HIGH PRODUCTION VOLUME (HPV)

CHEMICAL CHALLENGE PROGRAM

-

TEST DATA

For

C12, Branched Ketones
CAS No. 68514-41-0

Prepared by:

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EXECUTIVE SUMMARY

Under the U.S. Environmental Protection Agency (EPA) High Production Volume (HPV) Chemical Challenge Program (Program), ExxonMobil Chemical Company (EMCC) committed to voluntarily compile data that can be used to characterize the hazard of C12, branched ketones (C12 ketone fraction; CAS No. 68514-41-0). The data for this assessment includes selected physicochemical, environmental fate, and human and environmental effect endpoints identified by the U.S. HPV Program.

The C12 ketone fraction is a co-product of methyl ethyl ketone production (MEK) and is never isolated from the waste MEK production stream, although it is tanked together with other substances in that stream. The stream is subsequently used as part of a chemical feed to produce syngas, a reaction that completely destroys the constituent substances. Together, these processes do not provide an opportunity for human or environmental exposure. However, data are provided to assess the hazard of the C12 ketone fraction.

Based on data for analogs, the C12 ketone fraction is expected to present a low order of hazard for human health as indicated by acute, genetic, and a combined repeated dose toxicity study with the reproductive / developmental toxicity screening test and a Functional Observation Battery (tests assessing sensory and motor activity). Results of Quantitative Structure Activity Relationship (QSAR) modeling and measured data for two analogs show that the C12 ketone fraction will exhibit moderate aquatic toxicity with acute values that fall largely between 1 to 5 mg/L.

In the environment, the C12 ketone fraction is calculated to partition to air and soil compartments where biological and physical processes can mediate the fraction's degradation. Results of Mackay Level I distribution modeling at steady state, show that the C12 ketone fraction will partition primarily to the air compartment (82.6%) with a significant amount also partitioning to the soil compartment (15.5%). Level III modeling indicates that soil is the primary compartment on a percentage basis at steady state when the default emission to each of these compartments is included in the calculations. However, Level III modeling may not be representative of the ultimate disposition of C12 ketones because default emissions, which use 1000 kg/h/compartment, are not representative of chemical discharge.

C12 ketones are volatile and in the atmosphere can be quickly degraded by indirect photolysis. The C12 ketone fraction half-life from hydroxyl radical attack is calculated as approximately 7 hours. Ketones do absorb visible light in a range that can contribute to their degradation by direct photolysis. Therefore, this process could contribute to the degradation of the C12 ketone fraction in the environment. Hydrolysis will not contribute to the transformation of C12 ketones in aquatic environments because they are poorly susceptible to this reaction.

C12 ketones are not rapidly (readily) biodegradable based on results of biodegradation modeling and data from an analog. Although, the C12 ketone fraction is not readily biodegradable, it is not expected to bioaccumulate, based on a bioconcentration factor of 256.6.

Sufficient data are available to characterize the mammalian and environmental health and environmental fate of the C12 ketone fraction, CAS No. 68514-41-0, for the U.S. EPA HPV Program. Additional testing is not planned.

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CAS No. 68514-41-0

I. INTRODUCTION

Under the U.S. Environmental Protection Agency (EPA) High Production Volume (HPV) Chemical Challenge Program (Program), ExxonMobil Chemical Company (EMCC) committed to voluntarily compile data for C12, branched ketones (C12 ketone fraction; CAS No. 68514-41-0).

This substance is supported by selected screening data needed for an initial assessment of physicochemical properties, environmental fate, and human and environmental effects as defined by the U.S. HPV Program. Information cited within this test plan comes from existing data.

Procedures to assess the reliability of selected data for inclusion in this test plan were based on guidelines described by Klimisch *et al*. (1997) (Appendix A) and identified within the US EPA (1999a) document titled Determining the Adequacy of Existing Data.

