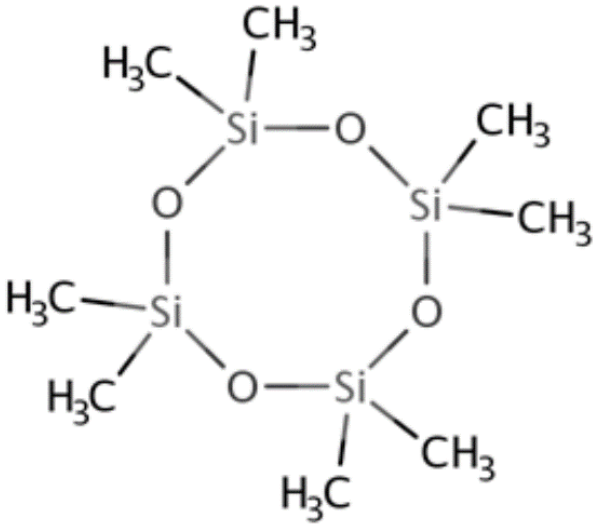
United States
Environmental Protection Agency

September 2025
Office of Chemical Safety and
Pollution Prevention

Data Extraction Information for Environmental Hazard and Human Health Hazard Animal Toxicology and Epidemiology for Octamethylcyclotetrasiloxane (D4)

Systematic Review Support Document for the Draft Risk Evaluation

CASRN: 556-67-2



September 2025

This supplemental file contains information regarding the data extraction results relevant to the *Draft Environmental Hazard Assessment for Octamethylcyclotetrasiloxane (D4)* and the *Draft Human Health Hazard Assessment for Octamethylcyclotetrasiloxane (D4)*. EPA used the TSCA systematic review process described in the *Draft Systematic Review Protocol Supporting TSCA Risk Evaluations for Chemical Substances* (also referred to as the '2021 Draft Systematic Review Protocol'). Any updated steps in the systematic review process for data extraction since the publication of the 2021 Draft Systematic Review Protocol are described in the *Draft Risk Evaluation for Octamethylcyclotetrasiloxane (D4) – Systematic Review Protocol*. EPA conducted data extraction based on author-reported descriptions and results; additional analyses (*e.g.*, statistical analyses performed during data integration into the risk evaluation) potentially conducted by EPA are not contained in this supplemental file.

Environmental Hazard Data Extraction: As explained in Section 6.4 of the 2021 Draft Systematic Review Protocol, key study details (*e.g.*, exposure duration vs. study duration) were extracted from references that underwent data quality evaluation; these study details are available in the tables below. The study details and respective endpoints were organized by first the chemical, then relevant habitat (*i.e.*, aquatic vs. terrestrial), followed by taxa categories (*e.g.*, vertebrates, invertebrates, vegetation), taxonomic groups (*e.g.*, fish, amphibian, mammalian, avian, worms, vascular plants), individual species, and finally exposure duration.

All the references that underwent data quality evaluation using the environmental hazard data quality metrics were extracted regardless of metric ranking and are included in this supplemental file. In the environmental hazard data extraction table, for some studies there were hazard health outcomes with multiple health effect levels extracted from ECOTOX; if all the data for one same health outcome were the same except for the health effect level (*e.g.*, LOEL level), multiple data extraction rows were combined into a single row in the table. All the extracted environmental hazard data will also be available in the ECOTOXicology Knowledgebase (ECOTOX) database; moreover, additional data sources and experimental details for these studies will also be available in ECOTOX.

Data Extraction of Rodent Data for the Application of Environmental Hazard: For DEHP, toxicity data gaps were identified for mammalian wildlife relevant to the terrestrial compartment of the environmental hazard assessment. This table includes rodent data for DEHP, which were used as proxy for mammalian wildlife. The rodent data were evaluated following the human health hazard animal toxicity evaluation and extraction process; however, additional data for health outcomes most relevant for environmental hazard assessment were extracted and are listed here.

Human Health Hazard Animal Toxicity Extraction: This supplemental file contains data extraction information for references that underwent data quality evaluation. Listed references with data extractions (1) met PECO screening criteria, (2) were published prior to 2014 which was the preferred literature cutoff date by EPA for data reported in previous assessments, and (3) reported human equivalent dose (HED) derived from points of departure (POD) that contained lowest-observable-effect levels (LOEL) greater than an order of magnitude of the lowest HED lowest-observable-adverse-effect level (LOAEL) identified across existing assessments. For a detailed description on these three criteria, see the *Draft Risk Evaluation for Octamethylcyclotetrasiloxane (D4) – Systematic Review Protocol*. Data from references that were within an order of magnitude of the existing assessment HED were extracted and detailed data were extracted from each individual health outcome within each organ/system. Any co-critical effects were reported along with OQD for the health outcome. A detailed summary statement of each study is reported along with the major limitations as identified by the reviewer and any guidelines used.

Epidemiological Study Information Extraction: All epidemiology references that met PECO screening criteria and further filtering criteria and had an overall quality determination of High, Medium, or Low were extracted as detailed in Section 6.4 of the 2021 Draft Systematic Review Protocol and the *Draft Risk Evaluation for Octamethylcyclotetrasiloxane (D4) – Systematic Review Protocol*. The data extracted include the measured health effect or endpoint, a description of the study population, the specific exposure compound measured and summary levels of exposure, the method of exposure measurement, and a summary of the results. Each health outcome assessed in a reference is extracted separately, and as such, each reference may have more than one record in the data extraction tables, with each record categorized by health outcome.

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Degradant: Dimethylsilanediol

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Aquatic: Arthropods Extraction Table

CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
556-67-2	24 Hour(s), (24 Hour(s))	*Aedes aegypti* (Yellow Fever Mosquito), Larva, 4 Instar, Not Reported, Laboratory (NR)	Fresh water, Aqueous (aquatic habitat), Static, Not Reported	Unmeasured	10 ppm	Mortality (Mortality-Mortality, Response Site: Not reported)	NR-ZERO (10 ppm)	Mortality	Uninformative	5885944
556-67-2	96 Hour(s), (96 Hour(s))	*Americamysis bahia* (Opossum Shrimp), <24 Hour(s), Not Reported, Laboratory (SPRINGBORN LABORATORIES)	Salt water, Aqueous (aquatic habitat), Flow-through, Not Reported	Measured	0 ug/L / 1.6 ug/L / 2.2 ug/L / 3.7 ug/L / 6.9 ug/L / 9.1 ug/L	Physiology (Intoxication-Immobile, Response Site: Not reported)	EC50 (>9.1 ug/L)	Mortality	High	6834101
556-67-2	96 Hour(s), (96 Hour(s))	*Americamysis bahia* (Opossum Shrimp), <24 Hour(s), Not Reported, Laboratory (SPRINGBORN LABORATORIES)	Salt water, Aqueous (aquatic habitat), Flow-through, Not Reported	Measured	0 ug/L / 1.6 ug/L / 2.2 ug/L / 3.7 ug/L / 6.9 ug/L / 9.1 ug/L	Physiology (Intoxication-Immobile, Response Site: Not reported)	NOEC (9.1 ug/L)	Mortality	High	6834101
556-67-2	48 Hour(s), (48 Hour(s))	*Americamysis bahia* (Opossum Shrimp), Juvenile, <=24 Hour(s), Not Reported, Laboratory (CULTURE AT SPRINGBORN LABS)	Salt water, Aqueous (aquatic habitat), Flow-through, Not Reported	Unmeasured	13-100 AI %	Mortality (Mortality-Mortality, Response Site: Not reported)	NR-ZERO (100 AI %)	Mortality	High	5889418
556-67-2	48 Hour(s), (48 Hour(s))	*Americamysis bahia* (Opossum Shrimp), Juvenile, 5 Day(s), Not Reported, Laboratory (CULTURE AT SPRINGBORN LABS)	Salt water, Aqueous (aquatic habitat), Flow-through, Not Reported	Unmeasured	13-100 AI %	Mortality (Mortality-Mortality, Response Site: Not reported)	NR-ZERO (100 AI %)	Mortality	High	5889418

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556-67-2	48 Hour(s), (48 Hour(s))	*Americamysis bahia* (Opossum Shrimp), Juvenile, <=24 Hour(s), Not Reported, Laboratory (CULTURE AT SPRINGBORN LABS)	Salt water, Aqueous (aquatic habitat), Flow-through, Not Reported	Unmeasured	13-100 AI %	Physiology (Intoxication-Intoxication, general, Response Site: Not reported)	NR (13-100 AI %)	Mortality	High	5889418
556-67-2	48 Hour(s), (48 Hour(s))	*Americamysis bahia* (Opossum Shrimp), Juvenile, 5 Day(s), Not Reported, Laboratory (CULTURE AT SPRINGBORN LABS)	Salt water, Aqueous (aquatic habitat), Flow-through, Not Reported	Unmeasured	13-100 AI %	Physiology (Intoxication-Intoxication, general, Response Site: Not reported)	NR (13-100 AI %)	Mortality	High	5889418
556-67-2	1-4 Day(s), (96 Hour(s))	*Americamysis bahia* (Opossum Shrimp), Juvenile, <=24 Hour(s), Not Reported, Laboratory (CULTURE AT SPRINGBORN LABS)	Salt water, Aqueous (aquatic habitat), Flow-through, 20 Organism	Measured	<1.00 AI ug/L / 1.6 (1.3-1.9) AI ug/L / 2.2 (2.0-2.6) AI ug/L / 3.7 (3.5-4.0) AI ug/L / 6.9 (4.5-12) AI ug/L / 9.1 (5.2-12) AI ug/L	Physiology (Intoxication-Intoxication, general, Response Site: Not reported)	NR (1.3-12 AI ug/L)	Mortality	High	5889418
556-67-2	4 Day(s), (4 Day(s))	*Americamysis bahia* (Opossum Shrimp), Juvenile, <=24 Hour(s), Not Reported, Laboratory (CULTURE AT SPRINGBORN LABS)	Salt water, Aqueous (aquatic habitat), Flow-through, Not Reported	Unmeasured	13-100 AI %	Mortality (Mortality-Mortality, Response Site: Not reported)	NR-ZERO (100 AI %)	Mortality	High	5889418

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CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
556-67-2	4 Day(s), (96 Hour(s))	*Americamysis bahia* (Opossum Shrimp), Juvenile, <=24 Hour(s), Not Reported, Laboratory (CULTURE AT SPRINGBORN LABS)	Salt water, Aqueous (aquatic habitat), Flow-through, 20 Organism	Measured	<1.00 AI ug/L / 1.6 (1.3-1.9) AI ug/L / 2.2 (2.0-2.6) AI ug/L / 3.7 (3.5-4.0) AI ug/L / 6.9 (4.5-12) AI ug/L / 9.1 (5.2-12) AI ug/L	Mortality (Mortality-Mortality, Response Site: Not reported)	NR-ZERO (9.1 (5.2-12) AI ug/L)	Mortality	High	5889418
556-67-2	18.0 Day(s), (28 Day(s))	*Chironomus riparius* (Midge), 1-3 Day(s), Both, Laboratory (ENVIRONMENTAL CONSULTING AND TESTING 1423 N 8TH ST SUITE 118 SUPERIOR, WI 54880)	Fresh water, Aqueous (aquatic habitat), Sediment, Not Reported	Measured	<18.5 mg/kg dw sediment / 6.5 mg/kg dw sediment / 7.9 mg/kg dw sediment / 19 (<15.9-26.6) mg/kg dw sediment / 44 (36.0-50.3) mg/kg dw sediment / 131 (101-173) mg/kg dw sediment / 355 (255-450) mg/kg dw sediment	Growth (Development-Developmental changes, general, Response Site: Not reported)	NOEC (131 (101-173) mg/kg dw sediment)	Development/Growth	High	7002244

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CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
556-67-2	21.1 Day(s), (28 Day(s))	*Chironomus riparius* (Midge), 1-3 Day(s), Both, Laboratory (ENVIRONMENTAL CONSULTING AND TESTING 1423 N 8TH ST SUITE 118 SUPERIOR, WI 54880)	Fresh water, Aqueous (aquatic habitat), Sediment, Not Reported	Measured	<18.5 mg/kg dw sediment / 6.5 mg/kg dw sediment / 7.9 mg/kg dw sediment / 19 (<15.9-26.6) mg/kg dw sediment / 44 (36.0-50.3) mg/kg dw sediment / 131 (101-173) mg/kg dw sediment / 355 (255-450) mg/kg dw sediment	Growth (Development-Developmental changes, general, Response Site: Not reported)	LOEC (355 (255-450) mg/kg dw sediment)	Development/Growth	High	7002244
556-67-2	15-28 Day(s), (28 Day(s))	*Chironomus riparius* (Midge), 1-3 Day(s), Both, Laboratory (ENVIRONMENTAL CONSULTING AND TESTING 1423 N 8TH ST SUITE 118 SUPERIOR, WI 54880)	Fresh water, Aqueous (aquatic habitat), Sediment, NA Both male and female	Measured	<18.5 mg/kg dw sediment / 6.5 mg/kg dw sediment / 7.9 mg/kg dw sediment / 19 (<15.9-26.6) mg/kg dw sediment / 44 (36.0-50.3) mg/kg dw sediment / 131 (101-173) mg/kg dw sediment / 355 (255-450) mg/kg dw sediment	Growth (Development-Emergence, Response Site: Not reported)	NR (6.5-450 mg/kg dw sediment)	Development/Growth	High	7002244

