201-15213A

High Production Volume (HPV) Challenge Program

Di-tertiary (C9-C12) Alkyl Polysulfides Category

Test Plan

CAS Numbers:

68425-16-1

68583-56-2

31565-23-8

68425-15-0

Chevron Phillips Chemical Company LP
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EXECUTIVE SUMMARY

Chevron Phillips Chemical Company LP (CPChem) and ATOFINA Chemicals, Inc. (ATOFINA) have jointly volunteered under the Polysulfides Scientific Research Program to assess the health and environmental hazards, including selected physicochemical characteristics, of the Di-Tertiary (C9-C12) Alkyl Polysulfides Category (referred to hereafter as the Category). The Di-Tertiary (C9-C12) Alkyl Polysulfides Category Test Plan is being submitted to fulfill the United States Environmental Protection Agency (USEPA) High Production Volume (HPV) Challenge Program commitment for di-tertiary nonyl polysulfide (CASN 68425-16-1). Other substances in this Category include the Organisation of Economic Cooperation and Development (OECD) listed HPV substance, di-tertiary dodecyl pentasulfide (CASN 31565-23-8) and di-tertiary dodecyl polysulfides (CASN 68583-56-2 and 68425-15-0). All members of this Category exist as a range of mixtures of isomers that are characterized by a common core polysulfide chain that can range from 2 to 8 sulfur atoms in length. These polysulfide chains are terminated with increasingly hydrophobic branched alkyl groups that contain a total of 9 or 12 carbon atoms on each end.

Data from company proprietary files, peer-reviewed literature, and/or calculated endpoints using widely accepted computer modeling programs have been identified for purposes of this program. The summary of available data for the Di-tertiary (C9-C12) Alkyl Polysulfides Category members presents evidence that the members of this Category have similar physical/chemical, environmental, and toxicological properties, and that they follow predictable patterns based upon their chemical composition. Importantly, the Category members are extremely hydrophobic and sorptive, and have very low water solubility and vapor pressure, both of which decrease with increasing carbon number in the tertiary alkyl groups. The hydrophobicity and low water solubility lead to very high predicted Log Kows (>9). These materials will be highly sorptive and tend to form complexes with organic substances in environmental matrices. They are unlikely to be in solution in the environment as free solutes, and therefore have low bioavailability and low predicted bioconcentration factors. They are also of relatively low toxicity to aquatic organisms and mammals.

Limited physiochemical data are available for members of this category, therefore it is proposed to conduct Melting Point (OECD 102), Boiling Point (OECD 103), Vapor Pressure (OECD 104), Partition Coefficient (OECD 117 or 107), and Water Solubility (OECD 105) testing for di-tertiary nonyl polysulfide.

A review of the existing data for the Category shows that sufficient data are available to characterize environmental fate and aquatic toxicity. Environmental fate data for the Category chemicals show that these substances are expected to be stable and resistant to biotic and abiotic degradation mechanisms in the environment, are extremely hydrophobic and sorptive, and have very low water solubility and bioavailability. Ultimately, they will not bioaccumulate, and will partition into soil and sediment compartments when released in the environment. Additionally, acute fish, daphnid, and algal growth inhibition studies were conducted on this Category and no toxicity was observed at the solubility limit.

The considerable existing mammalian toxicity information for the Category demonstrates that these substances share a similar order of toxicity. Mammalian acute toxicity data demonstrates a low order of toxicity via oral, dermal, and inhalation routes of exposure. Genotoxicity data exist for Category members and indicate that genotoxicity is not expected. Repeated dose toxicity testing on di-tertiary-dodecyl pentasulfide (28 day) showed a NOAEL of 250 mg/kg bw and a LOAEL of 1000 mg/kg bw in rats and no further repeated dose toxicity testing is required. No Reproductive Toxicity data were available for any of the Category members. A Developmental Toxicity study

was completed for di-tertiary dodecyl pentasulfide in Sprague-Dawley rats. Both the maternal and teratogen NOAEL were determined to be 1000 mg/kg bw and no clinical signs, unscheduled deaths, abortions, or total resorptions were observed in any group. Likewise, no treatment-related external anomalies or malformations; soft tissue malformations or anomalies; or skeletal malformations, anomalies or variations were observed in any group.

The majority of HPV endpoints have been satisfied for the USEPA HPV Challenge Program. Testing is proposed for the following endpoints for di-tertiary nonyl polysulfide:

- Melting Point
- Boiling Point
- Vapor Pressure
- Partition Coefficient
- Water Solubility
- Reproductive Toxicity (90-day Subchronic with reproductive endpoints)

In addition, there were insufficient data to fulfill the Reproductive Toxicity endpoint and therefore, testing is proposed. According to the annex VII of the proposal (dated 29.10.2003) for a regulation of the European parliament and of the council concerning the Registration, Evaluation, Authorisation and Restrictions of chemicals (REACH), an additional standard information requirement for substances manufactured or imported in quantities of 100 tonnes or more should be a sub-chronic toxicity study (90-day) (Commission of the European Communities [EC], 2003). In order to meet future ICCA and REACH testing requirements and to eliminate unnecessary and/or duplicate testing, the Polysulfides Scientific Research Program proposes to perform a Sub-chronic Oral Toxicity – Rodent 90-day Study (OECD 408) with a focus on reproductive endpoints. This study, in combination with the existing Developmental Toxicity study, will fulfill the Reproductive Toxicity endpoint. Current EPA and OECD guidance states that "When a 90-day repeated dose study is available and is sufficiently documented with respect to studying effects on the reproductive organs, and a developmental study is available, the requirements for the reproductive toxicity endpoints are satisfied" (USEPA, 1998; OECD 2002). Di-tertiary nonyl polysulfide is recommended for this test because of its lower molecular weight (and is therefore incrementally less hydrophobic) and represents a potentially more bioavailable fraction of the Di-tertiary (C9-C12) Alkyl Polysulfides Category.