II. CHEMICAL PROCESS, DESCRIPTION, AND EXPOSURE

For purposes of the HPV Program, the substance reported as CAS No. 68514-41-0 is a ketones fraction that is part of a reaction stream containing several component substances, each reported under a specific CAS No. (Table 1). Table 1 lists the average annual concentration and range in weight percent of the major constituents. CAS No. 68514-41-0 is never isolated from the stream during its chemical life, although it is tanked together with the other major substances as a stream (each CAS No. is reported separately). The stream is subsequently used as part of a chemical feed to produce syngas, a reaction that completely destroys the constituent substances. Together, these processes do not provide an opportunity for human or environmental exposure.

CAS No. 68514-41-0 is not synthesized on purpose and it is not purified. It is one component of a stream that, as a whole, is a co-product of the MEK (methyl ethyl ketone) manufacturing process. CAS No. 68514-41-0 is contained in the “bottoms” stream produced in the finishing section of the MEK production unit. This stream is stored in a tank and controllably fed with other input to a reaction that produces syngas. While there are specifications on the feed (carbon to hydrogen ratio, nitrogen content, water content), neither the concentration nor the different isomers of the “heavy ketones” fraction, which contains C12 ketones, of the stream are specified. The “heavy ketones” are produced via aldol condensation of 2 or 3 MEK molecules that produces C8 or C12 ketone fractions, respectively. This reaction occurs as a consequence of the MEK production process, the intended purpose of which is to produce MEK alone. Consequently, the C8 and C12 ketone fractions are stripped from the MEK product and become a production process stream that is tanked and used as the feedstock to produce syngas.

The fraction reported as CAS No. 68514-41-0 is not a pure chemical. It contains a series of C12 ketone isomers. The specific structures of the C12 ketones fraction components and their relative percent composition are not known.

Table 1. Composition Data for the "Bottoms" Stream Produced in the Finishing Section of the MEK Production Unit.

Substance (CAS Number)*	Average Constituent Concentration % wt. (s.d.)**	Constituent Concentration Range % wt.**
C8 Ketones Fraction (409-02-9)	49.33 (7.71)	22.85 - 64.61
C7-C9 Alkenes (68526-54-5)	3.69 (0.88)	1.95 - 6.34
sec-Butyl Ether (6863-58-7)	13.25 (8.01)	3.60 - 37.00
C12, Branched Ketone (68514-41-0)	27.86 (9.26)	4.56 - 46.78

* "Bottoms" stream constituents with average annual concentrations reported at ≥2% wt. (n=80) from 2005 data.

** Does not include one sample reported to contain 98.36% sec-butyl alcohol.

III. C12, BRANCHED KETONES DATA

No data were identified for the C12, branched ketone, fraction (CAS No. 68514-41-0) alone. Therefore, read-across data for two C12 ketones, trimethyl 4-nonanone (CAS No. 123-18-2) and 2-dodecanone (CAS No. 6175-49-1), and the C8 ketone fraction (CAS No. 409-02-9), which is part of the "bottoms" stream (Table 1), are used as analogs for assessing the human health hazards and environmental effects of the C12 ketone fraction. A single structure for CAS No. 68514-41-0 is not specified. This fraction is likely composed of various C12 ketone isomers. As an analog for the C12 ketones group, trimethyl 4-nonanone is a C12 ketone with a C9 carbon backbone containing methyl groups at carbons 2, 6, and 8. 2-Dodecanone is a linear C12 ketone with the ketone group at the second carbon.

The C8 ketone fraction can be used to characterize the C12 ketone fraction because the two fractions are created from the same starting material, methylethyl ketone (MEK), and same condensation reaction. C8 ketones in the C8 ketone fraction are formed from the condensation of two MEK molecules (4 carbon molecules), while the C12 ketone fraction is formed from the condensation of three MEK molecules. Consequently, the types of structures in the two fractions would be expected to be closely related and have similar activities. Indeed, the acute mammalian toxicity data for a C12 ketone analog, trimethyl 4-nonanone, and the C8 ketone fraction indicate that they both have a low order of acute toxicity.