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556-67-2	15-28 Day(s), (28 Day(s))	*Chironomus riparius* (Midge), 1-3 Day(s), Both (Measured in: Female organisms), Laboratory (ENVIRONMENTAL CONSULTING AND TESTING 1423 N 8TH ST SUITE 118 SUPERIOR, WI 54880)	Fresh water, Aqueous (aquatic habitat), Sediment, NA Female organisms	Measured	<18.5 mg/kg dw sediment / 6.5 mg/kg dw sediment / 7.9 mg/kg dw sediment / 19 (<15.9-26.6) mg/kg dw sediment / 44 (36.0-50.3) mg/kg dw sediment / 131 (101-173) mg/kg dw sediment / 355 (255-450) mg/kg dw sediment	Growth (Development-Emergence, Response Site: Not reported)	NR (6.5-450 mg/kg dw sediment)	Development/Growth	High	7002244
556-67-2	28 Day(s), (28 Day(s))	*Chironomus riparius* (Midge), 1-3 Day(s), Both, Laboratory (ENVIRONMENTAL CONSULTING AND TESTING 1423 N 8TH ST SUITE 118 SUPERIOR, WI 54880)	Fresh water, Aqueous (aquatic habitat), Sediment, NA Both male and female	Measured	<18.5 mg/kg dw sediment / 6.5 mg/kg dw sediment / 7.9 mg/kg dw sediment / 19 (<15.9-26.6) mg/kg dw sediment / 44 (36.0-50.3) mg/kg dw sediment / 131 (101-173) mg/kg dw sediment / 355 (255-450) mg/kg dw sediment	Mortality (Mortality-Mortality, Response Site: Not reported)	LC50 (114 (96-136) mg/kg dw sediment)	Mortality	High	7002244

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556-67-2	28 Day(s), (28 Day(s))	*Chironomus riparius* (Midge), 1-3 Day(s), Both, Laboratory (ENVIRONMENTAL CONSULTING AND TESTING 1423 N 8TH ST SUITE 118 SUPERIOR, WI 54880)	Fresh water, Aqueous (aquatic habitat), Sediment, NA Both male and female	Measured	<18.5 mg/kg dw sediment / 6.5 mg/kg dw sediment / 7.9 mg/kg dw sediment / 19 (<15.9-26.6) mg/kg dw sediment / 44 (36.0-50.3) mg/kg dw sediment / 131 (101-173) mg/kg dw sediment / 355 (255-450) mg/kg dw sediment	Growth (Development-Emergence, Response Site: Not reported)	LOEC (131 (101-173) mg/kg dw sediment)	Development/Growth	High	7002244
556-67-2	28 Day(s), (28 Day(s))	*Chironomus riparius* (Midge), 1-3 Day(s), Both, Laboratory (ENVIRONMENTAL CONSULTING AND TESTING 1423 N 8TH ST SUITE 118 SUPERIOR, WI 54880)	Fresh water, Aqueous (aquatic habitat), Sediment, Not Reported	Measured	<18.5 mg/kg dw sediment / 6.5 mg/kg dw sediment / 7.9 mg/kg dw sediment / 19 (<15.9-26.6) mg/kg dw sediment / 44 (36.0-50.3) mg/kg dw sediment / 131 (101-173) mg/kg dw sediment / 355 (255-450) mg/kg dw sediment	Mortality (Mortality-Survival, Response Site: Not reported)	LOEC (131 (101-173) mg/kg dw sediment)	Mortality	High	7002244

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556-67-2	28 Day(s), (28 Day(s))	*Chironomus riparius* (Midge), 1-3 Day(s), Both, Laboratory (ENVIRONMENTAL CONSULTING AND TESTING 1423 N 8TH ST SUITE 118 SUPERIOR, WI 54880)	Fresh water, Aqueous (aquatic habitat), Sediment, Not Reported	Measured	<18.5 mg/kg dw sediment / 6.5 mg/kg dw sediment / 7.9 mg/kg dw sediment / 19 (<15.9-26.6) mg/kg dw sediment / 44 (36.0-50.3) mg/kg dw sediment / 131 (101-173) mg/kg dw sediment / 355 (255-450) mg/kg dw sediment	Growth (Development-Developmental changes, general, Response Site: Not reported)	LOEC (355 (255-450) mg/kg dw sediment)	Development/Growth	High	7002244
556-67-2	28 Day(s), (28 Day(s))	*Chironomus riparius* (Midge), 1-3 Day(s), Both, Laboratory (ENVIRONMENTAL CONSULTING AND TESTING 1423 N 8TH ST SUITE 118 SUPERIOR, WI 54880)	Fresh water, Aqueous (aquatic habitat), Sediment, Not Reported	Measured	<18.5 mg/kg dw sediment / 6.5 mg/kg dw sediment / 7.9 mg/kg dw sediment / 19 (<15.9-26.6) mg/kg dw sediment / 44 (36.0-50.3) mg/kg dw sediment / 131 (101-173) mg/kg dw sediment / 355 (255-450) mg/kg dw sediment	Growth (Development-Developmental changes, general, Response Site: Not reported)	NOEC (131 (101-173) mg/kg dw sediment)	Development/Growth	High	7002244

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556-67-2	28 Day(s), (28 Day(s))	*Chironomus riparius* (Midge), 1-3 Day(s), Both, Laboratory (ENVIRONMENTAL CONSULTING AND TESTING 1423 N 8TH ST SUITE 118 SUPERIOR, WI 54880)	Fresh water, Aqueous (aquatic habitat), Sediment, NA Both male and female	Measured	<18.5 mg/kg dw sediment / 6.5 mg/kg dw sediment / 7.9 mg/kg dw sediment / 19 (<15.9-26.6) mg/kg dw sediment / 44 (36.0-50.3) mg/kg dw sediment / 131 (101-173) mg/kg dw sediment / 355 (255-450) mg/kg dw sediment	Growth (Development-Emergence, Response Site: Not reported)	NOEC (44 (36.0-50.3) mg/kg dw sediment)	Development/Growth	High	7002244
556-67-2	28 Day(s), (28 Day(s))	*Chironomus riparius* (Midge), 1-3 Day(s), Both, Laboratory (ENVIRONMENTAL CONSULTING AND TESTING 1423 N 8TH ST SUITE 118 SUPERIOR, WI 54880)	Fresh water, Aqueous (aquatic habitat), Sediment, Not Reported	Measured	<18.5 mg/kg dw sediment / 6.5 mg/kg dw sediment / 7.9 mg/kg dw sediment / 19 (<15.9-26.6) mg/kg dw sediment / 44 (36.0-50.3) mg/kg dw sediment / 131 (101-173) mg/kg dw sediment / 355 (255-450) mg/kg dw sediment	Mortality (Mortality-Survival, Response Site: Not reported)	NOEC (44 (36.0-50.3) mg/kg dw sediment)	Mortality	High	7002244

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556-67-2	15-28 Day(s), (28 Day(s))	*Chironomus riparius* (Midge), 1-3 Day(s), Both (Measured in: Male organisms), Laboratory (ENVIRONMENTAL CONSULTING AND TESTING 1423 N 8TH ST SUITE 118 SUPERIOR, WI 54880)	Fresh water, Aqueous (aquatic habitat), Sediment, NA Male organisms	Measured	<18.5 mg/kg dw sediment / 6.5 mg/kg dw sediment / 7.9 mg/kg dw sediment / 19 (<15.9-26.6) mg/kg dw sediment / 44 (36.0-50.3) mg/kg dw sediment / 131 (101-173) mg/kg dw sediment / 355 (255-450) mg/kg dw sediment	Growth (Development-Emergence, Response Site: Not reported)	NR (6.5-450 mg/kg dw sediment)	Development/Growth	High	7002244
556-67-2	14 Day(s), (14 Day(s))	*Chironomus tentans* (Midge), Larva, 2 Instar, Not Reported, Laboratory (NR)	Fresh water, Aqueous (aquatic habitat), Sediment, Not Reported	Measured	<0.33 mg/kg dw sediment / <0.33 mg/kg dw sediment / 2.6 mg/kg dw sediment / 7.4 mg/kg dw sediment / 19 mg/kg dw sediment / 54 mg/kg dw sediment / 170 mg/kg dw sediment	Accumulation (Accumulation-Residue, Response Site: Whole organism)	BCF (19 mg/kg dw sediment)	Other (please specify below)	Medium	6834021

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556-67-2	14 Day(s), (14 Day(s))	*Chironomus tentans* (Midge), Larva, 2 Instar, Not Reported, Laboratory (NR)	Fresh water, Aqueous (aquatic habitat), Sediment, Not Reported	Measured	<7.9 mg/kg dw sediment / <7.9 mg/kg dw sediment / 6.8 mg/kg dw sediment / 17 mg/kg dw sediment / 32 mg/kg dw sediment / 65 mg/kg dw sediment / 130 mg/kg dw sediment	Mortality (Mortality-Survival, Response Site: Not reported)	NOEC (130 mg/kg dw sediment)	Mortality	High	6834021
556-67-2	14 Day(s), (14 Day(s))	*Chironomus tentans* (Midge), Larva, 2 Instar, Not Reported, Laboratory (NR)	Fresh water, Aqueous (aquatic habitat), Sediment, Not Reported	Measured	<7.9 mg/kg dw sediment / <7.9 mg/kg dw sediment / 6.8 mg/kg dw sediment / 17 mg/kg dw sediment / 32 mg/kg dw sediment / 65 mg/kg dw sediment / 130 mg/kg dw sediment	Growth (Growth-Weight, Response Site: Whole organism)	NOEC (65 mg/kg dw sediment)	Development/Growth	High	6834021
556-67-2	14 Day(s), (14 Day(s))	*Chironomus tentans* (Midge), Larva, 2 Instar, Not Reported, Laboratory (NR)	Fresh water, Aqueous (aquatic habitat), Sediment, Not Reported	Measured	<0.33 mg/kg dw sediment / <0.33 mg/kg dw sediment / 2.6 mg/kg dw sediment / 7.4 mg/kg dw sediment / 19 mg/kg dw sediment / 54 mg/kg dw sediment / 170 mg/kg dw sediment	Mortality (Mortality-Mortality, Response Site: Not reported)	LC50 (>170 mg/kg dw sediment)	Mortality	High	6834021

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556-67-2	14 Day(s), (14 Day(s))	*Chironomus tentans* (Midge), Larva, 2 Instar, Not Reported, Laboratory (NR)	Fresh water, Aqueous (aquatic habitat), Sediment, Not Reported	Measured	<6.9 mg/kg dw sediment / <6.9 mg/kg dw sediment / 18 mg/kg dw sediment / 38 mg/kg dw sediment / 76 mg/kg dw sediment / 120 mg/kg dw sediment / 250 mg/kg dw sediment	Accumulation (Accumulation-Residue, Response Site: Whole organism)	BCF (18 mg/kg dw sediment)	Other (please specify below)	Medium	6834021
556-67-2	14 Day(s), (14 Day(s))	*Chironomus tentans* (Midge), Larva, 2 Instar, Not Reported, Laboratory (NR)	Fresh water, Aqueous (aquatic habitat), Sediment, Not Reported	Measured	<0.33 mg/kg dw sediment / <0.33 mg/kg dw sediment / 2.6 mg/kg dw sediment / 7.4 mg/kg dw sediment / 19 mg/kg dw sediment / 54 mg/kg dw sediment / 170 mg/kg dw sediment	Accumulation (Accumulation-Residue, Response Site: Whole organism)	BCF (54 mg/kg dw sediment)	Other (please specify below)	Medium	6834021
556-67-2	14 Day(s), (14 Day(s))	*Chironomus tentans* (Midge), Larva, 2 Instar, Not Reported, Laboratory (NR)	Fresh water, Aqueous (aquatic habitat), Flow-through, Not Reported	Measured	<0.00005 ug/L / 0.49 ug/L / 1.2 ug/L / 2.9 ug/L / 6.5 ug/L / 15 ug/L	Mortality (Mortality-Survival, Response Site: Not reported)	NOEC (15 ug/L)	Mortality	High	6834021

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CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
556-67-2	14 Day(s), (14 Day(s))	*Chironomus tentans* (Midge), Larva, 2 Instar, Not Reported, Laboratory (NR)	Fresh water, Aqueous (aquatic habitat), Sediment, Not Reported	Measured	<0.33 mg/kg dw sediment / <0.33 mg/kg dw sediment / 2.6 mg/kg dw sediment / 7.4 mg/kg dw sediment / 19 mg/kg dw sediment / 54 mg/kg dw sediment / 170 mg/kg dw sediment	Accumulation (Accumulation-Residue, Response Site: Whole organism)	BCF (2.6 mg/kg dw sediment)	Other (please specify below)	Medium	6834021
556-67-2	14 Day(s), (14 Day(s))	*Chironomus tentans* (Midge), Larva, 2 Instar, Not Reported, Laboratory (NR)	Fresh water, Aqueous (aquatic habitat), Flow-through, Not Reported	Measured	<0.00005 ug/L / 0.49 ug/L / 1.2 ug/L / 2.9 ug/L / 6.5 ug/L / 15 ug/L	Growth (Growth-Weight, Response Site: Whole organism)	NOEC (15 ug/L)	Development/Growth	High	6834021
556-67-2	14 Day(s), (14 Day(s))	*Chironomus tentans* (Midge), Larva, 2 Instar, Not Reported, Laboratory (NR)	Fresh water, Aqueous (aquatic habitat), Sediment, Not Reported	Measured	<7.9 mg/kg dw sediment / <7.9 mg/kg dw sediment / 6.8 mg/kg dw sediment / 17 mg/kg dw sediment / 32 mg/kg dw sediment / 65 mg/kg dw sediment / 130 mg/kg dw sediment	Growth (Growth-Weight, Response Site: Whole organism)	MATC (92 (65-130) mg/kg dw sediment)	Development/Growth	High	6834021

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Aquatic: Arthropods Extraction Table

CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
556-67-2	14 Day(s), (14 Day(s))	*Chironomus tentans* (Midge), Larva, 2 Instar, Not Reported, Laboratory (NR)	Fresh water, Aqueous (aquatic habitat), Sediment, Not Reported	Measured	<7.9 mg/kg dw sediment / <7.9 mg/kg dw sediment / 6.8 mg/kg dw sediment / 17 mg/kg dw sediment / 32 mg/kg dw sediment / 65 mg/kg dw sediment / 130 mg/kg dw sediment	Growth (Growth-Weight, Response Site: Whole organism)	LOEC (130 mg/kg dw sediment)	Development/Growth	High	6834021
556-67-2	14 Day(s), (14 Day(s))	*Chironomus tentans* (Midge), Larva, 2 Instar, Not Reported, Laboratory (NR)	Fresh water, Aqueous (aquatic habitat), Sediment, Not Reported	Measured	<7.9 mg/kg dw sediment / <7.9 mg/kg dw sediment / 6.8 mg/kg dw sediment / 17 mg/kg dw sediment / 32 mg/kg dw sediment / 65 mg/kg dw sediment / 130 mg/kg dw sediment	Accumulation (Accumulation-Residue, Response Site: Whole organism)	BCF (6.8 mg/kg dw sediment)	Other (please specify below)	Medium	6834021
556-67-2	14 Day(s), (14 Day(s))	*Chironomus tentans* (Midge), Larva, 2 Instar, Not Reported, Laboratory (NR)	Fresh water, Aqueous (aquatic habitat), Sediment, Not Reported	Measured	<0.33 mg/kg dw sediment / <0.33 mg/kg dw sediment / 2.6 mg/kg dw sediment / 7.4 mg/kg dw sediment / 19 mg/kg dw sediment / 54 mg/kg dw sediment / 170 mg/kg dw sediment	Accumulation (Accumulation-Residue, Response Site: Whole organism)	BCF (7.4 mg/kg dw sediment)	Other (please specify below)	Medium	6834021