The following table summarizes the available data for the Di-tertiary (C9-C12) Alkyl Polysulfides:

Matrix of Available and Adequate Data on Di-tertiary (C9-C12) Alkyl polysulfides Category

"SIDS ENDPOINT"	di-tertiary nonyl polysulfide US HPV SUBSTANCE Y/N	di-tertiary dodecyl polysulfide & di-tertiary dodecyl pentasulfide Y/N	Testing Planned? Y/N
Physical and Chemical Data			
Melting Point	N	Y	Y (nonyl)
Boiling Point	N	Y	Y (nonyl)
Vapor Pressure	N	Y	Y (nonyl)
Partition Coefficient	N	Y	Y (nonyl)
Water Solubility	N	Y	Y (nonyl)

Environmental Fate and Pathways			
Photodegradation	Y	Y	N
Stability in Water (Hydrolysis)	NA	NA	NA
Transport/Distribution	Y	Y	N
Biodegradation	Y	Y	N
Ecotoxicity			
Acute/Prolonged Toxicity to Fish	Y	N	N
Acute Toxicity to Aquatic Invertebrates (*Daphnia*)	N	Y	N
Acute Toxicity to Aquatic Plants (Algae)	N	Y	N
Toxicity			
Acute Toxicity (Oral)	Y	Y	N
Acute Toxicity (Dermal)	N	Y	N
Acute Toxicity (Inhalation)	Y	N	N
Repeated Dose	N	Y	N
GeneticToxicity *in vitro* – Gene Mutation	Y	Y	N
Genetic Toxicity *in vitro* – Chromosomal Aberration	Y	Y	N
Reproductive Toxicity	N	N	Y (nonyl)
Developmental Toxicity	N	Y	N

NA = not applicable

Note: **The data used to characterize the OECD SIDS endpoints for substances in this Test Plan were identified either in company proprietary files, peer-reviewed literature, and/or calculated using widely accepted computer modelling programs. All data were evaluated for study reliability in accordance with criteria outlined by the USEPA (1999a). Only studies that met the reliability criteria of "1" (reliable without restrictions) or "2" (reliable with restrictions) were used to fulfil OECD SIDS endpoints. Additional data for substances in this Category are also included in the IUCLID (International Uniform Chemical Information Dataset) attached in Annexes I and II. A more detailed discussion of the data quality and reliability assessment process used to develop this test plan is provided in Annex III.**

CONTENTS

Tables

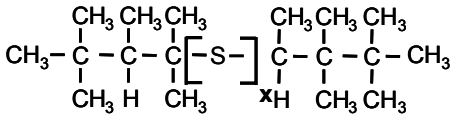
1 IDENTITY

1.1 Identification of the Substance

The Di-tertiary (C9-C12) Alkyl Polysulfides Category consists of the United States Environmental Protection Agency (USEPA) High Production Volume (HPV) listed substance, di-tertiary nonyl polysulfide (CAS # 68425-16-1); the Organisation of Economic Cooperation and Development (OECD) HPV listed substance, di-tertiary dodecyl pentasulfide (CAS Number 31565-23-8); and di-tertiary dodecyl polysulfides (CAS Number 68583-56-2 and 68425-15-0). Due to their close structural similarity, these compounds comprise the proposed Di-tertiary (C9-C12) Alkyl Polysulfides Category for the purpose of meeting the requirements of the US HPV Challenge Program and the International Council of Chemical Associations (ICCA) HPV Initiative.

In general, these dialkyl polysulfides exist as complex mixtures of isomers with varying distributions of alkyl chain length and tertiary branching, and sulfur atom chain length. All members of this Category exist as a range of mixtures of isomers that are characterized by a common core polysulfide chain that can range from 2 to 8 sulfur atoms in length. These polysulfide chains are terminated with increasingly hydrophobic branched alkyl groups that contain a total of 9 or 12 carbon atoms on each end.

1.1.1 Di-Tertiary-Nonyl Polysulfide

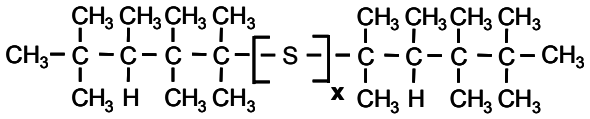
CAS Number:	68425-16-1
EINECS Number	270-336-2
IUPAC Name:	
EINECS Substance Name:	Polysulfides, di-tert-nonyl
Molecular Formula:	$C_{18}H_{38}S_X$
Structural Formula:	
	Where **x** = 2-5, predominantly 3
Molecular Weight:	~ 350
Synonyms:	TPS 37; TNPS; t-Nonyl polysulfide; tertiary-Nonyl polysulfide

1.1.2 Di-Tertiary-Dodecyl Polysulfide

CAS Number:	68583-56-2 / 68425-15-0
EINECS Number	271-518-4 / 270-335-7
IUPAC Name:	
EINECS Substance Name:	Tert-Dodecanethiol, sulfurized / Polysulfides, di-tert-dodecyl

Molecular Formula: $C_{24}H_{50}S_X$

Structural Formula:

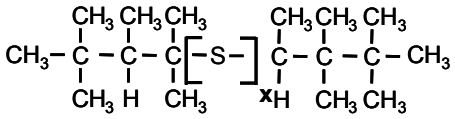


Where **x** = 2-8, predominantly 3-5

Molecular Weight: ~ 498
Synonyms: TDPS 320; t-Dodecyl polysulfide; tertiary-Dodecyl polysulfide; Di-t-dodecyl polysulfide; t-Dodecyl mercaptan, sulfurized; Di-tertiary dodecyl polysulfide (3S); tert-Dodecanethiol, sulfurized

1.1.3 Di-Tertiary Dodecyl Pentasulfide

CAS Number: 31565-23-8
EINECS Number 250-702-8
IUPAC Name:
EINECS Substance Name: Di(tert-dodecyl) pentasulphide
Molecular Formula: $C_{24}H_{50}S_X$
Structural Formula:



Where **x** = 5

Molecular Weight: ~ 498
Synonyms:

1.2 Purity/Impurities/Additives

1.2.1 Di-Tertiary-Nonyl Polysulfide

Purity: 100%
Main impurities**:** none

1.2.2 Di-Tertiary-Dodecyl Polysulfide and Di-Tertiary Dodecyl Pentasulfide

Purity: 100%
Main impurities**:** none

1.3 Physico-Chemical properties

Physico-chemical data for the Category chemicals were either tested or estimated using EPIWIN© (USEPA, 2000) and are provided in the following table.