The C8 ketone fraction has been analyzed and the following information is available for that stream:

- Approximately 50% C8 olefinic ketones
- 5-Methyl-4-hepten-3-one (CAS# 20685-43-2) and 5-Methyl-2-hepten-4-one (CAS# 81925-81-7) were tentatively identified (identification of all C8 olefinic ketone isomers is limited because of the lack of analytical standards and reference spectra in the NIST (National Institute of Standards and Technology) library)
- The balance of the C8 ketone fraction may contain smaller amounts of saturated C8 branched ketones, alcohols, and C12 olefins

There are no metabolism data for the C12 ketone fraction. Metabolism of ketones generally results in reduction to the corresponding secondary alcohol and elimination as a glucuronic acid conjugate.

A. Physicochemical Data

Physicochemical data (Table 2) include calculated data for a structure representative of the C12 ketone fraction and 2 analogs, trimethyl 4-nonanone and 2-dodecanone, as calculated by the EPI Suite™ model (EPI Suite, 2000), discussed in the EPA document titled The Use of Structure-Activity Relationships (SAR) in the High Production Volume Chemicals Challenge Program (US EPA, 1999b).

Table 2. Selected Physicochemical Properties for the C12 Ketone Fraction and C12 Ketone Analogs.

DATA SOURCE	MELTING POINT (º C)	BOILING POINT (º C)	VAPOR PRESSURE (hPa @ 25ºC)	WATER SOLUBILITY (mg/L@ 25ºC)	LOG K_{ow}
C12 Ketone Fraction (CAS 68514-41-0)	-6.7	220.2	0.261	18.7	4.04
Trimethyl 4-nonanone (CAS 123-18-2)	-17.6	208.6	0.459	21.6	3.96
2-Dodecanone (CAS 6175-49-1)	21*	246.5*	0.070	14.0	4.18

* Value provided by experimental database of EPI Suite.

B. Human Health Effects Data

Acute data on a C12 ketone fraction analog, trimethyl 4-nonanone, are available to characterize the potential acute human health hazards of the C12 ketone fraction. These data demonstrate a low order of acute toxicity by the oral, dermal, and inhalation routes of exposure. In addition, only mild ocular irritation was reported. No data are available to assess the genotoxic, or repeated-dose developmental and reproductive toxicity of the C12 ketone fraction. However, there are data for the C8 ketones fraction that can be used to characterize these 4 endpoints as well as the acute endpoint, which show a similar order of acute toxicity as was demonstrated with the C12 ketone fraction.

Acute Toxicity

Acute data on a C12 ketone fraction, trimethyl 4-nonanone, are available to characterize the potential acute human health hazards of the C12 ketone fraction. The oral rat LD_{50} value for trimethyl 4-nonanone was 8470 mg/kg (Carpenter, 1948). The dermal LD_{50} values for trimethyl 4-nonanone were 9030 mg/kg (Carpenter, 1948) and 11 mL/kg (Smyth *et al*., 1951). Mild skin irritation was reported following application of trimethyl 4-nonanone to the skin of rabbits for 24 hours under a cover or applied at a concentration of 500 mg/kg and left uncovered for 24 hours (Smyth *et al*., 1951). Inhalation of trimethyl 4-nonanone in the form of a substantially saturated vapor was administered to 6 rats at room temperature for 8 hrs. Two of the 6 rats died within the 8 hr exposure. The cause of death was considered to be direct damage to the lung, as evidenced by marked

congestion (Carpenter, 1948). A 4-hr exposure to saturated vapor caused no deaths in rats (Smyth *et al*., 1951). Trimethyl 4-nonanone was characterized as a mild irritant following application to rabbit eyes (Smyth *et al*., 1954).

The C8 ketone fraction demonstrated a rat oral LD_{50} value of >2000 mg/kg, which like trimethyl 4-nonanone, suggests a low order of acute toxicity (Huntingdon Life Sciences, Ltd., 2008a).

Thus, for purposes of the HPV Challenge Program, the available data on a similar C12 ketone and the C8 ketone are adequate to characterize the acute toxicity of the C12 ketone fraction. Therefore, no additional testing for acute toxicity is proposed.

Genotoxicity

Data are not available for the C12 ketone fraction. However, the C8 ketones fraction showed no evidence of mutagenic activity in an Ames test (Huntingdon Life Sciences, Ltd., 2008b). No substantial increases in revertant numbers over control counts were obtained with any tester strains following exposure to a C8 ketone fraction at any concentration up to 5000 µg/plate in either the presence or absence of S9 mix.

