this data confirms that substances in this Category are not eye irritants. EPA should review the Draize scoring methods (Draize et al., 1944).

EPA concludes the read-across value for in vitro Gene Mutation (HC Table 3) is "positive" for White Mineral Oil (CAS 8042-47-5). The Testing Group believes the read-across results for FDA approved oils for food preparation, cosmetics, and medicinal uses should be reported as "negative". EPA also reports CAS 8042-47-5 is a skin sensitizer although no reference is cited. The Testing Group believes FDA approved oils for food preparation, cosmetics, and medicinal uses are not skin sensitizers.

4. Hazard to the Environment

EPA did not use the lethal loading data provided by the Testing Group but instead cites lethal effects concentrations for this category (HC page 53 and Table 5).

EPA provides a summary of aquatic toxicity data submitted for SIDS endpoints in Table 5. The table also indicates where data for the supporting chemical, 1-tetradecene, (CASRN 1120-36-1) are used to read across to all the members of the Lubricating Oil Basestocks Category.

EPA considered submitted data for the CASRNs, 64741-89-5, 64742-01-4, CASRN 64742-55-8, CASRN 64742-57-0, and 64741-88-4 to be inadequate to address the toxicity to aquatic organisms because these substances were tested above their water solubility limit. In addition, these studies used WAF (water accommodated fraction) preparation methods without the analytical data to accompany the values for loading rates, which makes calculating an LC50 or EC50 value impossible. These studies are included here as a contribution to the weight of evidence for characterizing the available information on hazard associated with the Lubricating Oil Basestocks category members. Because the physical-chemical properties of the sponsored chemicals (high Log Kow and low water solubility) are reasonably similar to those of the supporting chemical CASRN 1120-36-1, the ecotoxicity for the Lubricating Oil Basestocks Category members is expected to be no effects at saturation.

EPA cites 1-tetradecene (CASRN 1120-36-1) as a supporting chemical that can be used to represent the aquatic toxicity of petroleum UVCB ('Class 2') substances having similar solubility and partitioning (Log Kow) characteristics. Yet the studies supporting the aquatic toxicity of 1-tetradecene employed the same testing methods that EPA criticized in their review of the studies submitted by the Testing Group for lubricating base oils. The supporting data for 1-tetradecene was submitted as part of the SIDS Initial Assessment Report for Alpha Olefins (11th SIAM, January 2001). The robust summary for the fish test is shown in the Appendix (page 8). This summary shows that exposure solutions were prepared as WAFs, at concentration well above the solubility limit of 1-tetradecene (calculated solubility of 0.004 mg/L by WSKOW V1.41, EPI-Suite^{TM} V4.0) without analytical data to accompany the values for loading rates.
EPA's use of these surrogate data, although redundant, supports the Testing Group's use of lethal loading based on WAF preparations. Therefore, the Testing Group interprets EPA's use of the surrogate data as accepting studies run employing WAF preparations.

The Testing Group agrees with EPA's conclusion that these substances show no aquatic toxicity at their water saturation limit. However, the Testing Group believes that results for petroleum UVCBs (multi-constituent, poorly soluble hydrocarbons) should be expressed as lethal loadings (LL) rather than lethal/effect concentrations (LC, EC). The Testing Group maintains that toxicity endpoints are more accurately expressed as 'loading rates'. Loading is a more effective means of comparing two substances to each other because the hydrocarbon composition in the WAF varies with composition of these streams. Loading is a reflection of the composition and chemistry of the substance and implicitly accounts for multicomponent dissolution and volatilization.

Aquatic toxicity of petroleum streams is attributed to the neutral organic hydrocarbon constituents whose toxic mode of action is non-polar narcosis. Hydrocarbons are equitoxic in tissues where the toxic mechanism of short-term toxicity for these chemicals is disruption of biological membrane function (van Wezel and Opperhuizen, 1995). The differences between toxicities (i.e., LC/LL5O, EC/EL50) can be explained by the differences between the target tissue-partitioning behaviors of the individual chemicals (Verbruggen et al., 2000). The existing fish toxicity database for hydrophobic neutral chemicals supports a critical body residue (CBR, the internal concentration that causes mortality) of approximately 2-8 mmol/kg fish (wet weight) (McGrath and Di Toro, 2009). When normalized to lipid content the CBR is approximately 50 µmol/g of lipid for most organisms (Di Toro et al., 2000).