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Aquatic: Arthropods Extraction Table

CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
556-67-2	14 Day(s), (14 Day(s))	*Chironomus tentans* (Midge), Larva, 2 Instar, Not Reported, Laboratory (NR)	Fresh water, Aqueous (aquatic habitat), Sediment, Not Reported	Measured	<0.33 mg/kg dw sediment / <0.33 mg/kg dw sediment / 2.6 mg/kg dw sediment / 7.4 mg/kg dw sediment / 19 mg/kg dw sediment / 54 mg/kg dw sediment / 170 mg/kg dw sediment	Mortality (Mortality-Survival, Response Site: Not reported)	LOEC (170 mg/kg dw sediment)	Mortality	High	6834021
556-67-2	14 Day(s), (14 Day(s))	*Chironomus tentans* (Midge), Larva, 2 Instar, Not Reported, Laboratory (NR)	Fresh water, Aqueous (aquatic habitat), Sediment, Not Reported	Measured	<0.33 mg/kg dw sediment / <0.33 mg/kg dw sediment / 2.6 mg/kg dw sediment / 7.4 mg/kg dw sediment / 19 mg/kg dw sediment / 54 mg/kg dw sediment / 170 mg/kg dw sediment	Mortality (Mortality-Survival, Response Site: Not reported)	MATC (96 (54-170) mg/kg dw sediment)	Mortality	High	6834021
556-67-2	14 Day(s), (14 Day(s))	*Chironomus tentans* (Midge), Larva, 2 Instar, Not Reported, Laboratory (NR)	Fresh water, Aqueous (aquatic habitat), Sediment, Not Reported	Measured	<0.33 mg/kg dw sediment / <0.33 mg/kg dw sediment / 2.6 mg/kg dw sediment / 7.4 mg/kg dw sediment / 19 mg/kg dw sediment / 54 mg/kg dw sediment / 170 mg/kg dw sediment	Growth (Growth-Weight, Response Site: Whole organism)	NOEC (170 mg/kg dw sediment)	Development/Growth	High	6834021

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Aquatic: Arthropods Extraction Table

CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
556-67-2	14 Day(s), (14 Day(s))	*Chironomus tentans* (Midge), Larva, 2 Instar, Not Reported, Laboratory (NR)	Fresh water, Aqueous (aquatic habitat), Sediment, Not Reported	Measured	<0.33 mg/kg dw sediment / <0.33 mg/kg dw sediment / 2.6 mg/kg dw sediment / 7.4 mg/kg dw sediment / 19 mg/kg dw sediment / 54 mg/kg dw sediment / 170 mg/kg dw sediment	Mortality (Mortality-Survival, Response Site: Not reported)	NOEC (54 mg/kg dw sediment)	Mortality	High	6834021
556-67-2	14 Day(s), (14 Day(s))	*Chironomus tentans* (Midge), Larva, 2 Instar, Not Reported, Laboratory (NR)	Fresh water, Aqueous (aquatic habitat), Sediment, Not Reported	Measured	<6.9 mg/kg dw sediment / <6.9 mg/kg dw sediment / 18 mg/kg dw sediment / 38 mg/kg dw sediment / 76 mg/kg dw sediment / 120 mg/kg dw sediment / 250 mg/kg dw sediment	Accumulation (Accumulation-Residue, Response Site: Whole organism)	BCF (38 mg/kg dw sediment)	Other (please specify below)	Medium	6834021
556-67-2	14 Day(s), (14 Day(s))	*Chironomus tentans* (Midge), Larva, 2 Instar, Not Reported, Laboratory (NR)	Fresh water, Aqueous (aquatic habitat), Sediment, Not Reported	Measured	<6.9 mg/kg dw sediment / <6.9 mg/kg dw sediment / 18 mg/kg dw sediment / 38 mg/kg dw sediment / 76 mg/kg dw sediment / 120 mg/kg dw sediment / 250 mg/kg dw sediment	Mortality (Mortality-Mortality, Response Site: Not reported)	LC50 (170 (110-390) mg/kg dw sediment)	Mortality	Uninformative	6834021

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Aquatic: Arthropods Extraction Table

CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
556-67-2	14 Day(s), (14 Day(s))	*Chironomus tentans* (Midge), Larva, 2 Instar, Not Reported, Laboratory (NR)	Fresh water, Aqueous (aquatic habitat), Sediment, Not Reported	Measured	<6.9 mg/kg dw sediment / <6.9 mg/kg dw sediment / 18 mg/kg dw sediment / 38 mg/kg dw sediment / 76 mg/kg dw sediment / 120 mg/kg dw sediment / 250 mg/kg dw sediment	Mortality (Mortality-Survival, Response Site: Not reported)	LOEC (250 mg/kg dw sediment)	Mortality	Uninformative	6834021
556-67-2	14 Day(s), (14 Day(s))	*Chironomus tentans* (Midge), Larva, 2 Instar, Not Reported, Laboratory (NR)	Fresh water, Aqueous (aquatic habitat), Sediment, Not Reported	Measured	<6.9 mg/kg dw sediment / <6.9 mg/kg dw sediment / 18 mg/kg dw sediment / 38 mg/kg dw sediment / 76 mg/kg dw sediment / 120 mg/kg dw sediment / 250 mg/kg dw sediment	Mortality (Mortality-Survival, Response Site: Not reported)	MATC (170 (120-250) mg/kg dw sediment)	Mortality	Uninformative	6834021
556-67-2	14 Day(s), (14 Day(s))	*Chironomus tentans* (Midge), Larva, 2 Instar, Not Reported, Laboratory (NR)	Fresh water, Aqueous (aquatic habitat), Sediment, Not Reported	Measured	<6.9 mg/kg dw sediment / <6.9 mg/kg dw sediment / 18 mg/kg dw sediment / 38 mg/kg dw sediment / 76 mg/kg dw sediment / 120 mg/kg dw sediment / 250 mg/kg dw sediment	Mortality (Mortality-Survival, Response Site: Not reported)	NOEC (120 mg/kg dw sediment)	Mortality	Uninformative	6834021

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Aquatic: Arthropods Extraction Table

CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
556-67-2	14 Day(s), (14 Day(s))	*Chironomus tentans* (Midge), Larva, 2 Instar, Not Reported, Laboratory (NR)	Fresh water, Aqueous (aquatic habitat), Sediment, Not Reported	Measured	<6.9 mg/kg dw sediment / <6.9 mg/kg dw sediment / 18 mg/kg dw sediment / 38 mg/kg dw sediment / 76 mg/kg dw sediment / 120 mg/kg dw sediment / 250 mg/kg dw sediment	Growth (Growth-Weight, Response Site: Whole organism)	NOEC (250 mg/kg dw sediment)	Development/Growth	High	6834021
556-67-2	14 Day(s), (14 Day(s))	*Chironomus tentans* (Midge), Larva, 2 Instar, Not Reported, Laboratory (NR)	Fresh water, Aqueous (aquatic habitat), Sediment, Not Reported	Measured	<7.9 mg/kg dw sediment / <7.9 mg/kg dw sediment / 6.8 mg/kg dw sediment / 17 mg/kg dw sediment / 32 mg/kg dw sediment / 65 mg/kg dw sediment / 130 mg/kg dw sediment	Accumulation (Accumulation-Residue, Response Site: Whole organism)	BCF (17 mg/kg dw sediment)	Other (please specify below)	Medium	6834021
556-67-2	14 Day(s), (14 Day(s))	*Chironomus tentans* (Midge), Larva, 2 Instar, Not Reported, Laboratory (NR)	Fresh water, Aqueous (aquatic habitat), Sediment, Not Reported	Measured	<7.9 mg/kg dw sediment / <7.9 mg/kg dw sediment / 6.8 mg/kg dw sediment / 17 mg/kg dw sediment / 32 mg/kg dw sediment / 65 mg/kg dw sediment / 130 mg/kg dw sediment	Mortality (Mortality-Mortality, Response Site: Not reported)	LC50 (>130 mg/kg dw sediment)	Mortality	High	6834021

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Aquatic: Arthropods Extraction Table

CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
556-67-2	14 Day(s), (14 Day(s))	*Chironomus tentans* (Midge), Larva, ~10 Day(s), Not Reported, Laboratory (CULTURED AT SPRING-BORN LABS)	Fresh water, Aqueous (aquatic habitat), Leaching , 14 Organism	Measured	<0.052 mg/L / <0.052 mg/L / <0.052-0.14 mg/L / 0.17 (<0.052-0.35) mg/L / 0.34 (0.10-0.71) mg/L / 0.47 (0.12-0.99) mg/L / 0.87 (0.25-2.5) mg/L	Accumulation (Accumulation-Residue, Response Site: Whole organism)	BCF (0.17 (<0.052-0.35) mg/L)	Other (please specify below)	High	5889402
556-67-2	14 Day(s), (14 Day(s))	*Chironomus tentans* (Midge), Larva, ~10 Day(s), Not Reported, Laboratory (CULTURED AT SPRING-BORN LABS)	Fresh water, Aqueous (aquatic habitat), Leaching , Not Reported	Measured	<0.052 mg/L / <0.052 mg/L / <0.052-0.14 mg/L / 0.17 (<0.052-0.35) mg/L / 0.34 (0.10-0.71) mg/L / 0.47 (0.12-0.99) mg/L / 0.87 (0.25-2.5) mg/L	Mortality (Mortality-Mortality, Response Site: Not reported)	LC50 (0.62 (0.46-1.2) mg/L)	Mortality	High	5889402
556-67-2	14 Day(s), (14 Day(s))	*Chironomus tentans* (Midge), Larva, ~10 Day(s), Not Reported, Laboratory (CULTURED AT SPRING-BORN LABS)	Fresh water, Aqueous (aquatic habitat), Leaching , 19 Organism	Measured	<0.052 mg/L / <0.052 mg/L / <0.052-0.14 mg/L / 0.17 (<0.052-0.35) mg/L / 0.34 (0.10-0.71) mg/L / 0.47 (0.12-0.99) mg/L / 0.87 (0.25-2.5) mg/L	Mortality (Mortality-Survival, Response Site: Not reported)	LOEC (0.87 (0.25-2.5) mg/L)	Mortality	High	5889402

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CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
556-67-2	14 Day(s), (14 Day(s))	*Chironomus tentans* (Midge), Larva, ~10 Day(s), Not Reported, Laboratory (CULTURED AT SPRING-BORN LABS)	Fresh water, Aqueous (aquatic habitat), Leaching , 30 Organism	Measured	<0.052 mg/L / <0.052 mg/L / <0.052-0.14 mg/L / 0.17 (<0.052-0.35) mg/L / 0.34 (0.10-0.71) mg/L / 0.47 (0.12-0.99) mg/L / 0.87 (0.25-2.5) mg/L	Mortality (Mortality-Survival, Response Site: Not reported)	NOEC (0.47 (0.12-0.99) mg/L)	Mortality	High	5889402
556-67-2	14 Day(s), (14 Day(s))	*Chironomus tentans* (Midge), Larva, ~10 Day(s), Not Reported, Laboratory (CULTURED AT SPRING-BORN LABS)	Fresh water, Aqueous (aquatic habitat), Leaching , 19 Organism	Measured	<0.052 mg/L / <0.052 mg/L / <0.052-0.14 mg/L / 0.17 (<0.052-0.35) mg/L / 0.34 (0.10-0.71) mg/L / 0.47 (0.12-0.99) mg/L / 0.87 (0.25-2.5) mg/L	Growth (Growth-Weight, Response Site: Whole organism)	NOEC (0.87 (0.25-2.5) mg/L)	Development/Growth	High	5889402
556-67-2	14 Day(s), (14 Day(s))	*Chironomus tentans* (Midge), Larva, ~10 Day(s), Not Reported, Laboratory (CULTURED AT SPRING-BORN LABS)	Fresh water, Aqueous (aquatic habitat), Leaching , 10 Organism	Measured	<0.053 mg/L / <0.053 mg/L / 0.76 (0.55-0.87) mg/L / 1.1 (0.51-1.9) mg/L / 1.1 (0.41-2.3) mg/L / 1.1 (0.25-2.1) mg/L / 3.6 (0.8-7.8) mg/L	Accumulation (Accumulation-Residue, Response Site: Whole organism)	BCF (0.76 (0.55-0.87) mg/L)	Other (please specify below)	High	5889402