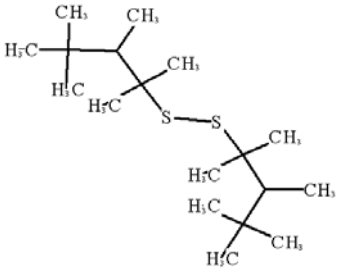
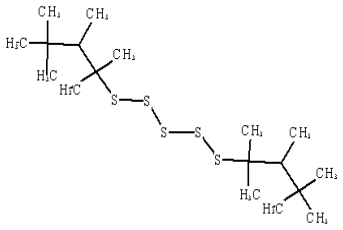
Table 1. Summary of Physical and Chemical Properties (Measured [M] and Calculated [C])

Test	M/C	di-tertiary nonyl polysulfide	M/C	di-tertiary dodecyl pentasulfide
Physical state	-	yellow to yellow-orange liquid		yellow to yellow-orange liquid
Odor	-	Mildly unpleasant		mildly unpleasant
Melting Point	-	ND	M[1]	< 0 °C
	C[2]	96.70 °C	C[2]	178.66 °C
Boiling Point	-	ND	M[1]	> 200 ºC at 1013 hPa
	C[2]	350.6 ºC	C[2]	463.57 ºC
Relative Density		ND		ND
Vapor Pressure	-	ND	M[1]	<0.03 hPa at 20 ºC
	C[2]	3.43 x10^{-5} hPa at 25 ºC	C[2]	7.6 x10^{-9} hPa at 25 ºC
Water Solubility	-	ND	M[1]	Not soluble
	C[3]	9.612 x10^{-5} mg/L	C[3]	5.368 x10^{-8} mg/L
Partition coefficient n-octanol/water (log value)	-	ND	C[4]	> 5
	C[5]	9.14	C[5]	11.86
Henry's Law Constant	C[6]	0.174 atm-m^3/mol at 25°C	C[6]	2.27 atm-m^3/mol at 25°C
Organic Carbon/Water Partition Coefficient (Log Koc)	C[7]	2.8 x 10^5	C[7]	1.9 x 10^7
Flammability	M[8]	Slight flammability Flash point 145°C (PMCC, ASTM D93)	M[8]	Slight flammability Flash point 132°C (PMCC, ASTM D93)

[1] Source: Atofina, 2003
[2] EPIWIN v3.10; calculated using MPBPWIN v1.40 (determined at 760 mmHg)
[3] EPIWIN v3.10; calculated using WSKOW v1.40
[4] Source: Atofina, 2003
[5] EPIWIN v3.10; calculated using KOWWIN v1.66
[6] EPIWIN v3.10; calculated using HENRYWIN v3.10
[7] EPIWIN v3.10; calculated using PCKOC v1.66
[8] Source: CPChem MSDS
ND = No Data Available

For additional perspective, Table 1a provides EPIWIN data developed for representative polysulfide structures containing 2 and 5 sulfurs.

Table 1a. EPIWIN Physicochemical Data for Representative Structures

Physical and Chemical Data		
Parameter	 (C_{18} H_{38} S_2)	 (C_{18} H_{38} S_5)
Melting Point	69.03 ºC [1]	143.65 ºC[1]
Boiling Point	314.76 ºC [1]	417.14 ºC[1]
Vapor Pressure	0.000342 mmHg at 25 ºC [1]	2 x 10^{-7} mmHg at 25 ºC [1]
Kow Partition Coefficient	9.14 [2]	9.14 [2]
Water Solubility	1.495 x 10^{-4} mg/L at 25 ºC [2]	3.881 x 10^{-5} mg/L at 25 ºC [2]

[1]EPIWIN v3.10; MPBPWIN v1.40.
[2]EPIWIN v3.10; calculated using WSKOW v1.40.

Conclusion

Limited physiochemical data are available for members of the Category and the Polysulfides Scientific Research Program therefore proposes to complete the following testing for di-tertiary nonyl polysulfide:

- Melting Point (OECD Guideline 102, "Melting Point/Melting Range")
- Boiling Point (OECD Guideline 103, "Boiling Point")
- Vapor Pressure (OECD Guideline 104, "Vapour Pressure")
- Partition Coefficient – (OECD Guideline 117 "Partition Coefficient (n-octanol/water), High Performance Liquid Chromatography (HPLC) Method" – Note: In general, calculated values greater than 6 are recognized to not be reliable and therefore, testing is required following either OECD Guideline 107 or 117. According to OECD guidelines, a high log Kow cannot be correctly determined using the OECD 107 (shake flask method). As a result, the OECD guideline 117 (HPLC method) is indicated. However, due to the expected low solution concentrations and the test material not being UV active, a non-specific HPLC method such as HPLC/UV or HPLC/Refractive Index, may not be possible, rather, HPLC with Radiochemical detection or HPLC/Mass Spectrometry detection may be recommended depending on sample availability and the results of preliminary studies.
- Water Solubility (OECD Guideline 105, "Water Solubility")

1.4 Category Justification

A chemical category is defined as a group of chemicals whose physicochemical and toxicological properties are likely to be similar to or follow a regular pattern as a result of structural similarity (USEPA, 1999a). The Polysulfides Scientific Research Program has evaluated the dialkyl polysulfides in this Test Plan with this guidance in mind, and has opted to form the Di-tertiary (C9-C12) Alkyl Polysulfides Category.

Common Dialkyl Polysulfide Structures and Functional Groups

In general, these dialkyl polysulfides exist as complex mixtures of isomers with varying distributions of alkyl chain length and tertiary branching, and sulfur atom chain length. All members of this Category exist as a range of mixtures of isomers that are characterized by a common core polysulfide chain that can range from 2 to 8 sulfur atoms in length. These polysulfide chains are terminated with increasingly hydrophobic branched alkyl groups that contain a total of 9 or 12 carbon atoms on each end.

GENERAL ALKYL POLYSULFIDE STRUCTURE $R—S_x—R'$	• Sulfur atom chains form the core of the molecule and range from 2 to 8 sulfurs in length. • R = highly methyl branched alkyl groups containing 9 or 12 carbons each and which terminate at the core sulfur atom chains

Similar or Even Identical Properties or Hazards

The summary of available data for the Di-tertiary (C9-C12) Alkyl Polysulfides Category members presents evidence that the members of this Category have similar physical/chemical, environmental, and toxicological properties, and that they follow predictable patterns based upon their chemical composition. Importantly, the Category members are extremely hydrophobic and sorptive, and have very low water solubility and vapor pressure, both of which decrease with increasing carbon number in the tertiary alkyl groups. The hydrophobicity and low water solubility lead to very high predicted Log Kows (>9). These materials will be highly sorptive and tend to form complexes with organic substances in environmental matrices. They are unlikely to be in solution in the environment as free solutes, and therefore have low bioavailability and low predicted bioconcentration factors. They are also of relatively low toxicity to aquatic organisms and mammals.