When compared on the basis of standard test methods and exposure solution preparation procedures, lubricating oil basestocks are expected to produce a similar range of toxicity for the three trophic level species. Results expressed as measured concentrations of the fraction of the substance in solution are of little value since it will be virtually impossible to extrapolate to spill situations where the only relevant measures of concentration will be the amount of product spilled and the volume of the receiving environment (i.e., the loading rates). Loading rates provide a unifying concept for expressing the results of a toxicity test with poorly-soluble substances (European Eco-Labeling Criteria; ASTM 2009; GESAMP; OECD 2006; ECHA). Preparation of independent WAFs based on test substance loading rates is the appropriate procedure for products in this category because these products are multi-constituent hydrocarbons whose constituent hydrocarbons vary in water solubility. The dissolution thermodynamics of a multi-constituent hydrocarbon in an aqueous medium limit the likelihood of consistent proportional concentrations of the constituent hydrocarbons at various test substance loading rates. For this reason,

- exposure solutions are not prepared from dilutions of a stock solution (the relative proportion of hydrocarbon constituents in the dilutions would not accurately reflect the relative concentration of those constituent chemicals in individually prepared, successively lower exposure solutions of the test material), and
- separate exposure solutions are prepared at each exposure loading for products that are multi-constituent hydrocarbons.

EPA is critical of the Testing Group's submitted data and claim they are inadequate because the test substances were tested above their solubility limit. When properly prepared, WAFs represent the equilibrium condition of maximally dissolved test substance for its respective loading rate. Any excess test substance is separated from the solutions used in testing, allowing the use of only dissolved constituents or those that create stable dispersions.

References cited in this response to EPA's HC for the Lubricating Oil Basestocks Category

ASTM. 2009. ASTM D6081 – 98 (2009) Standard Practice for Aquatic Toxicity Testing of Lubricants: Sample Preparation and Results Interpretation.

Di Toro DM, McGrath JA, Hansen DJ. (2000). Technical basis for narcotic chemicals and polycyclic aromatic hydrocarbon criteria. I. Water and tissue. Environ Toxicol Chem. 19:1951-1970.

Draize JH, Woodard G, Calvery HO. (1944). Methods for the study of irritation and toxicity of substances applied topically to the skin and mucous membranes. J. Pharmacol. Exp. Ther. 1944; 82:377-390

ECHA Guidance on information requirements and chemical safety assessment. Chapter R.7b: Endpoint http://echa.europa.eu/documents/10162/13632/information_requirements_r7b_en.pdf European eco-lubricant labeling criteria: http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2005:118:0026:0034:EN:PDF

GESAMP: The Revised GESAMP Hazard Evaluation Procedure for Chemical Substances Carried by Ships http://www.gesamp.org/publications/publicationdisplaypages/rs64

McGrath JA, Di Toro DM. (2009). Validation of the target limpid model for toxicity assessment of residual petroleum constituents: moncyclic and polycyclic aromatic hydrocarbons. Environ Toxicol Chem 28:1130-1148.

McKee, R.H., Schreiner, C., Nicolich, M.J., and Gray, T. (2013) Genetic toxicity of HPV petroleum streams containing polycyclic aromatic compounds. Regulatory Toxicology and Pharmacology. Accepted for publication.

Murray J, Roth R, Nicolich M, Gray T, Simpson B. (2013). The relationship between developmental toxicity and aromatic ring class content of high boiling petroleum substances. Regulatory Toxicology and Pharmacology. Accepted for publication.

Nicolich M, Simpson B, Murray J, Roth R, Gray T. (2013). The development of statistical models to determine the relationship between the aromatic ring class content and repeat-dose and developmental toxicities of high boiling petroleum substances. Regulatory Toxicology and Pharmacology. Accepted for publication.