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CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
556-67-2	14 Day(s), (14 Day(s))	*Chironomus tentans* (Midge), Larva, ~10 Day(s), Not Reported, Laboratory (CULTURED AT SPRINGBORN LABS)	Fresh water, Aqueous (aquatic habitat), Leaching , 13 Organism	Measured	<0.052 mg/L / <0.052 mg/L / <0.052-0.14 mg/L / 0.17 (<0.052-0.35) mg/L / 0.34 (0.10-0.71) mg/L / 0.47 (0.12-0.99) mg/L / 0.87 (0.25-2.5) mg/L	Accumulation (Accumulation-Residue, Response Site: Whole organism)	BCF (0.17 (<0.052-0.35) mg/L)	Other (please specify below)	High	5889402
556-67-2	14 Day(s), (14 Day(s))	*Chironomus tentans* (Midge), Larva, ~10 Day(s), Not Reported, Laboratory (CULTURED AT SPRINGBORN LABS)	Fresh water, Aqueous (aquatic habitat), Leaching , 13 Organism	Measured	<0.053 mg/L / <0.053 mg/L / 0.76 (0.55-0.87) mg/L / 1.1 (0.51-1.9) mg/L / 1.1 (0.41-2.3) mg/L / 1.1 (0.25-2.1) mg/L / 3.6 (0.8-7.8) mg/L	Accumulation (Accumulation-Residue, Response Site: Whole organism)	BCF (1.1 (0.51-1.9) mg/L)	Other (please specify below)	High	5889402
556-67-2	14 Day(s), (14 Day(s))	*Chironomus tentans* (Midge), Larva, ~10 Day(s), Not Reported, Laboratory (CULTURED AT SPRINGBORN LABS)	Fresh water, Aqueous (aquatic habitat), Leaching , Not Reported	Measured	<0.053 mg/L / <0.053 mg/L / 0.76 (0.55-0.87) mg/L / 1.1 (0.51-1.9) mg/L / 1.1 (0.41-2.3) mg/L / 1.1 (0.25-2.1) mg/L / 3.6 (0.8-7.8) mg/L	Mortality (Mortality-Mortality, Response Site: Not reported)	LC50 (>3.6 (0.8-7.8) mg/L)	Mortality	High	5889402

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CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
556-67-2	14 Day(s), (14 Day(s))	*Chironomus tentans* (Midge), Larva, ~10 Day(s), Not Reported, Laboratory (CULTURED AT SPRINGBORN LABS)	Fresh water, Aqueous (aquatic habitat), Leaching , 25 Organism	Measured	<0.053 mg/L / <0.053 mg/L / 0.76 (0.55-0.87) mg/L / 1.1 (0.51-1.9) mg/L / 1.1 (0.41-2.3) mg/L / 1.1 (0.25-2.1) mg/L / 3.6 (0.8-7.8) mg/L	Growth (Growth-Weight, Response Site: Whole organism)	LOEC (3.6 (0.8-7.8) mg/L)	Development/Growth	High	5889402
556-67-2	14 Day(s), (14 Day(s))	*Chironomus tentans* (Midge), Larva, ~10 Day(s), Not Reported, Laboratory (CULTURED AT SPRINGBORN LABS)	Fresh water, Aqueous (aquatic habitat), Leaching , 25 Organism	Measured	<0.053 mg/L / <0.053 mg/L / 0.76 (0.55-0.87) mg/L / 1.1 (0.51-1.9) mg/L / 1.1 (0.41-2.3) mg/L / 1.1 (0.25-2.1) mg/L / 3.6 (0.8-7.8) mg/L	Growth (Growth-Weight, Response Site: Whole organism)	MATC (2.0 mg/L)	Development/Growth	High	5889402
556-67-2	14 Day(s), (14 Day(s))	*Chironomus tentans* (Midge), Larva, ~10 Day(s), Not Reported, Laboratory (CULTURED AT SPRINGBORN LABS)	Fresh water, Aqueous (aquatic habitat), Leaching , 26 Organism	Measured	<0.053 mg/L / <0.053 mg/L / 0.76 (0.55-0.87) mg/L / 1.1 (0.51-1.9) mg/L / 1.1 (0.41-2.3) mg/L / 1.1 (0.25-2.1) mg/L / 3.6 (0.8-7.8) mg/L	Growth (Growth-Weight, Response Site: Whole organism)	NOEC (1.1 (0.25-2.1) mg/L)	Development/Growth	High	5889402
556-67-2	14 Day(s), (14 Day(s))	*Chironomus tentans* (Midge), Larva, ~10 Day(s), Not Reported, Laboratory (CULTURED AT SPRINGBORN LABS)	Fresh water, Aqueous (aquatic habitat), Leaching , 38 Organism	Measured	<0.053 mg/L / <0.053 mg/L / 0.76 (0.55-0.87) mg/L / 1.1 (0.51-1.9) mg/L / 1.1 (0.41-2.3) mg/L / 1.1 (0.25-2.1) mg/L / 3.6 (0.8-7.8) mg/L	Mortality (Mortality-Survival, Response Site: Not reported)	NOEC (3.6 (0.8-7.8) mg/L)	Mortality	High	5889402

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CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
556-67-2	14 Day(s), (14 Day(s))	*Chironomus tentans* (Midge), Larva, ~10 Day(s), Not Reported, Laboratory (CULTURED AT SPRING-BORN LABS)	Fresh water, Aqueous (aquatic habitat), Leaching , 6 Organism	Measured	<0.054 mg/L / <0.052-0.21 mg/L / 0.12 (0.082-0.20) mg/L / 0.22 (0.13-0.30) mg/L / 0.45 (0.31-0.60) mg/L / 0.74 (0.49-1.1) mg/L / 1.7 (1.3-2.3) mg/L	Accumulation (Accumulation-Residue, Response Site: Whole organism)	BCF (0.12 (0.082-0.20) mg/L)	Other (please specify below)	High	5889402
556-67-2	14 Day(s), (14 Day(s))	*Chironomus tentans* (Midge), Larva, ~10 Day(s), Not Reported, Laboratory (CULTURED AT SPRING-BORN LABS)	Fresh water, Aqueous (aquatic habitat), Leaching , 3 Organism	Measured	<0.053 mg/L / <0.053 mg/L / 0.76 (0.55-0.87) mg/L / 1.1 (0.51-1.9) mg/L / 1.1 (0.41-2.3) mg/L / 1.1 (0.25-2.1) mg/L / 3.6 (0.8-7.8) mg/L	Accumulation (Accumulation-Residue, Response Site: Whole organism)	BCF (1.1 (0.51-1.9) mg/L)	Other (please specify below)	High	5889402
556-67-2	14 Day(s), (14 Day(s))	*Chironomus tentans* (Midge), Larva, ~10 Day(s), Not Reported, Laboratory (CULTURED AT SPRING-BORN LABS)	Fresh water, Aqueous (aquatic habitat), Leaching , 13 Organism	Measured	<0.054 mg/L / <0.052-0.21 mg/L / 0.12 (0.082-0.20) mg/L / 0.22 (0.13-0.30) mg/L / 0.45 (0.31-0.60) mg/L / 0.74 (0.49-1.1) mg/L / 1.7 (1.3-2.3) mg/L	Mortality (Mortality-Survival, Response Site: Not reported)	LOEC (0.12 (0.082-0.20) mg/L)	Mortality	High	5889402

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Aquatic: Arthropods Extraction Table

CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
556-67-2	14 Day(s), (14 Day(s))	*Chironomus tentans* (Midge), Larva, ~10 Day(s), Not Reported, Laboratory (CULTURED AT SPRING-BORN LABS)	Fresh water, Aqueous (aquatic habitat), Leaching , 12 Organism	Measured	<0.054 mg/L / <0.052-0.21 mg/L / 0.12 (0.082-0.20) mg/L / 0.22 (0.13-0.30) mg/L / 0.45 (0.31-0.60) mg/L / 0.74 (0.49-1.1) mg/L / 1.7 (1.3-2.3) mg/L	Growth (Growth-Weight, Response Site: Whole organism)	NOEC (1.7 (1.3-2.3) mg/L)	Development/Growth	High	5889402
556-67-2	14 Day(s), (14 Day(s))	*Chironomus tentans* (Midge), Larva, ~10 Day(s), Not Reported, Laboratory (CULTURED AT SPRING-BORN LABS)	Fresh water, Aqueous (aquatic habitat), Leaching , 7 Organism	Measured	<0.054 mg/L / <0.052-0.21 mg/L / 0.12 (0.082-0.20) mg/L / 0.22 (0.13-0.30) mg/L / 0.45 (0.31-0.60) mg/L / 0.74 (0.49-1.1) mg/L / 1.7 (1.3-2.3) mg/L	Accumulation (Accumulation-Residue, Response Site: Whole organism)	BCF (0.12 (0.082-0.20) mg/L)	Other (please specify below)	High	5889402
556-67-2	14 Day(s), (14 Day(s))	*Chironomus tentans* (Midge), Larva, ~10 Day(s), Not Reported, Laboratory (CULTURED AT SPRING-BORN LABS)	Fresh water, Aqueous (aquatic habitat), Sediment, 4 Organism	Measured	<9.9 mg/kg dw sediment / <8.1 mg/kg dw sediment / 16 (14-17) mg/kg dw sediment / 32 (27-46) mg/kg dw sediment / 59 (54-62) mg/kg dw sediment / 110 (94-120) mg/kg dw sediment / 200 (170-230) mg/kg dw sediment	Accumulation (Accumulation-Residue, Response Site: Whole organism)	BCF (32 (27-46) mg/kg dw sediment)	Other (please specify below)	High	5889402

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Aquatic: Arthropods Extraction Table

CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
556-67-2	14 Day(s), (14 Day(s))	*Chironomus tentans* (Midge), Larva, ~10 Day(s), Not Reported, Laboratory (CULTURED AT SPRINGBORN LABS)	Fresh water, Aqueous (aquatic habitat), Sediment, Not Reported	Measured	<9.9 mg/kg dw sediment / <8.1 mg/kg dw sediment / 16 (14-17) mg/kg dw sediment / 32 (27-46) mg/kg dw sediment / 59 (54-62) mg/kg dw sediment / 110 (94-120) mg/kg dw sediment / 200 (170-230) mg/kg dw sediment	Mortality (Mortality-Mortality, Response Site: Not reported)	LC50 (<16 (14-17) mg/kg dw sediment)	Mortality	High	5889402
556-67-2	14 Day(s), (14 Day(s))	*Chironomus tentans* (Midge), Larva, ~10 Day(s), Not Reported, Laboratory (CULTURED AT SPRINGBORN LABS)	Fresh water, Aqueous (aquatic habitat), Sediment, 13 Organism	Measured	<9.9 mg/kg dw sediment / <8.1 mg/kg dw sediment / 16 (14-17) mg/kg dw sediment / 32 (27-46) mg/kg dw sediment / 59 (54-62) mg/kg dw sediment / 110 (94-120) mg/kg dw sediment / 200 (170-230) mg/kg dw sediment	Mortality (Mortality-Survival, Response Site: Not reported)	LOEC (16 (14-17) mg/kg dw sediment)	Mortality	High	5889402

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Aquatic: Arthropods Extraction Table

CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
556-67-2	14 Day(s), (14 Day(s))	*Chironomus tentans* (Midge), Larva, ~10 Day(s), Not Reported, Laboratory (CULTURED AT SPRINGBORN LABS)	Fresh water, Aqueous (aquatic habitat), Sediment, 12 Organism	Measured	<9.9 mg/kg dw sediment / <8.1 mg/kg dw sediment / 16 (14-17) mg/kg dw sediment / 32 (27-46) mg/kg dw sediment / 59 (54-62) mg/kg dw sediment / 110 (94-120) mg/kg dw sediment / 200 (170-230) mg/kg dw sediment	Growth (Growth-Weight, Response Site: Whole organism)	NOEC (200 (170-230) mg/kg dw sediment)	Development/Growth	High	5889402
556-67-2	14 Day(s), (14 Day(s))	*Chironomus tentans* (Midge), Larva, ~10 Day(s), Not Reported, Laboratory (CULTURED AT SPRINGBORN LABS)	Fresh water, Aqueous (aquatic habitat), Sediment, 6 Organism	Measured	<9.9 mg/kg dw sediment / <8.1 mg/kg dw sediment / 16 (14-17) mg/kg dw sediment / 32 (27-46) mg/kg dw sediment / 59 (54-62) mg/kg dw sediment / 110 (94-120) mg/kg dw sediment / 200 (170-230) mg/kg dw sediment	Accumulation (Accumulation-Residue, Response Site: Whole organism)	BCF (16 (14-17) mg/kg dw sediment)	Other (please specify below)	High	5889402

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Aquatic: Arthropods Extraction Table

CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
556-67-2	14 Day(s), (14 Day(s))	*Chironomus tentans* (Midge), Larva, ~10 Day(s), Not Reported, Laboratory (CULTURED AT SPRINGBORN LABS)	Fresh water, Aqueous (aquatic habitat), Sediment, 7 Organism	Measured	<9.9 mg/kg dw sediment / <8.1 mg/kg dw sediment / 16 (14-17) mg/kg dw sediment / 32 (27-46) mg/kg dw sediment / 59 (54-62) mg/kg dw sediment / 110 (94-120) mg/kg dw sediment / 200 (170-230) mg/kg dw sediment	Accumulation (Accumulation-Residue, Response Site: Whole organism)	BCF (16 (14-17) mg/kg dw sediment)	Other (please specify below)	High	5889402
556-67-2	14 Day(s), (14 Day(s))	*Chironomus tentans* (Midge), Larva, ~10 Day(s), Not Reported, Laboratory (CULTURED AT SPRINGBORN LABS)	Fresh water, Aqueous (aquatic habitat), Leaching , 2 Organism	Measured	<0.054 mg/L / <0.052-0.21 mg/L / 0.12 (0.082-0.20) mg/L / 0.22 (0.13-0.30) mg/L / 0.45 (0.31-0.60) mg/L / 0.74 (0.49-1.1) mg/L / 1.7 (1.3-2.3) mg/L	Accumulation (Accumulation-Residue, Response Site: Whole organism)	BCF (0.22 (0.13-0.30) mg/L)	Other (please specify below)	High	5889402
556-67-2	14 Day(s), (14 Day(s))	*Chironomus tentans* (Midge), Larva, ~10 Day(s), Not Reported, Laboratory (CULTURED AT SPRINGBORN LABS)	Fresh water, Aqueous (aquatic habitat), Leaching , 4 Organism	Measured	<0.054 mg/L / <0.052-0.21 mg/L / 0.12 (0.082-0.20) mg/L / 0.22 (0.13-0.30) mg/L / 0.45 (0.31-0.60) mg/L / 0.74 (0.49-1.1) mg/L / 1.7 (1.3-2.3) mg/L	Accumulation (Accumulation-Residue, Response Site: Whole organism)	BCF (0.22 (0.13-0.30) mg/L)	Other (please specify below)	High	5889402

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Aquatic: Arthropods Extraction Table

CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
556-67-2	14 Day(s), (14 Day(s))	*Chironomus tentans* (Midge), Larva, ~10 Day(s), Not Reported, Laboratory (CULTURED AT SPRINGBORN LABS)	Fresh water, Aqueous (aquatic habitat), Leaching , Not Reported	Measured	<0.054 mg/L / <0.052-0.21 mg/L / 0.12 (0.082-0.20) mg/L / 0.22 (0.13-0.30) mg/L / 0.45 (0.31-0.60) mg/L / 0.74 (0.49-1.1) mg/L / 1.7 (1.3-2.3) mg/L	Mortality (Mortality-Mortality, Response Site: Not reported)	LC50 (<0.12 (0.082-0.20) mg/L)	Mortality	High	5889402
556-67-2	14 Day(s), (14 Day(s))	*Chironomus tentans* (Midge), Larva, ~10 Day(s), Not Reported, Laboratory (CULTURED AT SPRINGBORN LABS)	Fresh water, Aqueous (aquatic habitat), Sediment, 2 Organism	Measured	<9.9 mg/kg dw sediment / <8.1 mg/kg dw sediment / 16 (14-17) mg/kg dw sediment / 32 (27-46) mg/kg dw sediment / 59 (54-62) mg/kg dw sediment / 110 (94-120) mg/kg dw sediment / 200 (170-230) mg/kg dw sediment	Accumulation (Accumulation-Residue, Response Site: Whole organism)	BCF (32 (27-46) mg/kg dw sediment)	Other (please specify below)	High	5889402
556-67-2	14 Day(s), (14 Day(s))	*Chironomus tentans* (Midge), Larva, ~10 Day(s), Not Reported, Laboratory (SPRINGBORN LABORATORIES CULTURE)	Fresh water, Aqueous (aquatic habitat), Leaching , 18 Organism	Measured	<0.013 mg/L / <0.011 mg/L / 0.019 (0.011-0.028) mg/L / 0.034 (0.018-0.097) mg/L / 0.21 (0.10-0.26) mg/L / 1.0 mg/L / 1.1 (0.86-1.3) mg/L	Accumulation (Accumulation-Residue, Response Site: Whole organism)	BCF (0.019 (0.011-0.028) mg/L)	Other (please specify below)	High	5898831

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Aquatic: Arthropods Extraction Table

CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
556-67-2	14 Day(s), (14 Day(s))	*Chironomus tentans* (Midge), Larva, ~10 Day(s), Not Reported, Laboratory (SPRINGBORN LABORATORIES CULTURE)	Fresh water, Aqueous (aquatic habitat), Leaching , 21 Organism	Measured	<0.013 mg/L / <0.011 mg/L / 0.019 (0.011-0.028) mg/L / 0.034 (0.018-0.097) mg/L / 0.21 (0.10-0.26) mg/L / 1.0 mg/L / 1.1 (0.86-1.3) mg/L	Accumulation (Accumulation-Residue, Response Site: Whole organism)	BCF (0.019 (0.011-0.028) mg/L)	Other (please specify below)	High	5898831
556-67-2	14 Day(s), (14 Day(s))	*Chironomus tentans* (Midge), Larva, ~10 Day(s), Not Reported, Laboratory (SPRINGBORN LABORATORIES CULTURE)	Fresh water, Aqueous (aquatic habitat), Leaching , 20 Organism	Measured	<0.013 mg/L / <0.011 mg/L / 0.019 (0.011-0.028) mg/L / 0.034 (0.018-0.097) mg/L / 0.21 (0.10-0.26) mg/L / 1.0 mg/L / 1.1 (0.86-1.3) mg/L	Accumulation (Accumulation-Residue, Response Site: Whole organism)	BCF (1.0 mg/L)	Other (please specify below)	High	5898831
556-67-2	14 Day(s), (14 Day(s))	*Chironomus tentans* (Midge), Larva, ~10 Day(s), Not Reported, Laboratory (SPRINGBORN LABORATORIES CULTURE)	Fresh water, Aqueous (aquatic habitat), Leaching , 23 Organism	Measured	<0.013 mg/L / <0.011 mg/L / 0.019 (0.011-0.028) mg/L / 0.034 (0.018-0.097) mg/L / 0.21 (0.10-0.26) mg/L / 1.0 mg/L / 1.1 (0.86-1.3) mg/L	Accumulation (Accumulation-Residue, Response Site: Whole organism)	BCF (0.21 (0.10-0.26) mg/L)	Other (please specify below)	High	5898831
556-67-2	14 Day(s), (14 Day(s))	*Chironomus tentans* (Midge), Larva, ~10 Day(s), Not Reported, Laboratory (SPRINGBORN LABORATORIES CULTURE)	Fresh water, Aqueous (aquatic habitat), Leaching , 21 Organism	Measured	<0.013 mg/L / <0.011 mg/L / 0.019 (0.011-0.028) mg/L / 0.034 (0.018-0.097) mg/L / 0.21 (0.10-0.26) mg/L / 1.0 mg/L / 1.1 (0.86-1.3) mg/L	Accumulation (Accumulation-Residue, Response Site: Whole organism)	BCF (0.034 (0.018-0.097) mg/L)	Other (please specify below)	High	5898831

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Aquatic: Arthropods Extraction Table

CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
556-67-2	14 Day(s), (14 Day(s))	*Chironomus tentans* (Midge), Larva, ~10 Day(s), Not Reported, Laboratory (SPRINGBORN LABORATORIES CULTURE)	Fresh water, Aqueous (aquatic habitat), Leaching , 34 Organism	Measured	<0.013 mg/L / <0.011 mg/L / 0.019 (0.011-0.028) mg/L / 0.034 (0.018-0.097) mg/L / 0.21 (0.10-0.26) mg/L / 1.0 mg/L / 1.1 (0.86-1.3) mg/L	Mortality (Mortality-Survival, Response Site: Not reported)	LOEC (1.1 (0.86-1.3) mg/L)	Mortality	High	5898831
556-67-2	14 Day(s), (14 Day(s))	*Chironomus tentans* (Midge), Larva, ~10 Day(s), Not Reported, Laboratory (SPRINGBORN LABORATORIES CULTURE)	Fresh water, Aqueous (aquatic habitat), Leaching , Not Reported	Measured	<0.013 mg/L / <0.011 mg/L / 0.019 (0.011-0.028) mg/L / 0.034 (0.018-0.097) mg/L / 0.21 (0.10-0.26) mg/L / 1.0 mg/L / 1.1 (0.86-1.3) mg/L	Mortality (Mortality-Mortality, Response Site: Not reported)	LC50 (>1.1 (0.86-1.3) mg/L)	Mortality	High	5898831
556-67-2	14 Day(s), (14 Day(s))	*Chironomus tentans* (Midge), Larva, ~10 Day(s), Not Reported, Laboratory (SPRINGBORN LABORATORIES CULTURE)	Fresh water, Aqueous (aquatic habitat), Leaching , 23 Organism	Measured	<0.013 mg/L / <0.011 mg/L / 0.019 (0.011-0.028) mg/L / 0.034 (0.018-0.097) mg/L / 0.21 (0.10-0.26) mg/L / 1.0 mg/L / 1.1 (0.86-1.3) mg/L	Accumulation (Accumulation-Residue, Response Site: Whole organism)	BCF (1.0 mg/L)	Other (please specify below)	High	5898831
556-67-2	14 Day(s), (14 Day(s))	*Chironomus tentans* (Midge), Larva, ~10 Day(s), Not Reported, Laboratory (SPRINGBORN LABORATORIES CULTURE)	Fresh water, Aqueous (aquatic habitat), Leaching , 21 Organism	Measured	<0.013 mg/L / <0.011 mg/L / 0.019 (0.011-0.028) mg/L / 0.034 (0.018-0.097) mg/L / 0.21 (0.10-0.26) mg/L / 1.0 mg/L / 1.1 (0.86-1.3) mg/L	Accumulation (Accumulation-Residue, Response Site: Whole organism)	BCF (0.21 (0.10-0.26) mg/L)	Other (please specify below)	High	5898831

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Aquatic: Arthropods Extraction Table

CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
556-67-2	14 Day(s), (14 Day(s))	*Chironomus tentans* (Midge), Larva, ~10 Day(s), Not Reported, Laboratory (SPRINGBORN LABORATORIES CULTURE)	Fresh water, Aqueous (aquatic habitat), Leaching , 43 Organism	Measured	<0.013 mg/L / <0.011 mg/L / 0.019 (0.011-0.028) mg/L / 0.034 (0.018-0.097) mg/L / 0.21 (0.10-0.26) mg/L / 1.0 mg/L / 1.1 (0.86-1.3) mg/L	Mortality (Mortality-Survival, Response Site: Not reported)	NOEC (1.0 mg/L)	Mortality	High	5898831
556-67-2	14 Day(s), (14 Day(s))	*Chironomus tentans* (Midge), Larva, ~10 Day(s), Not Reported, Laboratory (SPRINGBORN LABORATORIES CULTURE)	Fresh water, Aqueous (aquatic habitat), Sediment, 23 Organism	Measured	<0.48 mg/kg dw sediment / <=0.96 mg/kg dw sediment / 2.6 (2.3-2.9) mg/kg dw sediment / 7.4 (6.7-9.1) mg/kg dw sediment / 19 (17-22) mg/kg dw sediment / 54 (49-60) mg/kg dw sediment / 170 (150-180) mg/kg dw sediment	Accumulation (Accumulation-Residue, Response Site: Whole organism)	BCF (19 (17-22) mg/kg dw sediment)	Other (please specify below)	High	5898831

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Aquatic: Arthropods Extraction Table

CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
556-67-2	14 Day(s), (14 Day(s))	*Chironomus tentans* (Midge), Larva, ~10 Day(s), Not Reported, Laboratory (SPRINGBORN LABORATORIES CULTURE)	Fresh water, Aqueous (aquatic habitat), Sediment, 18 Organism	Measured	<0.48 mg/kg dw sediment / <=0.96 mg/kg dw sediment / 2.6 (2.3-2.9) mg/kg dw sediment / 7.4 (6.7-9.1) mg/kg dw sediment / 19 (17-22) mg/kg dw sediment / 54 (49-60) mg/kg dw sediment / 170 (150-180) mg/kg dw sediment	Accumulation (Accumulation-Residue, Response Site: Whole organism)	BCF (2.6 (2.3-2.9) mg/kg dw sediment)	Other (please specify below)	High	5898831
556-67-2	14 Day(s), (14 Day(s))	*Chironomus tentans* (Midge), Larva, ~10 Day(s), Not Reported, Laboratory (SPRINGBORN LABORATORIES CULTURE)	Fresh water, Aqueous (aquatic habitat), Sediment, 20 Organism	Measured	<0.48 mg/kg dw sediment / <=0.96 mg/kg dw sediment / 2.6 (2.3-2.9) mg/kg dw sediment / 7.4 (6.7-9.1) mg/kg dw sediment / 19 (17-22) mg/kg dw sediment / 54 (49-60) mg/kg dw sediment / 170 (150-180) mg/kg dw sediment	Accumulation (Accumulation-Residue, Response Site: Whole organism)	BCF (54 (49-60) mg/kg dw sediment)	Other (please specify below)	High	5898831

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Aquatic: Arthropods Extraction Table

CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
556-67-2	14 Day(s), (14 Day(s))	*Chironomus tentans* (Midge), Larva, ~10 Day(s), Not Reported, Laboratory (SPRINGBORN LABORATORIES CULTURE)	Fresh water, Aqueous (aquatic habitat), Sediment, 23 Organism	Measured	<0.48 mg/kg dw sediment / <=0.96 mg/kg dw sediment / 2.6 (2.3-2.9) mg/kg dw sediment / 7.4 (6.7-9.1) mg/kg dw sediment / 19 (17-22) mg/kg dw sediment / 54 (49-60) mg/kg dw sediment / 170 (150-180) mg/kg dw sediment	Accumulation (Accumulation-Residue, Response Site: Whole organism)	BCF (54 (49-60) mg/kg dw sediment)	Other (please specify below)	High	5898831
556-67-2	14 Day(s), (14 Day(s))	*Chironomus tentans* (Midge), Larva, ~10 Day(s), Not Reported, Laboratory (SPRINGBORN LABORATORIES CULTURE)	Fresh water, Aqueous (aquatic habitat), Sediment, 15 Organism	Measured	<0.48 mg/kg dw sediment / <=0.96 mg/kg dw sediment / 2.6 (2.3-2.9) mg/kg dw sediment / 7.4 (6.7-9.1) mg/kg dw sediment / 19 (17-22) mg/kg dw sediment / 54 (49-60) mg/kg dw sediment / 170 (150-180) mg/kg dw sediment	Accumulation (Accumulation-Residue, Response Site: Whole organism)	BCF (7.4 (6.7-9.1) mg/kg dw sediment)	Other (please specify below)	High	5898831

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Aquatic: Arthropods Extraction Table

CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
556-67-2	14 Day(s), (14 Day(s))	*Chironomus tentans* (Midge), Larva, ~10 Day(s), Not Reported, Laboratory (SPRINGBORN LABORATORIES CULTURE)	Fresh water, Aqueous (aquatic habitat), Sediment, 21 Organism	Measured	<0.48 mg/kg dw sediment / <=0.96 mg/kg dw sediment / 2.6 (2.3-2.9) mg/kg dw sediment / 7.4 (6.7-9.1) mg/kg dw sediment / 19 (17-22) mg/kg dw sediment / 54 (49-60) mg/kg dw sediment / 170 (150-180) mg/kg dw sediment	Accumulation (Accumulation-Residue, Response Site: Whole organism)	BCF (7.4 (6.7-9.1) mg/kg dw sediment)	Other (please specify below)	High	5898831
556-67-2	14 Day(s), (14 Day(s))	*Chironomus tentans* (Midge), Larva, ~10 Day(s), Not Reported, Laboratory (SPRINGBORN LABORATORIES CULTURE)	Fresh water, Aqueous (aquatic habitat), Sediment, 21 Organism	Measured	<0.48 mg/kg dw sediment / <=0.96 mg/kg dw sediment / 2.6 (2.3-2.9) mg/kg dw sediment / 7.4 (6.7-9.1) mg/kg dw sediment / 19 (17-22) mg/kg dw sediment / 54 (49-60) mg/kg dw sediment / 170 (150-180) mg/kg dw sediment	Accumulation (Accumulation-Residue, Response Site: Whole organism)	BCF (2.6 (2.3-2.9) mg/kg dw sediment)	Other (please specify below)	High	5898831