Additionally, the C8 ketones fraction showed no evidence of causing an increase in the frequency of structural chromosome aberrations in *in vitro* cytogenetic tests (Huntingdon Life Sciences, Ltd., 2008c). No statistically significant increases in the proportion of polyploid cells were observed during metaphase analysis. Studies were conducted in the absence of S9 activation, after 3-hr treatment and 17-hr recovery periods at 25, 125, and 200 µg/ml, and in the presence of S9 activation after 3-hr treatment and 17-hr recovery periods at 200, 600, and 1000 µg/ml.

Based on these results, the C12 ketone fraction would not be expected to be genotoxic.

Repeated Dose Toxicity and Developmental/Reproductive Toxicity

Data are not available for the C12 ketone fraction. However, a combined repeated dose toxicity study with a reproductive/developmental toxicity screen (with a functional observation battery for sensory and motor activity) for the C8 ketones fraction can be used as read-across to the C12 ketone fraction (Huntingdon Life Sciences, Ltd., 2009).

Oral administration of C8 ketone at dose levels of 100, 300 and 1000 mg/kg/day was not tolerated by F0 parental animals at 1000 mg/kg/day. Physical signs observed in association with dosing, in conjunction with bodyweight loss and significantly low food consumption at 1000 mg/kg/day after 2 days of treatment, were considered too severe for prolonged treatment. A decision was made to reduce the high dose to 500 mg/kg/day from Day 3 for the remainder of the study. F0 male animals dosed at levels of 100 mg/kg/day (absolute body weight ~3% below controls at dosing initiation) or more had low bodyweight gain throughout the treatment period. As there was no clear effect on food consumption for male animals at dose levels up to 500 mg/kg/day, the effect on bodyweight at the 500 mg/kg/day dose level (absolute body weight ~8% below controls) was considered to be a non-specific indicator of toxicity.

F0 female animals at 500 mg/kg/day showed low bodyweight throughout the treatment period. Similar to the male animals there was no clear effect on food consumption in the two week period before pairing, however food consumption for females at 500 mg/kg/day was low during both the gestation and lactation phases. At 300 mg/kg/day

females also showed low bodyweight gain and food consumption but this was only apparent during the lactation phase. F0 females receiving 100 mg/kg/day were unaffected by treatment. Males receiving 500 mg/kg/day showed a high incidence of weak tail pinch response (six out of ten animals compared with one out of ten Controls) during Week 5 of treatment. Responses of treated males in the other sensory reactivity tests, and responses of treated females in all tests on Day 6 of lactation, were, however, considered to be unaffected. Motor activity for males, during Week 5 of treatment, the low beam scores (cage floor activity) in all treated groups were low, compared with Controls, during the first 6 minutes of recording, with a dose relationship being evident. Scores for males receiving 500 or 300 mg/kg/day continued to be low at 12, 18 and 24 minutes, although the dose relationship was no longer apparent. High beam scores (rearing activity), usually the more sensitive of the two beam level measures, were unaffected through the same time period. Motor activity scores for females on Day 6 of lactation showed considerable inter and intra-group variation but there was no evidence of an effect of treatment. There were no premature deaths that could be attributed to treatment. Mating performance, fertility, and the offspring survival and development up to Day 7 of age was unaffected by treatment at dose levels up to 500 mg/kg/day. Parental males at 500 mg/kg/day had significantly high liver weights. Slight hepatocyte centrilobular hypertrophy was observed in the liver of all treated males and females. This effect was observed in a dose-related manner and correlated with the increase in liver mean weight for high dose males. These observations, common findings in the livers of rodents that have been administered xenobiotics, are considered to be an adaptive change and not a toxic effect of treatment. The histopathological findings in the thyroid were also considered to be rodent-specific secondary changes due to the induction of hepatic enzymes as suggested by the presence of hepatocyte hypertrophy. The changes are not considered to be of toxicological significance to man because the hormone-binding profiles differ and the rodent thyroid is many times more responsive to hormonal imbalance than the human thyroid. The kidneys showed an increased incidence and severity (minimal to moderate severity) of cortical tubular hyaline droplets, tubular granular casts and cortical tubular basophilia in all the treated male groups, in a dose dependant manner. The kidney findings in this study are similar to those described as occurring in the toxicological syndrome known as “hydrocarbon nephropathy”, a male rat specific toxic response,