GENERAL INFORMATION ON EXPOSURE

1.5 Production Volumes and Use Pattern

1.5.1 Manufacturers:

- Chevron Phillips Chemical Company LP (CPChem)
- ATOFINA Chemicals, Inc.

1.5.2 Use Pattern:

The principal uses of polysulfides are as reagents for catalyst sulfidation in metalworking and metal processing industries. These sulphide reagents improve initial catalyst activity and lengthen production cycles for nickel, molybdenum, cobalt, and tungsten hydrotreating catalysts.

Polysulfides are also commonly used in the metal working, steel rolling, and wire drawing industries in the formulation of lubricant additives to improve equipment functionality at extreme pressures. The sulphur reacts with the metal under extreme heat and pressure to form a metal sulphide layer that allows for slippage and movement and reduces friction and damage to metal equipment.

Tert-nonyl polysulfide and tert-dodecyl polysulfide are used in general metalworking applications. Tert-dodecyl polysulfide is also used in steel rolling oils and non-ferrous metalworking applications. Tert-butyl polysulfide can be used as a replacement for sulfurized isobutylene for gear oil lubricants.

1.6 Environmental Exposure and Fate

The weight of evidence indicates that no further environmental fate testing is necessary to meet HPV SIDS endpoints for the Di-tertiary (C9-C12) Alkyl Polysulfides Category. Environmental fate data for the Category chemicals were either tested or estimated using EPIWIN and are provided in the following sections. Overall, these substances are expected to be stable and resistant to biotic and abiotic degradation mechanisms in the environment, are extremely hydrophobic and sorptive, and have very low water solubility and bioavailability. Ultimately they will not bioaccumulate, and will partition into soil and sediment compartments when released to the environment.

1.6.1 Sources of Environmental Exposure

1.6.2 Photodegradation

Values for atmospheric oxidation were calculated based upon the representative chemical structures for this Category using EPIWIN. No reaction with ozone could be estimated due to lack of suitable labile functional groups. These results demonstrate that substances in this Category are similar in estimated atmospheric stability or reactivity.

Table 2. Photodegradation and Atmospheric Oxidation Data.

Test	di-tertiary nonyl polysulfide	di-tertiary dodecyl pentasulfide
OH Half-Life	0.023 Days	0.016 Days
OH Rate Constant	473 $x10^{-12}$ cm^3/molecule-sec	683 $x10^{-12}$ cm^3/molecule-sec

Source: EPIWIN v3.10; calculated using AOP Program v1.90

1.6.3 Stability in Water

EPIWIN was unable to calculate a hydrolysis rate for any of the polysulfides (di-tertiary dodecyl or di-tertiary nonyl) due to the absence of functional groups that are labile to hydrolysis. Given the very low water solubility of these materials and the lack of a functional group to hydrolyze, further testing for hydrolytic stability is not warranted.

1.6.4 Transport between Environmental Compartments

Fugacity modeling for the Category and representative di-tertiary nonyl polysulfide structures (S2 and S5) members using EPIWIN (v3.10) produced the following results for di-tertiary-nonyl polysulfide:

Table 3. Fugacity Results for Di-tertiary Nonyl Polysulfide

Compartment	100% to air	100% to water	100% to soil	Equally to each compartment
Air	75%	0.0%	0.0%	0.00474%
Water	0.0745%	1.87%	0.0021%	1.28%
Soil	21%	0.0%	99.9%	31.6%
Sediment	3.91%	98.1%	0.11%	67.1%

for di-tertiary-dodecyl pentasulfide:

Table 4. Fugacity Results for Di-tertiary Dodecyl Polysulfide

Compartment	100% to air	100% to water	100% to soil	Equally to each compartment
Air	4.35%	0.0%	0.0%	0.00323%
Water	0.346%	1.87%	0.0021%	1.27%
Soil	77.1%	0.0%	99.9%	31.9%
Sediment	18.2%	98.1%	0.11%	66.9%

Results are similar and show ultimate partitioning to soil and sediments where these substances will likely be tightly bound to organic phases and unavailable to exert toxicity. Predictably, there is a difference for releases directly to air, where the lower molecular weight di-tertiary nonyl polysulfide Category member is predicted to be slower to partition from the air into the soil compartment. Overall, these data are of adequate quality, and no further fugacity modeling is warranted for this Category.

1.6.5 Biodegradation

The members of this Category have both been tested in European Economic Community/Organisation for Economic Co-operation and Development (EEC/OECD) Ready Biodegradation tests (OECD 301D – Closed Bottle Test) that show no biodegradation for either di-tertiary nonyl polysulfide or di-tertiary dodecyl pentasulfide. These experiments are consistent with EPIWIN, where this Category is predicted not to quickly biodegrade. This is to be expected, given the highly branched nature of the carbon chains. These data are considered valid without restriction, and further Ready Biodegradability testing will not add additional value for this Category.

Table 5. Biodegradation Data.

Test	di-tertiary nonyl polysulfide	di-tertiary dodecyl pentasulfide
Biodegradation	0 in 28 days (non-biodegradable)	0 in 28 days (non-biodegradable)

Source: Atofina, 2003.

1.6.6 Bioaccumulation

The predicted bioconcentration factor (BCF) is low for this Category, suggesting no bioaccumulation hazard. There are 18 to 24 carbon atoms per molecule in the representative molecules used in the modeling of this Category in EPIWIN. The predicted Log Kows for this Category are, therefore, very high, reflecting the very low water solubility and high hydrophobicity of these materials. The predicted organic carbon partition coefficient shows that these materials will be highly sorptive. This also translates into a low predicted fish BCF since these materials will not be bioavailable in the environment due to the combination of low water solubility and tendency to adsorb to surfaces and other hydrophobic constituents in the environment.

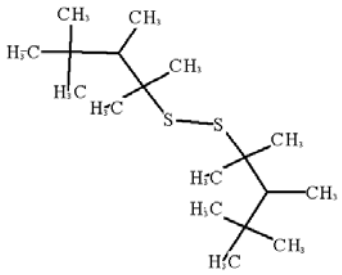
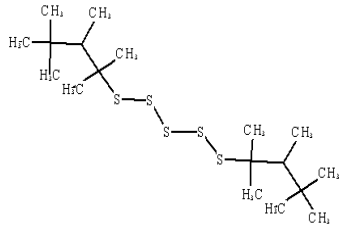
Table 6. Bioaccumulation Data

Test	di-tertiary nonyl polysulfide	di-tertiary dodecyl pentasulfide
Estimated BCF	75.66	3.162

Source: EPIWIN v3.10; calculated using BCF Program v2.14.