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Aquatic: Arthropods Extraction Table

CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
556-67-2	14 Day(s), (14 Day(s))	*Chironomus tentans* (Midge), Larva, ~10 Day(s), Not Reported, Laboratory (SPRINGBORN LABORATORIES CULTURE)	Fresh water, Aqueous (aquatic habitat), Leaching , 34-43 Organism	Measured	<0.013 mg/L / <0.011 mg/L / 0.019 (0.011-0.028) mg/L / 0.034 (0.018-0.097) mg/L / 0.21 (0.10-0.26) mg/L / 1.0 mg/L / 1.1 (0.86-1.3) mg/L	Mortality (Mortality-Survival, Response Site: Not reported)	MATC (1.0 (1.0-1.1) mg/L)	Mortality	High	5898831
556-67-2	14 Day(s), (14 Day(s))	*Chironomus tentans* (Midge), Larva, ~10 Day(s), Not Reported, Laboratory (SPRINGBORN LABORATORIES CULTURE)	Fresh water, Aqueous (aquatic habitat), Sediment, 21 Organism	Measured	<0.48 mg/kg dw sediment / <=0.96 mg/kg dw sediment / 2.6 (2.3-2.9) mg/kg dw sediment / 7.4 (6.7-9.1) mg/kg dw sediment / 19 (17-22) mg/kg dw sediment / 54 (49-60) mg/kg dw sediment / 170 (150-180) mg/kg dw sediment	Accumulation (Accumulation-Residue, Response Site: Whole organism)	BCF (19 (17-22) mg/kg dw sediment)	Other (please specify below)	High	5898831
556-67-2	14 Day(s), (14 Day(s))	*Chironomus tentans* (Midge), Larva, ~10 Day(s), Not Reported, Laboratory (SPRINGBORN LABORATORIES CULTURE)	Fresh water, Aqueous (aquatic habitat), Leaching , 34 Organism	Measured	<0.013 mg/L / <0.011 mg/L / 0.019 (0.011-0.028) mg/L / 0.034 (0.018-0.097) mg/L / 0.21 (0.10-0.26) mg/L / 1.0 mg/L / 1.1 (0.86-1.3) mg/L	Growth (Growth-Weight, Response Site: Whole organism)	NOEC (1.1 (0.86-1.3) mg/L)	Development/Growth	High	5898831

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Aquatic: Arthropods Extraction Table

CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
556-67-2	14 Day(s), (14 Day(s))	*Chironomus tentans* (Midge), Larva, ~10 Day(s), Not Reported, Laboratory (SPRINGBORN LABORATORIES CULTURE)	Fresh water, Aqueous (aquatic habitat), Leaching , 15 Organism	Measured	<0.013 mg/L / <0.011 mg/L / 0.019 (0.011-0.028) mg/L / 0.034 (0.018-0.097) mg/L / 0.21 (0.10-0.26) mg/L / 1.0 mg/L / 1.1 (0.86-1.3) mg/L	Accumulation (Accumulation-Residue, Response Site: Whole organism)	BCF (0.034 (0.018-0.097) mg/L)	Other (please specify below)	High	5898831
556-67-2	24 Hour(s), (24 Hour(s))	*Daphnia magna* (Water Flea), Multiple, Not Reported, Laboratory	Fresh water, Aqueous (aquatic habitat), Flow-through, Not Reported	Measured	0 ug/L / 24.8-50.8 ug/L	Mortality (Mortality-Mortality, Response Site: Not reported)	NR (24.8-50.8 ug/L)	ADME (biotransformation)	Medium	5885396
556-67-2	24 Hour(s), (24 Hour(s))	*Daphnia magna* (Water Flea), Multiple, Not Reported, Laboratory	Fresh water, Aqueous (aquatic habitat), Flow-through, Not Reported	Measured	0 ug/L / 24.8-50.8 ug/L	Accumulation (Accumulation-Residue, Response Site: Whole organism)	BCF (24.8-50.8 ug/L)	ADME (biotransformation)	Medium	5885396
556-67-2	72 Hour(s), (72 Hour(s))	*Daphnia magna* (Water Flea), Not reported, Not Reported, Not reported	Fresh water, Aqueous (aquatic habitat), Aquatic - not reported, Not Reported	Unmeasured	0 ppm / 3.125 ppm / 6.25 ppm / 10.0 ppm / 12.5 ppm / 100 ppm / 250 ppm / 500 ppm / 750 ppm / 1000 ppm	Mortality (Mortality-Mortality, Response Site: Not reported)	LC50 (23.44 (14.53-35.73) ppm)	Mortality	Medium	5900580
556-67-2	72 Hour(s), (72 Hour(s))	*Daphnia magna* (Water Flea), Not reported, Not Reported, Not reported	Fresh water, Aqueous (aquatic habitat), Aquatic - not reported, Not Reported	Unmeasured	0 ppm / 3.125 ppm / 6.25 ppm / 10.0 ppm / 12.5 ppm / 100 ppm / 250 ppm / 500 ppm / 750 ppm / 1000 ppm	Mortality (Mortality-Mortality, Response Site: Not reported)	LC10 (1.85 (0.65-3.68) ppm)	Mortality	Medium	5900580

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Aquatic: Arthropods Extraction Table

CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
556-67-2	72 Hour(s), (72 Hour(s))	*Daphnia magna* (Water Flea), Not reported, Not Reported, Not reported	Fresh water, Aqueous (aquatic habitat), Aquatic - not reported, Not Reported	Unmeasured	0 ppm / 3.125 ppm / 6.25 ppm / 10.0 ppm / 12.5 ppm / 100 ppm / 250 ppm / 500 ppm / 750 ppm / 1000 ppm	Mortality (Mortality-Mortality, Response Site: Not reported)	LC90 (297.74 (171.63-657.20) ppm)	Mortality	Medium	5900580
556-67-2	21 Day(s), (21 Day(s))	*Daphnia magna* (Water Flea), Flower opening, <24 Hour(s), Not Reported, Laboratory (CONTINUOUS LABORATORY CULTURES)	Fresh water, Aqueous (aquatic habitat), Renewal, Not Reported	Unmeasured	0 mg/L / 10 mg/L / 10 mg/L / 100 mg/L	Mortality (Mortality-Mortality, Response Site: Not reported)	NR-ZERO (100 mg/L)	Mortality	High	5903815
556-67-2	21 Day(s), (21 Day(s))	*Daphnia magna* (Water Flea), Flower opening, <24 Hour(s), Not Reported, Laboratory (CONTINUOUS LABORATORY CULTURES)	Fresh water, Aqueous (aquatic habitat), Renewal, Not Reported	Unmeasured	0 mg/L / 10 mg/L / 10 mg/L / 100 mg/L	Reproduction (Reproduction-Progeny counts/numbers, Response Site: Not reported)	NOEC (100 mg/L)	Reproductive/Teratogenic	High	5903815
556-67-2	48 Hour(s), (48 Hour(s))	*Daphnia magna* (Water Flea), <24 Hour(s), Not Reported, Laboratory (SPRINGBORN LABORATORIES)	Fresh water, Aqueous (aquatic habitat), Flow-through, Not Reported	Measured	0 ug/L / 1.7 ug/L / 2.9 ug/L / 3.7 ug/L / 7.8 ug/L / 15 ug/L	Physiology (Intoxication-Immobile, Response Site: Not reported)	EC50 (>15 ug/L)	Immobilization	High	6834101
556-67-2	48 Hour(s), (48 Hour(s))	*Daphnia magna* (Water Flea), <24 Hour(s), Not Reported, Laboratory (SPRINGBORN LABORATORIES)	Fresh water, Aqueous (aquatic habitat), Flow-through, Not Reported	Measured	0 ug/L / 1.7 ug/L / 2.9 ug/L / 3.7 ug/L / 7.8 ug/L / 15 ug/L	Physiology (Intoxication-Immobile, Response Site: Not reported)	NOEC (15 ug/L)	Immobilization	High	6834101

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Aquatic: Arthropods Extraction Table

CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
556-67-2	21 Day(s), (21 Day(s))	*Daphnia magna* (Water Flea), <24 Hour(s), Not Reported, Laboratory (SPRINGBORN LABORATORIES)	Fresh water, Aqueous (aquatic habitat), Flow-through, Not Reported	Measured	0 ug/L / 1.7 ug/L / 1.8 ug/L / 4.2 ug/L / 7.9 ug/L / 15 ug/L	Reproduction (Reproduction-Progeny counts/numbers, Response Site: Not reported)	NOEC (7.9 ug/L)	Reproductive/Teratogenic	High	6834101
556-67-2	21 Day(s), (21 Day(s))	*Daphnia magna* (Water Flea), <24 Hour(s), Not Reported, Laboratory (SPRINGBORN LABORATORIES)	Fresh water, Aqueous (aquatic habitat), Flow-through, Not Reported	Measured	0 ug/L / 1.7 ug/L / 1.8 ug/L / 4.2 ug/L / 7.9 ug/L / 15 ug/L	Mortality (Mortality-Survival, Response Site: Not reported)	NOEC (7.9 ug/L)	Mortality	High	6834101
556-67-2	21 Day(s), (21 Day(s))	*Daphnia magna* (Water Flea), <24 Hour(s), Not Reported, Laboratory (SPRINGBORN LABORATORIES)	Fresh water, Aqueous (aquatic habitat), Flow-through, Not Reported	Measured	0 ug/L / 1.7 ug/L / 1.8 ug/L / 4.2 ug/L / 7.9 ug/L / 15 ug/L	Reproduction (Reproduction-Progeny counts/numbers, Response Site: Not reported)	LOEC (15 ug/L)	Reproductive/Teratogenic	High	6834101
556-67-2	21 Day(s), (21 Day(s))	*Daphnia magna* (Water Flea), <24 Hour(s), Not Reported, Laboratory (SPRINGBORN LABORATORIES)	Fresh water, Aqueous (aquatic habitat), Flow-through, Not Reported	Measured	0 ug/L / 1.7 ug/L / 1.8 ug/L / 4.2 ug/L / 7.9 ug/L / 15 ug/L	Mortality (Mortality-Survival, Response Site: Not reported)	LOEC (15 ug/L)	Mortality	High	6834101
556-67-2	21 Day(s), (21 Day(s))	*Daphnia magna* (Water Flea), <24 Hour(s), Not Reported, Laboratory (SPRINGBORN LABORATORIES)	Fresh water, Aqueous (aquatic habitat), Flow-through, Not Reported	Measured	0 ug/L / 1.7 ug/L / 1.8 ug/L / 4.2 ug/L / 7.9 ug/L / 15 ug/L	Physiology (Intoxication-Immobile, Response Site: Not reported)	EC50 (>15 ug/L)	Immobilization	High	6834101

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Aquatic: Arthropods Extraction Table

CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
556-67-2	48 Hour(s), (48 Hour(s))	*Daphnia magna* (Water Flea), <=24 Hour(s), Not Reported, Laboratory (LABORATORY CULTURES MAINTAINED AT SPRING-BORN LABORATORIES, INC., WAREHAM, MASSACHUSETTS)	Fresh water, Aqueous (aquatic habitat), Flow-through, Not Reported	Measured	<1.00 AI ug/L / 1.7 (1.3-2.1) AI ug/L / 2.9 (2.3-3.9) AI ug/L / 3.7 (3.1-4.7) AI ug/L / 7.8 (4.0-9.0) AI ug/L / 15 (13-18) AI ug/L	Multiple (Multiple-Multiple effects reported as one result, Response Site: Not reported)	NOEC (15 (13-18) AI ug/L)	Behavioral	High	5889395
556-67-2	48 Hour(s), (48 Hour(s))	*Daphnia magna* (Water Flea), <=24 Hour(s), Not Reported, Laboratory (LABORATORY CULTURES MAINTAINED AT SPRING-BORN LABORATORIES, INC., WAREHAM, MASSACHUSETTS)	Fresh water, Aqueous (aquatic habitat), Flow-through, Not Reported	Unmeasured	0 % sat / 13 % sat / NR / NR / NR / 100 % sat	Behavior (Behavior-Displaying behavior,Swimming, Response Site: Not reported)	NR (13-100 % sat)	Behavioral	High	5889395
556-67-2	48 Hour(s), (48 Hour(s))	*Daphnia magna* (Water Flea), <=24 Hour(s), Not Reported, Laboratory (LABORATORY CULTURES MAINTAINED AT SPRING-BORN LABORATORIES, INC., WAREHAM, MASSACHUSETTS)	Fresh water, Aqueous (aquatic habitat), Flow-through, Not Reported	Measured	<1.00 AI ug/L / 1.7 (1.3-2.1) AI ug/L / 2.9 (2.3-3.9) AI ug/L / 3.7 (3.1-4.7) AI ug/L / 7.8 (4.0-9.0) AI ug/L / 15 (13-18) AI ug/L	Mortality (Mortality-Mortality, Response Site: Not reported)	NR-ZERO (15 (13-18) AI ug/L)	Immobilization	High	5889395

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Aquatic: Arthropods Extraction Table

CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
556-67-2	48 Hour(s), (48 Hour(s))	*Daphnia magna* (Water Flea), <=24 Hour(s), Not Reported, Laboratory (LABORATORY CULTURES MAINTAINED AT SPRING-BORN LABORATORIES, INC., WAREHAM, MASSACHUSETTS)	Fresh water, Aqueous (aquatic habitat), Flow-through, Not Reported	Measured	<1.00 AI ug/L / 1.7 (1.3-2.1) AI ug/L / 2.9 (2.3-3.9) AI ug/L / 3.7 (3.1-4.7) AI ug/L / 7.8 (4.0-9.0) AI ug/L / 15 (13-18) AI ug/L	Physiology (Intoxication-Immobile, Response Site: Not reported)	EC50 (>15 AI ug/L)	Immobilization	High	5889395
556-67-2	48 Hour(s), (48 Hour(s))	*Daphnia magna* (Water Flea), <=24 Hour(s), Not Reported, Laboratory (LABORATORY CULTURES MAINTAINED AT SPRING-BORN LABORATORIES, INC., WAREHAM, MASSACHUSETTS)	Fresh water, Aqueous (aquatic habitat), Flow-through, Not Reported	Unmeasured	0 % sat / 13 % sat / NR / NR / NR / 100 % sat	Mortality (Mortality-Mortality, Response Site: Not reported)	NR-ZERO (100 % sat)	Immobilization	High	5889395
556-67-2	1 Day(s), (21 Day(s))	*Daphnia magna* (Water Flea), <=24 Hour(s), Not Reported, Laboratory (OBTAINED FROM LABORATORY CULTURES MAINTAINED AT SPRING-BORN LABORATORIES, INC., WAREHAM, MASSACHUSETTS)	Fresh water, Aqueous (aquatic habitat), Flow-through, Not Reported	Measured	<1.0 ug/L / 1.7 (<1.0-2.3) ug/L / 1.8 (<1.0-2.8) ug/L / 4.2 (2.9-5.9) ug/L / 7.9 (6.6-10) ug/L / 15 (13-20) ug/L	Mortality (Mortality-Survival, Response Site: Not reported)	NOEC (15 (13-20) ug/L)	Mortality	High	7006323