It was concluded in this study that in terms of general toxicity, 100 mg/kg/day was the no observed adverse effect level (NOAEL), based on bodyweight and food consumption decreases. Despite evidence of systemic effects in the rat at 500 mg/kg/day, there was no consequential impairment of reproductive function and the high dose of 500 mg/kg/day was considered to be the NOAEL in terms of reproductive function and fertility.

C. Aquatic Toxicity Data

Experimental fish, invertebrate, and green algae data are not available for the C12 ketone fraction. However, Quantitative data determined using a Structure Activity Relationship (QSAR) model, the ECOSAR computer model (Cash and Nabholz, 1990), together with measured data for the analogs, 2-dodecanone and the C8 ketones fraction, can be used to characterize the aquatic toxicity of the C12 ketone fraction. The CAS number (68514-41-0) was used with the ECOSAR model to estimate toxicity. The model identifies a dimethyl 5-decanone with the CAS number, 68514-41-0. Estimates

included a 96-hr LC_{50} value of 1.7 mg/l for a freshwater fish, a 48-hr EC_{50} value of 2.0 mg/l for a daphnid (freshwater invertebrate), and a 96-hr EC_{50} value of 1.4 mg/l for a green alga (Table 3). Table 3 also includes modeled chronic data for a fish, invertebrate, and green alga. The values for both C12 ketones and 2-dodecanone range from approximately 0.2 to 0.5 mg/L for the three trophic levels.

There are measured and calculated data for the analog ketone, 2-dodecanone (CAS No. 6175-49-1), that support using the invertebrate and alga calculated data for the C12 ketone fraction. A study that evaluated 2-dodecanone acute toxicity to fish was reported by the Center for Lake Superior Environmental Studies (Geiger *et al*, 1988). The study reported a 96-hr LC_{50} value of 1.2 mg/l for the Fathead Minnow (*Pimephales promelas*). The calculated fish 96-hr LC_{50} value for 2-dodecanone was also 1.2 mg/l. Because the measured and estimated acute fish values compare favorably, the use of the model is supported to estimate the invertebrate and alga aquatic toxicity values.

Table 3. Calculated and Measured Aquatic Toxicity Data for the C12 Ketone Fraction and the Analog, 2-Dodecanone.

ENDPOINT	RESULT (mg/l)	
	C12 Ketone Fraction (CAS No. 68514-41-0)	**2-Dodecanone (CAS No. 6175-49-1)**
ACUTE		
Fish 96-hr LC_{50}	1.7 (c)	1.2 (m,c)
Daphnid 48-hr EC_{50}	2.0 (c)	1.5 (c)
Alga 96-hr EC_{50}	1.4 (c)	1.1 (c)
CHRONIC		
Fish 30-d ChV	0.3 (c)	0.2 (c)
Daphnid 16-d EC_{50}	0.3 (c)	0.2 (c)
Alga 96-hr ChV	0.5 (c)	0.4 (c)

m measured value
c calculated value

Measured invertebrate and alga results from the C8 ketone fraction also support the use of the estimated C12 ketone fraction data for these two endpoints. The daphnid 48-hr EC_{50} value was 5.2 mg/L (ExxonMobil Biomedical Sciences, Inc., 2007b) and the alga 72-hr EbC_{50} and NOECb values were 8.0 and 0.7 mg/L (ExxonMobil Biomedical Sciences, Inc., 2008), respectively (the biomass endpoint was the lower value of the two values, biomass and growth rate). The measured and calculated data for the C12 ketone fraction are lower than the C8 ketone fraction, which is expected since the C12 ketone fraction has a higher log K_{ow} value (4.04 for the C12 ketone fraction in comparison to 2.5 to 2.8 for the C8 ketone fraction).

D. Environmental Fate Data

Biodegradation

Biodegradation of an organic substance by bacteria can provide energy and carbon for microbial growth. This process results in a structural change of an organic substance and can lead to the complete degradation of that substance, producing carbon dioxide and water.