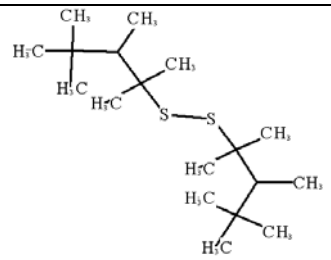
For additional perspective, two additional polysulfides, one containing 2 sulfurs and one containing 5 sulfurs, were run in EPIWIN and the following environmental fate and pathways data were obtained:

Table 6a. Related Structures EPIWIN Environmental Fate and Pathways Data

Environmental Fate and Pathways		
Parameter	 (C_{18} H_{38} S_2)	 (C_{18} H_{38} S_5)
Photodegradation & Atmos. Oxidation: • OH Rate Constant • OH Half Life	232.8774 x 10^{-12} cm^3/molecule-sec[1] 0.551 Hrs[1]	682.8774 x 10^{-12} cm^3/molecule-sec[1] 11.277 Min[1]
Transport/ Distribution Fugacity Estimated Koc: Estimated BCF:	 See Table 6b. 1.418 x 10^5 [(2)] 75.66[3]	 See Table 6b. 8.9 x 10^5 [(2)] 75.66[3]

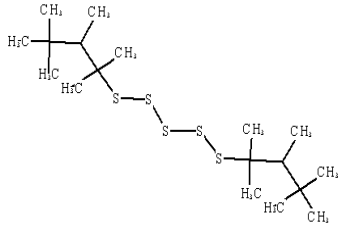
[1]EPIWIN v3.10; calculated using AOP Program v1.90.
[2]EPIWIN v3.10; calculated using PCKOC Program v1.66.
[3]EPIWIN v3.10; calculated using BCF Program v2.14.

Table 6b. EPIWIN Level III Fugacity Results for Representative Structures



(C_{18} H_{38} S_2)

Compartment	100% to air	100% to water	100% to soil	Equally to each compartment
Air	85.7%	0.00%	0.00%	0.00955%
Water	0.0388%	1.87%	0.0021%	1.28%
Soil	12.2%	0.00%	99.9%	31.6%
Sediment	2.03%	98.1%	0.11%	67.1%



(C_{18} H_{38} S_5)

Compartment	100% to air	100% to water	100% to soil	Equally to each compartment
Air	22.0%	0.00%	0.00%	0.00328%
Water	0.277%	1.87%	0.0021%	1.28%
Soil	63.2%	0.00%	99.9%	31.7%
Sediment	14.5%	98.1%	0.11%	67.0%

2 HUMAN HEALTH HAZARDS

2.1 Effects on Human Health

2.1.1 Acute Toxicity

Acute toxicity studies via oral, dermal, and inhalation routes for this Category have been conducted according to relevant OECD/EEC guidelines or methods comparable to those guidelines.

Studies in Animals

Inhalation

An acute study using di-tertiary-nonyl polysulfide was performed on Sprague-Dawley rats using methods comparable to OECD Guideline 403. This study featured exposure to a nominal

concentration of 15.5 mg/l (g/m^3) di-tertiary-nonyl polysulfide and fulfills the requirements for a critical study for this SIDS endpoint. Adequate data are available for this endpoint, and no additional testing is proposed (see Table 7 and IUCLID documents).

Table 7. Acute Toxicity – Results of Inhalation Studies in Animals

Test	di-tertiary nonyl polysulfide	di-tertiary dodecyl pentasulfide
Acute Inhalation	LC_{50} = >15.5 mg/L	No Data Available

Source: Atofina, 2003.

Dermal

Acute dermal toxicity of di-tertiary dodecyl pentasulfide was evaluated in a GLP study performed using Sprague-Dawley rats according to OECD Guideline 402 (Acute Dermal Toxicity). Fourteen days following administration of the test substance there was no evidence of lesion (erythema or oedema), mortality, or behavioral anomaly. This study fulfills the requirements for a critical study for this SIDS endpoint and no additional testing is proposed (see Table 8 and IUCLID documents).

Table 8. Acute Toxicity – Results of Dermal Studies in Animals

Test	di-tertiary nonyl polysulfide	di-tertiary dodecyl pentasulfide
Acute Dermal	No Data Available	$LD_0 \geq$ 2000 mg/kg bw

Source: Atofina, 2003.

Oral

Valid acute oral toxicity studies have been performed for this Category, which show mortality at high doses. These studies fulfill the requirements for a critical study for this SIDS endpoint and no additional testing is proposed (see Table 9 and IUCLID documents).

Table 9. Acute Toxicity – Results of Oral Studies in Animals

Test	di-tertiary nonyl polysulfide	di-tertiary dodecyl pentasulfide
Acute Oral	LD_{50} = 17781 – 21495 mg/kg bw	LD_0 = 12625 mg/kg bw

Source: Atofina, 2003.

Other Routes of Exposure

An acute study using di-tertiary-nonyl polysulfide was performed on Sprague-Dawley rats via intraperitoneal (i.p.) exposure. This study featured exposure to 3350 – 4375 mg/kg body weight di-tertiary-nonyl polysulfide and measurement of behavioral endpoints. Adequate data are available for this endpoint, and no additional testing is proposed (see Table 10 and IUCLID documents).

Table 10. Acute Toxicity – Results of Other Studies in Animals

Test	di-tertiary nonyl polysulfide	di-tertiary dodecyl pentasulfide
Acute Toxicity (i.p.)	LD_{50} = 3350 – 4375 mg/kg bw	No Data Available

Source: Atofina, 2003.

Conclusion

The collective data for the Di-tertiary (C9-C12) Alkyl Polysulfides Category fulfill the requirements for the acute toxicity endpoints. As a result, no additional testing is proposed for purposes of the HPV program (see Tables 7 to 10 and IUCLID documents).

2.1.2 Irritation

Skin Irritation

Studies in Animals

Several valid irritation studies have been performed for the Polysulfides in this Category, all of which show polysulfides to be mild to non-irritants (see Table 11 and IUCLID documents).

Table 11. Irritation – Results of Skin Irritation Studies in Animals

Test	di-tertiary-nonyl polysulfide	di-tertiary dodecyl pentasulfide
Skin Irritation	Slightly Irritating	Slightly irritating

Source: Atofina, 2003.