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Aquatic: Arthropods Extraction Table

CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
556-67-2	2 Day(s), (21 Day(s))	*Daphnia magna* (Water Flea), <=24 Hour(s), Not Reported, Laboratory (OBTAINED FROM LABORATORY CULTURES MAINTAINED AT SPRING-BORN LABORATORIES, INC., WAREHAM, MASSACHUSETTS)	Fresh water, Aqueous (aquatic habitat), Flow-through, Not Reported	Measured	<1.0 ug/L / 1.7 (<1.0-2.3) ug/L / 1.8 (<1.0-2.8) ug/L / 4.2 (2.9-5.9) ug/L / 7.9 (6.6-10) ug/L / 15 (13-20) ug/L	Mortality (Mortality-Survival, Response Site: Not reported)	NOEC (15 (13-20) ug/L)	Mortality	High	7006323
556-67-2	4 Day(s), (21 Day(s))	*Daphnia magna* (Water Flea), <=24 Hour(s), Not Reported, Laboratory (OBTAINED FROM LABORATORY CULTURES MAINTAINED AT SPRING-BORN LABORATORIES, INC., WAREHAM, MASSACHUSETTS)	Fresh water, Aqueous (aquatic habitat), Flow-through, Not Reported	Measured	<1.0 ug/L / 1.7 (<1.0-2.3) ug/L / 1.8 (<1.0-2.8) ug/L / 4.2 (2.9-5.9) ug/L / 7.9 (6.6-10) ug/L / 15 (13-20) ug/L	Mortality (Mortality-Survival, Response Site: Not reported)	NOEC (15 (13-20) ug/L)	Mortality	High	7006323
556-67-2	7 Day(s), (7 Day(s))	*Daphnia magna* (Water Flea), <=24 Hour(s), Not Reported, Laboratory (OBTAINED FROM LABORATORY CULTURES MAINTAINED AT SPRING-BORN LABORATORIES, INC., WAREHAM, MASSACHUSETTS)	Fresh water, Aqueous (aquatic habitat), Flow-through, Not Reported	Unmeasured	NR / NR / NR / NR / NR / 100 % sat	Mortality (Mortality-Mortality, Response Site: Not reported)	NR (NR)	Mortality	High	7006323

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CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
556-67-2	7 Day(s), (21 Day(s))	*Daphnia magna* (Water Flea), <=24 Hour(s), Not Reported, Laboratory (OBTAINED FROM LABORATORY CULTURES MAINTAINED AT SPRING-BORN LABORATORIES, INC., WAREHAM, MASSACHUSETTS)	Fresh water, Aqueous (aquatic habitat), Flow-through, Not Reported	Measured	<1.0 ug/L / 1.7 (<1.0-2.3) ug/L / 1.8 (<1.0-2.8) ug/L / 4.2 (2.9-5.9) ug/L / 7.9 (6.6-10) ug/L / 15 (13-20) ug/L	Reproduction (Reproduction-Progeny counts/numbers, Response Site: Not reported)	NOEC (15 (13-20) ug/L)	Reproductive/Teratogenic	High	7006323
556-67-2	7 Day(s), (7 Day(s))	*Daphnia magna* (Water Flea), <=24 Hour(s), Not Reported, Laboratory (OBTAINED FROM LABORATORY CULTURES MAINTAINED AT SPRING-BORN LABORATORIES, INC., WAREHAM, MASSACHUSETTS)	Fresh water, Aqueous (aquatic habitat), Flow-through, Not Reported	Unmeasured	NR / NR / NR / NR / NR / 100 % sat	Reproduction (Reproduction-Progeny counts/numbers, Response Site: Not reported)	NR (NR)	Reproductive/Teratogenic	High	7006323
556-67-2	7 Day(s), (21 Day(s))	*Daphnia magna* (Water Flea), <=24 Hour(s), Not Reported, Laboratory (OBTAINED FROM LABORATORY CULTURES MAINTAINED AT SPRING-BORN LABORATORIES, INC., WAREHAM, MASSACHUSETTS)	Fresh water, Aqueous (aquatic habitat), Flow-through, Not Reported	Measured	<1.0 ug/L / 1.7 (<1.0-2.3) ug/L / 1.8 (<1.0-2.8) ug/L / 4.2 (2.9-5.9) ug/L / 7.9 (6.6-10) ug/L / 15 (13-20) ug/L	Mortality (Mortality-Survival, Response Site: Not reported)	NOEC (15 (13-20) ug/L)	Mortality	High	7006323

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CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
556-67-2	10 Day(s), (21 Day(s))	*Daphnia magna* (Water Flea), <=24 Hour(s), Not Reported, Laboratory (OBTAINED FROM LABORATORY CULTURES MAINTAINED AT SPRING-BORN LABORATORIES, INC., WAREHAM, MASSACHUSETTS)	Fresh water, Aqueous (aquatic habitat), Flow-through, Not Reported	Measured	<1.0 ug/L / 1.7 (<1.0-2.3) ug/L / 1.8 (<1.0-2.8) ug/L / 4.2 (2.9-5.9) ug/L / 7.9 (6.6-10) ug/L / 15 (13-20) ug/L	Reproduction (Reproduction-Progeny counts/numbers, Response Site: Not reported)	NOEC (15 (13-20) ug/L)	Reproductive/Teratogenic	High	7006323
556-67-2	12 Day(s), (21 Day(s))	*Daphnia magna* (Water Flea), <=24 Hour(s), Not Reported, Laboratory (OBTAINED FROM LABORATORY CULTURES MAINTAINED AT SPRING-BORN LABORATORIES, INC., WAREHAM, MASSACHUSETTS)	Fresh water, Aqueous (aquatic habitat), Flow-through, Not Reported	Measured	<1.0 ug/L / 1.7 (<1.0-2.3) ug/L / 1.8 (<1.0-2.8) ug/L / 4.2 (2.9-5.9) ug/L / 7.9 (6.6-10) ug/L / 15 (13-20) ug/L	Reproduction (Reproduction-Progeny counts/numbers, Response Site: Not reported)	NOEC (15 (13-20) ug/L)	Reproductive/Teratogenic	High	7006323
556-67-2	14 Day(s), (21 Day(s))	*Daphnia magna* (Water Flea), <=24 Hour(s), Not Reported, Laboratory (OBTAINED FROM LABORATORY CULTURES MAINTAINED AT SPRING-BORN LABORATORIES, INC., WAREHAM, MASSACHUSETTS)	Fresh water, Aqueous (aquatic habitat), Flow-through, Not Reported	Measured	<1.0 ug/L / 1.7 (<1.0-2.3) ug/L / 1.8 (<1.0-2.8) ug/L / 4.2 (2.9-5.9) ug/L / 7.9 (6.6-10) ug/L / 15 (13-20) ug/L	Reproduction (Reproduction-Progeny counts/numbers, Response Site: Not reported)	NOEC (15 (13-20) ug/L)	Reproductive/Teratogenic	High	7006323

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CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
556-67-2	14 Day(s), (21 Day(s))	*Daphnia magna* (Water Flea), <=24 Hour(s), Not Reported, Laboratory (OBTAINED FROM LABORATORY CULTURES MAINTAINED AT SPRING-BORN LABORATORIES, INC., WAREHAM, MASSACHUSETTS)	Fresh water, Aqueous (aquatic habitat), Flow-through, Not Reported	Measured	<1.0 ug/L / 1.7 (<1.0-2.3) ug/L / 1.8 (<1.0-2.8) ug/L / 4.2 (2.9-5.9) ug/L / 7.9 (6.6-10) ug/L / 15 (13-20) ug/L	Mortality (Mortality-Survival, Response Site: Not reported)	NOEC (15 (13-20) ug/L)	Mortality	High	7006323
556-67-2	17 Day(s), (21 Day(s))	*Daphnia magna* (Water Flea), <=24 Hour(s), Not Reported, Laboratory (OBTAINED FROM LABORATORY CULTURES MAINTAINED AT SPRING-BORN LABORATORIES, INC., WAREHAM, MASSACHUSETTS)	Fresh water, Aqueous (aquatic habitat), Flow-through, Not Reported	Measured	<1.0 ug/L / 1.7 (<1.0-2.3) ug/L / 1.8 (<1.0-2.8) ug/L / 4.2 (2.9-5.9) ug/L / 7.9 (6.6-10) ug/L / 15 (13-20) ug/L	Reproduction (Reproduction-Progeny counts/numbers, Response Site: Not reported)	NOEC (15 (13-20) ug/L)	Reproductive/Teratogenic	High	7006323
556-67-2	19 Day(s), (21 Day(s))	*Daphnia magna* (Water Flea), <=24 Hour(s), Not Reported, Laboratory (OBTAINED FROM LABORATORY CULTURES MAINTAINED AT SPRING-BORN LABORATORIES, INC., WAREHAM, MASSACHUSETTS)	Fresh water, Aqueous (aquatic habitat), Flow-through, Not Reported	Measured	<1.0 ug/L / 1.7 (<1.0-2.3) ug/L / 1.8 (<1.0-2.8) ug/L / 4.2 (2.9-5.9) ug/L / 7.9 (6.6-10) ug/L / 15 (13-20) ug/L	Reproduction (Reproduction-Progeny counts/numbers, Response Site: Not reported)	NOEC (15 (13-20) ug/L)	Reproductive/Teratogenic	High	7006323

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Aquatic: Arthropods Extraction Table

CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
556-67-2	21 Day(s), (21 Day(s))	*Daphnia magna* (Water Flea), <=24 Hour(s), Not Reported, Laboratory (OBTAINED FROM LABORATORY CULTURES MAINTAINED AT SPRING-BORN LABORATORIES, INC., WAREHAM, MASSACHUSETTS)	Fresh water, Aqueous (aquatic habitat), Flow-through, Not Reported	Measured	<1.0 ug/L / 1.7 (<1.0-2.3) ug/L / 1.8 (<1.0-2.8) ug/L / 4.2 (2.9-5.9) ug/L / 7.9 (6.6-10) ug/L / 15 (13-20) ug/L	Mortality (Mortality-Survival, Response Site: Not reported)	NOEC (7.9 (6.6-10) ug/L)	Mortality	High	7006323
556-67-2	21 Day(s), (21 Day(s))	*Daphnia magna* (Water Flea), <=24 Hour(s), Not Reported, Laboratory (OBTAINED FROM LABORATORY CULTURES MAINTAINED AT SPRING-BORN LABORATORIES, INC., WAREHAM, MASSACHUSETTS)	Fresh water, Aqueous (aquatic habitat), Flow-through, Not Reported	Measured	<1.0 ug/L / 1.7 (<1.0-2.3) ug/L / 1.8 (<1.0-2.8) ug/L / 4.2 (2.9-5.9) ug/L / 7.9 (6.6-10) ug/L / 15 (13-20) ug/L	Physiology (Intoxication-Immobile, Response Site: Not reported)	EC50 (>15 ug/L)	Mortality	High	7006323
556-67-2	21 Day(s), (21 Day(s))	*Daphnia magna* (Water Flea), <=24 Hour(s), Not Reported, Laboratory (OBTAINED FROM LABORATORY CULTURES MAINTAINED AT SPRING-BORN LABORATORIES, INC., WAREHAM, MASSACHUSETTS)	Fresh water, Aqueous (aquatic habitat), Flow-through, Not Reported	Measured	<1.0 ug/L / 1.7 (<1.0-2.3) ug/L / 1.8 (<1.0-2.8) ug/L / 4.2 (2.9-5.9) ug/L / 7.9 (6.6-10) ug/L / 15 (13-20) ug/L	Mortality (Mortality-Survival, Response Site: Not reported)	LOEC (15 (13-20) ug/L)	Mortality	High	7006323

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Aquatic: Arthropods Extraction Table

CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
556-67-2	21 Day(s), (21 Day(s))	*Daphnia magna* (Water Flea), <=24 Hour(s), Not Reported, Laboratory (OBTAINED FROM LABORATORY CULTURES MAINTAINED AT SPRING-BORN LABORATORIES, INC., WAREHAM, MASSACHUSETTS)	Fresh water, Aqueous (aquatic habitat), Flow-through, Not Reported	Measured	<1.0 ug/L / 1.7 (<1.0-2.3) ug/L / 1.8 (<1.0-2.8) ug/L / 4.2 (2.9-5.9) ug/L / 7.9 (6.6-10) ug/L / 15 (13-20) ug/L	Mortality (Mortality-Mortality, Response Site: Not reported)	MATC (11 (7.9-15) ug/L)	Mortality	High	7006323
556-67-2	21 Day(s), (21 Day(s))	*Daphnia magna* (Water Flea), <=24 Hour(s), Not Reported, Laboratory (OBTAINED FROM LABORATORY CULTURES MAINTAINED AT SPRING-BORN LABORATORIES, INC., WAREHAM, MASSACHUSETTS)	Fresh water, Aqueous (aquatic habitat), Flow-through, Not Reported	Measured	<1.0 ug/L / 1.7 (<1.0-2.3) ug/L / 1.8 (<1.0-2.8) ug/L / 4.2 (2.9-5.9) ug/L / 7.9 (6.6-10) ug/L / 15 (13-20) ug/L	Reproduction (Reproduction-Progeny counts/numbers, Response Site: Not reported)	NOEC (7.9 (6.6-10) ug/L)	Reproductive/Teratogenic	High	7006323

* If multiple extractions contained all identical information except the effect level, extraction rows were collapsed and the differing levels are listed by comma in this row.