OECD: Guidance for Testing of difficult substances and mixtures: http://search.oecd.org/officialdocuments/displaydocumentpdf/?cote=env/jm/mono(2000)6&doclanguage=en

Roth R, Simpson B, Nicolich M, Murray R, Gray T. (2013). The relationship between repeat dose toxicity and the aromatic ring class content of high boiling petroleum substances. Regulatory Toxicology and Pharmacology. Accepted for publication.

TERA (2008) "Peer Consultation on Relationship Between PAC Profile and Toxicity of Petroleum Substances" (API Report), http://www.tera.org/peer/API/APIWelcome.htm, accessed 28 Oct 2009 and "Report of the Peer Consultation on Relationship between PAC Profile and Toxicity of Petroleum Substances Volume I" (TERA peer review) http://www.tera.org/peer/API/PAC MEETING REPORT Final.pdf, accessed 28 Oct 2009

Toxic Substances Control Act Inventory Representation for Chemical Substances of Unknown or Variable Composition, Complex Reaction Products and Biological Materials: UVCB Substances (March 29, 1995a); available from http://www.epa.gov/oppt/newchems/pubs/uvcb.txt

Toxic Substances Control Act Inventory Representation for Certain Chemical Substances containing Varying Carbon Chain Lengths (Alkyl Ranges Using the Cx-y Notation) (March 29, 1995b); available from: http://www.epa.gov/oppt/newchems/pubs/alkyl-rg.txt

U.S. EPA (2011). Screening Level Hazard Characterization of High Production Volume Chemicals; Lubricating Oil Basestocks Category. http://ofmpub.epa.gov/oppthpv/hpv_hc_characterization.get_report?srtCol=last_update_date&srtDir=asc&doctype=2

U.S. FDA (2002). Food Additives Permitted for Direct Addition to Food for Human Consumption Code of Federal Regulation Title 21, Vol 3 Part 172, Subpart I, Section 172.878.

van Wezel AP, Opperhuizen A. (1995). Narcosis due to environmental pollutants in aquatic organisms: residue-based toxicity, mechanisms, and membrane burdens. Critical Rev Toxicol. 25(3):255-279.

Verbruggen EMJ, Vaes WHJ, Parkerton TH, and Hermens JLM. (2000). Polyacrylate-coated SPME fibers as a tool to simulate body residues and target concentrations of complex organic mixtures for estimation of baseline toxicity. Environ Sci Technol. 34:324-331.

APPENDIX – Excerpt from Alpha Olefins SIAR, for 11th SIAM, January 2001

4.1 Acute/Prolonged Toxicity to Fish

Test substance: Blend of three suppliers' 1-tetradecene, 99% purity

Type:	Semistatic
Species:	Oncorhynchus mykiss
Exposure Period:	96 hour
Analyt. Monitoring:	No
Method:	OECD Guideline 203
GLP:	Yes
Test Results:	LC50 >1000 mg/L (author assigned)

LL0 = 1000 mg/L (EPA reviewed)

Comment: Water-accommodated fractions (WAFs) were prepared by adding the appropriate amount of 1-tetradecene to dilution water on a weight-volume basis. The WAFs were mixed for 24 hour inside a covered glass vessel using a magnetic stirrer. After the mixing period, the mixture was allowed to settle for one hour before the water phase containing the WAF was siphoned off to use. Test solutions were renewed daily using freshly prepared WAFs.

The range finding test used test concentrations of WAFs from 10, 100, and 1000 mg test article per liter, and five fish per chamber. No deaths were seen during the range finding test.

A definitive limit test was then conducted using 7 fish per chamber and two replicates each in the control and treatment (WAF from 1000 mg/L) groups. No deaths or abnormal signs were noted at any time point in the control or treated groups. The 96-hour LC50 was thus greater than WAF from 1000 mg test article/liter.

LL0 = lethal loading based on the WAF testing procedure, no mortality observed at the highest loading indicated.

Reference:

Drottar, L.R., and Swigert, J.P., "1-Tetradecene: A Water-Accommodated Fraction 96-hour Semistatic Acute Toxicity Test with the Rainbow Trout (Oncorhyncus mykiss)". Wildlife International Ltd., Easton, Maryland 1995b. Chemical Manufacturers Association, Alpha Olefins Panel, Sponsor