- Di-tertiary nonyl polysulfide – In a rabbit skin irritation test (undiluted, 24 hours, occlusive), the Primary Dermal Irritation Index (PDII) was 1.88. Di-tertiary nonyl polysulfide was slightly irritating.
- Di-tertiary dodecyl pentasulfide – In a rabbit skin irritation test following OECD Guideline 404, (undiluted, 4 hours, semiocclusive), di-tertiary dodecyl pentasulfide produced a slight erythema in one rabbit and a moderate erythema in 5 rabbits. A slight edema was observed in 3 rabbits. The mean score (24 + 48 + 72 h) for erythema was 1.72 and for edema was 0.39 and di-tertiary dodecyl pentasulfide was slightly irritating.

Eye Irritation

Studies in Animals

Several valid irritation studies have been performed for the Polysulfides Category, all of which show polysulfides to be non-irritants (see Table 12 and IUCLID documents).

Table 12. Irritation – Results of Eye Irritation Studies in Animals

Test	di-tertiary-nonyl polysulfide	di-tertiary dodecyl pentasulfide
Eye Irritation	Slightly irritating	Slightly irritating

Source: Atofina, 2003.

- Di-tertiary nonyl polysulfide – In a rabbit eye irritation test (undiluted, 24 hours, not rinsed), di-tertiary nonyl polysulfide was slightly irritating.
- Di-tertiary dodecyl pentasulfide – In a rabbit eye irritation test following OECD Guideline 405, (undiluted, 24 hours, not rinsed), di-tertiary dodecyl pentasulfide induced a slight chemosis and/or enanthema which persisted for up to 72 hours in 2 animals. Slight iridal congestion was observed up to 48 hours in some animals. The mean score (24 + 48 + 72 h) for chemosis was 0.89; for enanthema was 0.61; for iris was 0.33; and for cornea was 0.00. Di-tertiary dodecyl pentasulfide was slightly irritating.

Conclusion

Several valid skin and eye irritation studies have been performed for the Di-tertiary (C9-C12) Alkyl Polysulfides Category, all of which show polysulfides to be mild to non-irritants. (see Tables 11 and 12 and IUCLID documents).

2.1.3 Sensitisation

Studies in Animals

Skin

Several valid sensitisation studies have been performed for the Polysulfides Category. Data for di-tertiary nonyl polysulfide and di-tertiary dodecyl pentasulfide show ambiguous results, with both positive and negative results being reported. (see Table 13 and IUCLID documents).

Table 13. Sensitisation – Results of Skin Sensitisation Studies in Animals

Test	di-tertiary-nonyl polysulfide	di-tertiary dodecyl pentasulfide
Sensitization	1. Not sensitizing (Guinea pig maximization)	Not sensitizing (ambiguous results)

Source: Atofina, 2003.

- Di-tertiary nonyl polysulfide
    - In a Guinea Pig Maximization test following Directive 96/54/EC, B.6, no cutaneous reactions were observed after the challenge application. According to the maximization method of Magnusson and Kligman, di-tertiary nonyl polysulfide did not induce delayed contact hypersensitivity in guinea pigs.

- Di-tertiary dodecyl pentasulfide – In a Guinea Pig Maximization test following OECD Guideline 406, di-tertiary dodecyl pentasulfide was classified as "not sensitising." However, from the macroscopic and histological results obtained under the experimental conditions, it was concluded that the test article had provoked an aspecific reaction of irritation of weak intensity in 4 out of the 20 treated guinea-pigs. This phenomenon can hide possible weak reactions of cutaneous sensitisation.

Conclusion

Several valid sensitisation studies have been performed for the Di-tertiary (C9-C12) Alkyl Polysulfides Category (see Table 13 and IUCLID documents).

2.1.4 Repeated Dose Toxicity

Studies in Animals

Oral

For this Category, a GLP 28-day subchronic repeated dose study was performed on rats according to EEC guidelines using di-tertiary-dodecyl pentasulfide. This study featured gavage dosing, measurement of mortality, body weight changes, food consumption, hematological and blood biochemical examinations, urinalysis, and organ weights and fulfills the USEPA HPV requirements for this SIDS endpoint. Results from this study showed no deaths related to the treatment during the treatment period or the recovery period. Ptyalism was observed in all the animals of both sexes given 1000 mg/kg/day during the treatment period. During the recovery period no clinical signs were observed. No abnormalities of toxicological importance were noted among hematological and blood biochemical parameters, urinalysis, organ weights, or macro- and microscopic examinations.

An 8-day repeated dose study with rats gavaged with di-tertiary-dodecyl pentasulfide was also completed. No mortality occurred during the treatment period and ptyalism was observed in all the males given 1250 or 2500 mg/kg/day and in 2/4 or 3/4 females given 1250 or 2500 mg/kg/day, respectively. . A slightly lower mean food consumption and body weight gain was observed in the males given 2500 mg/kg/day. A thickened and/or translucent wall of the forestomach was noted for 3/4 females given 2500 mg/kg/day. This study reported NOAEL and LOAEL values similar to those of the longer subchronic repeated dose study and further supports the results of that study.

Table 14. Repeated Dose Toxicity – Results of Oral Studies in Animals

Test	di-tertiary nonyl polysulfide	di-tertiary dodecyl pentasulfide
Repeated Dose (28 Day and 8 Day)	No Data Available	1. 28-Day Rat Oral Gavage Study: No Observed Adverse Effect Levels (NOAEL) =1000 mg/kg bw
		2. 8 Day Rat Oral Gavage Study: NOAEL =1250 mg/kg bw (based on a lower body weight gain in males at 2500 mg/kg) LOAEL = 2500 mg/kg bw

Source: Atofina, 2003.

Conclusion

Adequate data are available for the Di-tertiary (C9-C12) Alkyl Polysulfides Category for this endpoint, and no additional testing is proposed for purposes of the HPV program (see Table 14 and IUCLID documents).

2.1.5 Mutagenicity

Studies in Animals

In vitro Studies

Several valid *in vitro* genetic toxicity/mutagenicity studies have been performed for the Polysulfides Category, all which show no mutagenic activity.

Table 15. Mutagenicity – Results of *In vitro* Studies in Animals

Test	di-tertiary nonyl polysulfide	di-tertiary dodecyl pentasulfide
Genetic – Gene Mutation	Negative with and without activation	Negative with and without activation
Genetic – Chromosomal Aberration	Negative with and without activation	Negative with and without activation

Source: Atofina, 2003.