Experimental data are not available for the C12 ketone fraction. However, there are modeled data and measured data for the C8 ketone fraction that can be used to assess the potential biodegradability of the C12 ketone fraction. The BIOWIN model, a subroutine within the EPI Suite (2000) computer model, estimates that the representative structure for the C12 ketone fraction will not occur at a rapid rate (not readily biodegradable). The BIOWIN3 model, which evaluates ultimate biodegradability to CO_2 and H_2O, estimates a biodegradability of weeks, while the BIOWIN4 model, which estimates primary biodegradation, estimates the C12 ketone fraction will degrade in days to weeks. These data appear to be a good estimate as the C8 ketone fraction biodegraded to 59.8% after 28 days in a test of ready biodegradability, indicating that it is not readily biodegradable (ExxonMobil Biomedical Sciences, Inc., 2007a). A slightly lower extent of biodegradation would be expected for the C12 ketone fraction because of its higher molecular weight and potential for additional methyl branching, which clearly places it at a lower expected extent of biodegradation and below the pass criteria for ready biodegradability.

Photodegradation – Photolysis

Direct photochemical degradation occurs through the absorbance of solar radiation by chemical molecules in aqueous solution. If the absorbed energy is high enough, then the resultant excited state of the molecule may undergo a structural transformation, which can lead to further reactions and its ultimate degradation. A prerequisite for direct photodegradation to occur is the ability of one or more bonds within a molecule to absorb ultraviolet (UV)/visible light in the 290 to 750 nm range. Light wavelengths longer than 750 nm do not contain sufficient energy to break chemical bonds, and wavelengths below 290 nm are shielded from the earth by the stratospheric ozone layer (Harris, 1982a).

An approach to assessing the potential for a substance to undergo photochemical degradation is to assume that degradation will occur in proportion to the amount of light wavelengths >290 nm absorbed by constituent molecules (Zepp and Cline, 1977).

Ketones do absorb visible light between 300 and 450 nm (Mill T, 2000), therefore, direct photolysis can contribute to the degradation of the C12 ketone fraction in the environment.

Photodegradation – Atmospheric Oxidation

Photodegradation can be measured (U.S. EPA, 1999a) or estimated using an atmospheric oxidation potential (AOP) model accepted by the EPA (U.S. EPA, 1999b). Atmospheric oxidation as a result of hydroxyl radical attack is not direct photochemical degradation, but rather indirect degradation.

The C12 ketone fraction has the potential to volatilize to air, based on a calculated vapor pressure of 0.26 hPa @ 25º C, where it is subject to atmospheric oxidation. In air, C12 ketones can react with photosensitized oxygen in the form of hydroxyl radicals ($^{\bullet}OH$). The computer program AOPWIN (atmospheric oxidation program for Microsoft

Windows) (EPI Suite, 2000) calculates a chemical half-life for a 12-hr day based on an •OH reaction rate constant and a defined •OH concentration (the 12-hr day half-life value normalizes degradation to a standard day light period during which hydroxyl radicals needed for degradation are generated).

The C12 ketone fraction has a calculated half-life in air of 7.3 hours or 0.61 days, based on a representative structure, a rate constant of 1.75E-13 cm^3/molecule*sec and an •OH concentration of 1.5E6 •OH /cm^3.

Stability in Water (Hydrolysis)

Hydrolysis of an organic chemical is the transformation process in which a water molecule or hydroxide ion reacts to form a new carbon-oxygen bond. Chemicals that have a potential to hydrolyze include alkyl halides, amides, carbamates, carboxylic acid esters and lactones, epoxides, phosphate esters, and sulfonic acid esters (Neely, 1985). The lack of a suitable leaving group renders a compound resistant to hydrolysis. The C12 ketone fraction is expected to be resistant to hydrolysis because ketones lack a functional group that is hydrolytically reactive (Harris, 1982b). Therefore, hydrolysis will not contribute to its removal from the environment.

Chemical Distribution in the Environment (Fugacity Modeling)

Fugacity-based multimedia modeling provides basic information on the relative distribution of a chemical between selected environmental compartments. Two widely used fugacity models are the EQC (Equilibrium Criterion) Level I and Level III model (Mackay, 1996; Mackay, 2003).

The input data required to run a Level I model include basic physicochemical parameters; distribution is calculated as the percent of chemical partitioned to six compartments (air, soil, water, suspended sediment, sediment, and biota) within a unit world. Level I data are basic partitioning data that allow for comparisons between chemicals and indicate the compartment(s) to which a chemical may partition, based on the selected physical parameters. The Level III model uses the same physical parameters as the Level I model, but also requires half-life degradation data for the air, soil, water, and sediment compartments, as well as emission parameters for the air, water, and soil compartments. Distribution in the Level III model is calculated as percent of chemical partitioned to 4 compartments (air, water, soil, and sediment) within a unit world. As with Level I data, Level III data are basic partitioning data that allow for comparisons between chemicals and indicate the compartment(s) to which a chemical may partition.

Results of the Mackay Level I environmental distribution model (Table 4) suggest that the C12 ketone fraction will partition primarily to the air (>80%). These results can be largely explained by its vapor pressure, 26.1 Pa at 25°C, one of the physical parameters used by the model. In comparison, the Level III model suggests that the majority of the C12 ketone fraction will partition primarily to the soil (>94) with a small percentage (3.6%) partitioning to the water compartment (Table 5).

Table 4. Environmental Distribution as Calculated by the Mackay (2003) Level I Fugacity Model.

Environmental Compartment	Percent Distribution*
Air	82.6
Water	1.6
Soil	15.5
Sediment	0.3
Suspended Sediment	0.01
Biota	<0.01

* Distribution is based on the following model input parameters for the C12 ketone fraction:

Molecular Weight	184.32
Temperature	25°C
Log K_{ow}	4.04
Water Solubility	18.7 g/m^3
Vapor Pressure	26.1 Pa
Melting Point	-6.7°C

Table 5. Environmental Distribution as Calculated by the Mackay (2003) Level III Fugacity Model

Environmental Compartment	Percent Distribution*
Air	0.3
Water	3.6
Soil	94.2
Sediment	1.9

* Distribution is based on the following model input parameters for the C12 ketone fraction:

Molecular Weight	184.32	Degradation half-lives:	
Temperature	25°C	Air	7.3 hrs
Log K_{ow}	4.04	Water	360 hrs
Water Solubility	18.7 g/m^3	Soil	7200 hrs
Vapor Pressure	26.1 Pa	Sediment	72000 hrs
Melting Point	-6.7°C		

Bioaccumulation Potential

A bioconcentration factor (BCF) of 256.6 (log BCF = 2.4) is calculated for a representative structure of the C12 ketone fraction (CAS No. 68514-41-0) (EPI Suite, 2000) using a log K_{ow} value of 4.04. These data indicate that the C12 ketone fraction has a relatively low BCF and is not expected to bioaccumulate.

IV. C12, BRANCHED KETONES DATA SUMMARY

A search for existing studies/information and their review identified data to characterize the C12 ketone fraction for all HPV endpoints. A dossier containing the robust summaries of the data presented in this test plan is also submitted. Data for the C12 ketone fraction and analog substances are summarized in Table 6.

Table 6. Summary of HPV Endpoints for the C12 Ketone Fraction.

Endpoint	Characterization / Value	Source
Physicochemical		
Melting Point (ºC)	-6.7 (c)	EPI Suite, 2000
Boiling Point (ºC)	220.2 (c)	EPI Suite, 2000
Vapor Pressure (hPa @ 25ºC)	0.261 (c)	EPI Suite, 2000
Water Solubility (mg/L @ 25ºC)	18.7 (c)	EPI Suite, 2000
Log K_{ow} (25ºC)	4.04 (c)	EPI Suite, 2000
Environmental Fate		
Biodegradation	Weeks (c) Not readily biodegradable (a) (<59% in 28 days)	EPI Suite, 2000 ExxonMobil Biomedical Sciences, Inc., 2007a
Direct Photolysis	Direct photolysis can contribute to degradation	Harris, 1982a Mill, 2000 Zepp and Cline, 1977
Indirect Photolysis (half- life; days)	7.3 (c)	EPI Suite, 2000
Hydrolysis	Hydrolysis will not contribute to degradation	Harris, 1982b Neely, 1985
Fugacity - Level I (Distribution to compartment)	Partitions primarily to: air (>82%) (c)	Mackay *et al.*, 1996 Mackay *et al.*, 2003
Fugacity - Level III (Distribution to compartment)	Partitions primarily to: soil (>94%) (c)	Mackay *et al.*, 1996 Mackay *et al.*, 2003