Conclusion

Adequate data are available for the Di-tertiary (C9-C12) Alkyl Polysulfides Category for this endpoint which indicate that these materials are not mutagenic. No additional testing is proposed for purposes of the HPV program (see Table 15 and IUCLID documents).

2.1.6 Toxicity for Reproduction

No reproduction toxicity data were available for any of the Category members. Therefore, testing to fulfill the Reproductive Toxicity endpoint is proposed.

The Subchronic Oral Toxicity – Rodent 90-day Study (OECD 408) with a focus on reproductive endpoints is proposed, which in combination with the Developmental Toxicity study will fulfill the Reproductive Toxicity endpoint. Current EPA and OECD guidance states that "When a 90-day repeated dose study is available and demonstrates no effect on reproductive organs, in particular the testes, then a developmental study (e.g. OECD Test guidelines 414) can be considered as an adequate test to complete information on reproduction/developmental effect" (USEPA, 1998; OECD, 2002). The 90-Day Subchronic study was chosen by the Polysulfides Scientific Research Program in order to meet future ICCA and REACH[1] testing requirements and to eliminate unnecessary and/or duplicate testing. Di-tertiary nonyl polysulfide is recommended for this test because of its lower molecular weight (and is therefore incrementally less hydrophobic) and represents a potentially more bioavailable fraction of the Di-tertiary (C9-C12) Alkyl Polysulfides Category.

Studies in Animals

Effects on Fertility

No data available.

Developmental Toxicity

A Developmental Toxicity test was completed for di-tertiary dodecyl pentasulfide in Sprague-Dawley rats following OECD Guideline 414 "Teratogenicity." No clinical signs, no unscheduled deaths, no abortions or total resorptions were observed in any group. The food consumption and body weight gain of the pregnant females from all treated groups were similar to those of controls. No treatment-related macroscopic findings were observed in any group. In the 1000 mg/kg/day group, a slightly increased post-implantation loss (represented mainly by late resorptions in one female) was observed, however, it could not be demonstrated that this single event was related to treatment. No treatment-related effects were observed on the number of live fetuses per animal, the fetal body weight, or the sex ratio. Likewise, no treatment-related external anomalies or malformations; soft tissue malformations or anomalies; or skeletal malformations, anomalies or variations were observed in any group.

Table 16. Toxicity for Reproduction – Results of Developmental Toxicity Studies in Animals

Test	di-tertiary nonyl polysulfide	di-tertiary dodecyl pentasulfide
Developmental/ Teratogenicity	No Data Available	NOAEL maternal tox. = 1000 mg/kg bw NOAEL teratogen = 1000 mg/kg bw

Source: Atofina, 2003.

[1] According to the annex VII of the proposal (dated 29.10.2003) for a regulation of the European parliament and of the council concerning the Registration, Evaluation, Authorisation and Restrictions of chemicals (REACH), establishing a European chemicals agency and amending directive 1999/45/EC and regulation (EC) {on persistent organic pollutants}, an additional standard information requirements for substances manufactured or imported in quantities of 100 tonnes or more should be a sub-chronic toxicity study (90-day).

Conclusion

The Di-tertiary (C9-C12) Alkyl Polysulfides Category underwent the developmental teratology screening test pursuant to OECD Test Guideline 414 (Teratogenicity). This study fulfills the HPV requirements for this SIDS endpoint, and no additional testing is proposed (see Table 16 and IUCLID Documents).

The Subchronic Oral Toxicity – Rodent 90-day Study (OECD 408) with a focus on reproductive endpoints is proposed for di-tertiary nonyl polysulfide, which in combination with the Developmental Toxicity study will fulfill the Reproductive Toxicity endpoint. Current EPA and OECD guidance states that "When a 90-day repeated dose study is available and demonstrates no effect on reproductive organs, in particular the testes, then a developmental study (e.g. OECD Test guidelines 414) can be considered as an adequate test to complete information on reproduction/developmental effect" (USEPA, 1998; OECD, 2002). Reproductive endpoints to be incorporated into the 90-Day Subchronic Toxicity study might include: gonadal weight and size, gonadal histopathology, accessory sex organ weight and size, accessory sex organ gross pathological appearance, accessory sex organ histopathology, spermatogenesis, sperm count and quality assessment, and estrus cyclicity. OECD (2002) has determined that these reproductive endpoints are either already incorporated into the 90-Day Subchronic Guidelines (OECD 407, 408, 409, and 412) or can be included in the study design without significant disruption to study methodology (OECD, 2002).

The Subchronic Oral Toxicity – Rodent 90-day Study was also chosen by the Polysulfides Scientific Research Program in order to meet future anticipated ICCA and REACH testing requirements and to eliminate unnecessary and/or duplicate testing. This is consistent with USEPA's position on chemicals which are being tested in multiple programs (e.g., HPV Challenge Program and the VCCEP program) where EPA states that "sponsors should consider conducting appropriate upper tier test(s) instead of the screening studies (such as OECD 422 or OECD 407 and 415/421 studies) included in the HPV Challenge Program to avoid conducting the lower tier studies unnecessarily" (USEPA, 2000).

2.2 Initial Assessment for Human Health

Data are available for the majority of the human health toxicity endpoints, as provided in Tables 7 through 16 and described above. However, there were insufficient data to fulfill the Reproductive Toxicity endpoint. The 90-day Subchronic Oral Toxicity study in rodents (OECD 408) is proposed.

3 HAZARDS TO THE ENVIRONMENT

3.1 Aquatic Effects

Acute Toxicity Test Results

Acute fish, daphnid, and algal growth inhibition studies were conducted on this Category according to the relevant OECD/EPA guidelines, and no toxicity was observed at the solubility limit.

Table 17. Aquatic Effects - Acute Toxicity Test Results.

Test	di-tertiary nonyl polysulfide	di-tertiary dodecyl pentasulfide
Acute/Prolonged Toxicity to Fish	Not toxic at maximal conc. corresponding to solubility limit (<0.11 mg/L)	ND
Acute Toxicity to Aquatic Invertebrates (*Daphnia*)	ND	No immobilization after reaching solubility limit of TS. Solubility limit was below the range of quantification (0.1 mg/L) and above the detection limit (0.02 mg/L) of the analytical method. 0.03 mg/L < Solubility limit <0.1 mg/L
Acute Toxicity to Aquatic Plants (Algae)	ND	No inhibition of growth at solubility limit (0.08 mg/L)

Source: Atofina, 2003.
ND = No Data Available

Toxicity to Microorganisms

Toxicity to microorganisms was determined for di-tertiary dodecyl pentasulfide. In this study, it was not possible to detect an inhibitory effect of the substance toward *Pseudomonas putida* even when dimethylformamide or ultrasonic dispersions were used. The maximum concentration tested was 10 g/L.