c Calculated for C12, branched ketones (CAS No. 68514-41-0)
a Analog data

Table 6 (Cont'd). Summary of HPV Endpoints for the C12 Ketone Fraction.

Endpoint	Characterization / Value	Source
Aquatic Toxicity		
Freshwater Fish 96-hr LC_{50} (mg/L)	1.7 (c) 1.2 (md)	Cash and Nabholz, 1990 Geiger *et al.*, 1988
Freshwater Fish 30-d ChV* (mg/L)	0.3 (c)	Cash and Nabholz, 1990
Freshwater Invertebrate 48-hr EC_{50} (mg/L)	2.0 (c) 5.2 (mk)	Cash and Nabholz, 1990 ExxonMobil Biomedical Sciences, Inc., 2007b
Freshwater Invertebrate 16-d EC_{50}* (mg/L)	0.3 (c)	Cash and Nabholz, 1990
Freshwater Alga 96-hr EC_{50} (mg/L)	1.4 (c) 16.0 (72-hr ErC_{50}) 8.0 (72-hr EbC_{50}) 3.3 (72-hr NOECr) 0.7 (72-hr NOECb)	Cash and Nabholz, 1990 ExxonMobil Biomedical Sciences, Inc., 2008
Freshwater Alga 96-hr ChV* (mg/L)	0.5 (c)	Cash and Nabholz, 1990

c Calculated for C12, branched ketones (CAS No. 68514-41-0)
md Measured for the analog, 2-dodecanone (CAS No. 6175-49-1)
mk Measured for the analog, C8 ketone fraction (CAS No. 409-02-9)
* Chronic value

Table 6 (Cont'd). Summary of HPV Endpoints for the C12 Ketone Fraction.

Endpoint		Characterization / Value	Source
Mammalian Toxicity			
Acute	Oral	LD_{50} >2000 mg/kg bw (mk) No effect at limit dose	Huntingdon Life Sciences, Ltd., 2008a
Acute	Oral	LD_{50} = 8470 mg/kg bw (mt)	Carpenter, 1948
	Dermal	LD_{50} = 9030 mg/kg bw (mt)	Carpenter, 1948
	Inhalation	Substantially Saturated Vapor, 2/6 rats died (8 hr) (mt)	Carpenter, 1948
Irritation	Skin	Mild Irritant (mt)	Smyth *et al*., 1951
	Eye	Mild Irritant (mt)	Smyth *et al*., 1954
Mutagenicity		Bacterial Reverse Mutation Negative Chromosome Aberration Negative	Huntingdon Life Sciences, Ltd., 2008b Huntingdon Life Sciences, Ltd., 2008c
Combined Repeated Dose Toxicity Study with Reproductive/ Developmental Toxicity Screening		100, 300, 500 mg/kg/day was associated with effects on parental bodyweight and marginally low food consumption. Males at 500 mg/kg/day showed a high incidence of weak tail pinch response sensory reactivity. Motor activity (cage floor exploring, but not rearing activity) diminished in males compared to controls. There were adaptive changes in liver morphology and rat specific changes in thyroid and kidney pathology. Parental Toxicity NOAEL = 100 mg/kg/day based on bodyweight and food consumption decreases. Reproductive NOAEL = 500 mg/kg/day based on reproductive function and fertility.	Huntingdon Life Sciences, Ltd., 2009

mt Measured for the analog, trimethyl 4-nonanone (CAS No. 123-18-2)
mk Measured for the analog, C8 ketone fraction (CAS No. 409-02-9)
* Chronic value

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