3.2 Terrestrial Effects

No data available

3.3 Other Environmental Effects

3.4 Initial Assessment for the Environment

Adequate data are available for the Di-tertiary (C9-C12) Alkyl Polysulfides Category for the HPV-required SIDS environmental endpoints. No additional testing is proposed for the purposes of the HPV program.

4 RECOMMENDATIONS

The chemical is a candidate for further testing to fulfill SIDS endpoints as follows:

Limited physiochemical data are available for members of the Category and the Polysulfides Scientific Research Program therefore proposes to complete the following testing for di-tertiary nonyl polysulfide:

- Melting Point (OECD Guideline 102, "Melting Point/Melting Range")
- Boiling Point (OECD Guideline 103, "Boiling Point")
- Vapor Pressure (OECD Guideline 104, "Vapour Pressure")
- Partition Coefficient (OECD Guideline 117,"Partition Coefficient (n-octanol/water), High Performance Liquid Chromatography (HPLC) Method")
- Water Solubility (OECD Guideline 105, "Water Solubility")

Data are available for the majority of the human health toxicity endpoints, however; there were insufficient data to fulfill the Reproductive Toxicity endpoint and therefore, testing is proposed. According to the annex VII of the proposal (dated 29.10.2003) for a regulation of the European parliament and of the council concerning the Registration, Evaluation, Authorisation and Restrictions of chemicals (REACH), an additional standard information requirement for substances manufactured or imported in quantities of 100 tonnes or more should be a sub-chronic toxicity study (90-day). In order to meet future ICCA and REACH testing requirements and to eliminate unnecessary and/or duplicate testing, the Polysulfides Scientific Research Program proposes to perform a Sub-chronic Oral Toxicity – Rodent 90-day Study (OECD 408) with a focus on reproductive endpoints. This study, in combination with the existing Developmental Toxicity study, will fulfill the Reproductive Toxicity endpoint. Current EPA and OECD guidance states that "When a 90-day repeated dose study is available and is sufficiently documented with respect to studying effects on the reproductive organs, and a developmental study is available, the requirements for the reproductive toxicity endpoints are satisfied" (USEPA, 1998; OECD 2002). Di-tertiary nonyl polysulfide is recommended for this test because of its lower molecular weight (and is therefore incrementally less hydrophobic) and represents a potentially more bioavailable fraction of the Di-tertiary (C9-C12) Alkyl Polysulfides Category.

5 REFERENCES

Atofina, 2003. IUCLID Data Set, CAS No. 31565-23-8, di(tert-dodecyl) pentasulphide. Atofina, Paris, France.

Commission of the European Communities (EC). 2003. Proposal for a Regulation of the European Parliament and of the Council Concerning the Registration, Evaluation, Authorisation and Restrictions of Chemicals (REACH), COM(2003) 644, Volume II, Brussels, 29 October 2003.

Klimisch, H.J., E. Andreae, and U. Tillmann. 1997. A systematic approach for evaluating the quality of experimental and ecotoxicological data. *Reg. Tox. and Pharm*. 25: 1-5.

Organisation for Economic Co-operation and Development (OECD) Secretariat. 2002. *Manual for Investigation of HPV Chemicals* (November 2002).

OECD, 2002. OECD Series on Testing and Assessment No. 21, Detailed Review Paper Appraisal of Test Methods for Sex Hormone Disrupting Chemicals. ENV/JM/MONO(2002)8, 07-Mar-2002.

U.S. Environmental Protection Agency (USEPA), Office of Pollution Prevention and Toxics. 1998. Guidance for Meeting the SIDS Requirements: Chemical Right-to-Know Initiative.

USEPA, Office of Pollution Prevention and Toxics. 1999a. Development of Chemical Categories in the HPV Challenge Program.

USEPA, Office of Pollution Prevention and Toxics. 1999b. Draft Determining the Adequacy of Existing Data.

USEPA, Office of Pollution Prevention and Toxics. 2000. Federal Register Notice; Voluntary Children's Chemical Evaluation Program, OPPTS-00274D; FRL-6758-5. FR Doc. 00-32767, filed 12/22/00.

USEPA, Office of Pollution Prevention and Toxics and Syracuse Research Corporation. 2000. EPI Suite v 3.10 (April, 2001).

ANNEX I: DI-TERT NONYL POLYSULFIDE IUCLID DOCUMENTS

See attached IUCLID documents.

ANNEX II: DI-TERT DODECYL PENTASULFIDE IUCLID DOCUMENTS

See attached IUCLID documents.

ANNEX III: DATA QUALITY ASSESSMENT

Available environmental, ecotoxicity, and mammalian toxicity studies were reviewed and assessed for reliability according to standards specified by Klimisch et al., (1997), as recommended by the USEPA (1999a) and the OECD (OECD, 2002). The following reliability classification (Klimisch rating) has been applied to each study assessed:

- *1 = Reliable without Restriction* – Includes studies that comply with USEPA- and/or OECD-accepted testing guidelines and were conducted using Good Laboratory Practices (GLPs) and for which test parameters are complete and well documented;

- *2 = Reliable with Restriction* – Includes studies that were conducted according to national/international testing guidance and are well documented. May include studies that were conducted prior to establishment of testing standards or GLPs but meet the test parameters and data documentation of subsequent guidance; also includes studies with test parameters that are well documented and scientifically valid but vary slightly from current testing guidance. Also included in this category were physical-chemical property data obtained from reference handbooks, as well as environmental endpoint values obtained from an accepted method of estimation (e.g., USEPA's EPIWIN estimation program);

- *3 = Not Reliable* – Includes studies in which there are interferences in either the study design or results that provide scientific uncertainty or in which documentation is insufficient; and,

- *4 = Not Assignable* – This designation is used in this dossier for studies that appear scientifically valid but for which insufficient information is available to adequately judge robustness.

Those studies receiving a Klimisch rating of 1 or 2 are considered adequate to support data assessment needs in this dossier. Those key studies selected for inclusion are considered typical of the endpoint responses observed in other studies of a similar nature and design that were identified during our search of the literature.