Aquatic: Fish Extraction Table

CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
556-67-2	14 Day(s), (14 Day(s))	*Cyprinodon variegatus* (Sheepshead Minnow), Not reported, Not Reported, Laboratory (COMMERCIAL FISH HATCHERIES)	Salt water, Aqueous (aquatic habitat), Flow-through, Not Reported	Measured	0 ug/L / 1.3 ug/L / 1.6 ug/L / 2.3 ug/L / 4.2 ug/L / 6.3 ug/L	Mortality (Mortality-Mortality, Response Site: Not reported)	LC50 (>6.3 ug/L)	Mortality	High	6834101
556-67-2	14 Day(s), (14 Day(s))	*Cyprinodon variegatus* (Sheepshead Minnow), Not reported, Not Reported, Laboratory (COMMERCIAL FISH HATCHERIES)	Salt water, Aqueous (aquatic habitat), Flow-through, Not Reported	Measured	0 ug/L / 1.3 ug/L / 1.6 ug/L / 2.3 ug/L / 4.2 ug/L / 6.3 ug/L	Mortality (Mortality-Mortality, Response Site: Not reported)	NOEC (6.3 ug/L)	Mortality	High	6834101
556-67-2	12 Day(s), (12 Day(s))	*Cyprinodon variegatus* (Sheepshead Minnow), Not reported, Not Reported, Laboratory (SLI IN HOUSE CULTURE)	Salt water, Aqueous (aquatic habitat), Flow-through, Not Reported	Unmeasured	0 ug/L / ~6.0 ug/L	Mortality (Mortality-Mortality, Response Site: Not reported)	NR (~6.0 ug/L)	Mortality	High	5889397
556-67-2	14 Day(s), (14 Day(s))	*Cyprinodon variegatus* (Sheepshead Minnow), Not reported, Not Reported, Laboratory (SLI IN HOUSE CULTURE)	Salt water, Aqueous (aquatic habitat), Flow-through, 20 Organism	Measured	0 ug/L / 1.3 ug/L / 1.6 ug/L / 2.3 ug/L / 4.2 ug/L / 6.3 ug/L	Mortality (Mortality-Mortality, Response Site: Not reported)	LC50 (>6.3 ug/L)	Mortality	High	5889397

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Aquatic: Fish Extraction Table

CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
556-67-2	4 Hour(s), (96 Hour(s))	*Leuciscus idus ssp. melanotus* (Carp), Not reported, Not Reported, Laboratory (OBTAINED FROM VOGEL. D-5650 SOLINGEN, FRG)	Fresh water, Aqueous (aquatic habitat), Flow-through, Not Reported	Unmeasured	0 mg/L / 0 mg/L / 2.854625 (2.449-3.267) mg/L / 4.42425 (3.487-5.215) mg/L / 0.005-2.326 mg/L / 0.053-0.985 mg/L / 0.204-3.483 mg/L	Mortality (Mortality-Mortality, Response Site: Not reported)	LC50 (0.204->3.483 mg/L)	Mortality	High	5899897
556-67-2	24 Hour(s), (96 Hour(s))	*Leuciscus idus ssp. melanotus* (Carp), Not reported, Not Reported, Laboratory (OBTAINED FROM VOGEL. D-5650 SOLINGEN, FRG)	Fresh water, Aqueous (aquatic habitat), Flow-through, Not Reported	Unmeasured	0 mg/L / 0 mg/L / 2.854625 (2.449-3.267) mg/L / 4.42425 (3.487-5.215) mg/L / 0.005-2.326 mg/L / 0.053-0.985 mg/L / 0.204-3.483 mg/L	Mortality (Mortality-Mortality, Response Site: Not reported)	LC50 (0.204->3.483 mg/L)	Mortality	High	5899897
556-67-2	48 Hour(s), (96 Hour(s))	*Leuciscus idus ssp. melanotus* (Carp), Not reported, Not Reported, Laboratory (OBTAINED FROM VOGEL. D-5650 SOLINGEN, FRG)	Fresh water, Aqueous (aquatic habitat), Flow-through, Not Reported	Unmeasured	0 mg/L / 0 mg/L / 2.854625 (2.449-3.267) mg/L / 4.42425 (3.487-5.215) mg/L / 0.005-2.326 mg/L / 0.053-0.985 mg/L / 0.204-3.483 mg/L	Mortality (Mortality-Mortality, Response Site: Not reported)	LC50 (0.204->3.483 mg/L)	Mortality	High	5899897

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Aquatic: Fish Extraction Table

CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
556-67-2	72 Hour(s), (96 Hour(s))	*Leuciscus idus ssp. melanotus* (Carp), Not reported, Not Reported, Laboratory (OBTAINED FROM VOGEL. D-5650 SOLINGEN, FRG)	Fresh water, Aqueous (aquatic habitat), Flow-through, Not Reported	Unmeasured	0 mg/L / 0 mg/L / 2.854625 (2.449-3.267) mg/L / 4.42425 (3.487-5.215) mg/L / 0.005-2.326 mg/L / 0.053-0.985 mg/L / 0.204-3.483 mg/L	Mortality (Mortality-Mortality, Response Site: Not reported)	LC50 (0.204->3.483 mg/L)	Mortality	High	5899897
556-67-2	96 Hour(s), (96 Hour(s))	*Leuciscus idus ssp. melanotus* (Carp), Not reported, Not Reported, Laboratory (OBTAINED FROM VOGEL. D-5650 SOLINGEN, FRG)	Fresh water, Aqueous (aquatic habitat), Flow-through, Not Reported	Unmeasured	0 mg/L / 0 mg/L / 2.854625 (2.449-3.267) mg/L / 4.42425 (3.487-5.215) mg/L / 0.005-2.326 mg/L / 0.053-0.985 mg/L / 0.204-3.483 mg/L	Mortality (Mortality-Mortality, Response Site: Not reported)	LC50 (0.204->3.483 mg/L)	Mortality	High	5899897
556-67-2	96 Hour(s), (96 Hour(s))	*Leuciscus idus ssp. melanotus* (Carp), Not reported, Not Reported, Laboratory (OBTAINED FROM VOGEL. D-5650 SOLINGEN, FRG)	Fresh water, Aqueous (aquatic habitat), Flow-through, Not Reported	Unmeasured	0 mg/L / 0 mg/L / 2.854625 (2.449-3.267) mg/L / 4.42425 (3.487-5.215) mg/L / 0.005-2.326 mg/L / 0.053-0.985 mg/L / 0.204-3.483 mg/L	Mortality (Mortality-Mortality, Response Site: Not reported)	NR-ZERO (0.204-3.483 mg/L)	Mortality	High	5899897

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Aquatic: Fish Extraction Table

CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
556-67-2	96 Hour(s), (96 Hour(s))	*Leuciscus idus ssp. melanotus* (Carp), Not reported, Not Reported, Not Reported, Laboratory (OBTAINED FROM VOGEL. D-5650 SOLINGEN, FRG)	Fresh water, Aqueous (aquatic habitat), Flow-through, Not Reported	Unmeasured	0 mg/L / 0 mg/L / 2.854625 (2.449-3.267) mg/L / 4.42425 (3.487-5.215) mg/L / 0.005-2.326 mg/L / 0.053-0.985 mg/L / 0.204-3.483 mg/L	Mortality (Mortality-Mortality, Response Site: Not reported)	NOEC (0.204-3.483 mg/L)	Mortality	High	5899897
556-67-2	4 Hour(s), (96 Hour(s))	*Leuciscus idus ssp. melanotus* (Carp), Not reported, Not Reported, Not reported (NR)	Fresh water, Aqueous (aquatic habitat), Flow-through, 10 Organism	Unmeasured values (some measured values reported in article)	0 ug/L / 0 ug/L / 65 ug/L / 130 ug/L / 260 ug/L / 521 ug/L / 1041 ug/L	Mortality (Mortality-Mortality, Response Site: Not reported)	LC50 (>1041 ug/L)	Mortality	Medium	5899898
556-67-2	24 Hour(s), (96 Hour(s))	*Leuciscus idus ssp. melanotus* (Carp), Not reported, Not Reported, Not reported (NR)	Fresh water, Aqueous (aquatic habitat), Flow-through, 10 Organism	Unmeasured values (some measured values reported in article)	0 ug/L / 0 ug/L / 65 ug/L / 130 ug/L / 260 ug/L / 521 ug/L / 1041 ug/L	Mortality (Mortality-Mortality, Response Site: Not reported)	LC50 (>1041 ug/L)	Mortality	Medium	5899898
556-67-2	48 Hour(s), (96 Hour(s))	*Leuciscus idus ssp. melanotus* (Carp), Not reported, Not Reported, Not reported (NR)	Fresh water, Aqueous (aquatic habitat), Flow-through, 10 Organism	Unmeasured values (some measured values reported in article)	0 ug/L / 0 ug/L / 65 ug/L / 130 ug/L / 260 ug/L / 521 ug/L / 1041 ug/L	Mortality (Mortality-Mortality, Response Site: Not reported)	LC50 (>1041 ug/L)	Mortality	Medium	5899898
556-67-2	72 Hour(s), (96 Hour(s))	*Leuciscus idus ssp. melanotus* (Carp), Not reported, Not Reported, Not reported (NR)	Fresh water, Aqueous (aquatic habitat), Flow-through, 10 Organism	Unmeasured values (some measured values reported in article)	0 ug/L / 0 ug/L / 65 ug/L / 130 ug/L / 260 ug/L / 521 ug/L / 1041 ug/L	Mortality (Mortality-Mortality, Response Site: Not reported)	LC50 (>1041 ug/L)	Mortality	Medium	5899898
556-67-2	96 Hour(s), (96 Hour(s))	*Leuciscus idus ssp. melanotus* (Carp), Not reported, Not Reported, Not reported (NR)	Fresh water, Aqueous (aquatic habitat), Flow-through, 10 Organism	Unmeasured values (some measured values reported in article)	0 ug/L / 0 ug/L / 65 ug/L / 130 ug/L / 260 ug/L / 521 ug/L / 1041 ug/L	Mortality (Mortality-Mortality, Response Site: Not reported)	LC50 (>1041 ug/L)	Mortality	Medium	5899898

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Aquatic: Fish Extraction Table

CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
556-67-2	96 Hour(s), (96 Hour(s))	*Leuciscus idus ssp. melanotus* (Carp), Not reported, Not Reported, Not reported (NR)	Fresh water, Aqueous (aquatic habitat), Flow-through, 10 Organism	Unmeasured values (some measured values reported in article)	0 ug/L / 0 ug/L / 65 ug/L / 130 ug/L / 260 ug/L / 521 ug/L / 1041 ug/L	Mortality (Mortality-Mortality, Response Site: Not reported)	NR-ZERO (1041 ug/L)	Mortality	Medium	5899898
556-67-2	14 Day(s), (14 Day(s))	*Oncorhynchus mykiss* (Rainbow Trout), Not reported, Not Reported, Laboratory (OBTAINED FROM G. MULLER, D-3413, MORINGEN, FRG)	Fresh water, Aqueous (aquatic habitat), Flow-through, 10 Organism	Measured	0 ug/L / 0 ug/L / 5.7 ug/L / 9.4 ug/L / 16.9 ug/L / 34.2 ug/L / 51.7 ug/L	Mortality (Mortality-Mortality, Response Site: Not reported)	LC50 (>76.0 ug/L)	Mortality	High	5898990
556-67-2	14 Day(s), (14 Day(s))	*Oncorhynchus mykiss* (Rainbow Trout), Not reported, Not Reported, Laboratory (OBTAINED FROM G. MULLER, D-3413, MORINGEN, FRG)	Fresh water, Aqueous (aquatic habitat), Flow-through, 10 Organism	Measured	0 ug/L / 0 ug/L / 5.7 ug/L / 9.4 ug/L / 16.9 ug/L / 34.2 ug/L / 51.7 ug/L	Mortality (Mortality-Mortality, Response Site: Not reported)	NR-ZERO (51.7 ug/L)	Mortality	High	5898990
556-67-2	14 Day(s), (14 Day(s))	*Oncorhynchus mykiss* (Rainbow Trout), Not reported, Not Reported, Laboratory (OBTAINED FROM G. MULLER, D-3413, MORINGEN, FRG)	Fresh water, Aqueous (aquatic habitat), Flow-through, 10 Organism	Measured	0 ug/L / 0 ug/L / 5.7 ug/L / 9.4 ug/L / 16.9 ug/L / 34.2 ug/L / 51.7 ug/L	Multiple (Multiple-Multiple effects reported as one result, Response Site: Not reported)	LOEC (34.2 ug/L)	Other (please specify below)	High	5898990

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Aquatic: Fish Extraction Table

CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
556-67-2	14 Day(s), (14 Day(s))	*Oncorhynchus mykiss* (Rainbow Trout), Not reported, Not Reported, Laboratory (OBTAINED FROM G. MULLER, D-3413, MORINGEN, FRG)	Fresh water, Aqueous (aquatic habitat), Flow-through, 10 Organism	Measured	0 ug/L / 0 ug/L / 5.7 ug/L / 9.4 ug/L / 16.9 ug/L / 34.2 ug/L / 51.7 ug/L	Multiple (Multiple-Multiple effects reported as one result, Response Site: Not reported)	NOEC (16.9 ug/L)	Other (please specify below)	High	5898990
556-67-2	4 Day(s), (7 Day(s))	*Oncorhynchus mykiss* (Rainbow Trout), Not reported, Not Reported, Not reported (NR)	Fresh water, Aqueous (aquatic habitat), Flow-through, Not Reported	Measured	11 (9-13) ug/L / 41 (31-59) ug/L / 89 (56-116) ug/L	Mortality (Mortality-Mortality, Response Site: Not reported)	NR-ZERO (41 ug/L)	Mortality	Uninformative	5899898
556-67-2	5 Day(s), (7 Day(s))	*Oncorhynchus mykiss* (Rainbow Trout), Not reported, Not Reported, Not reported (NR)	Fresh water, Aqueous (aquatic habitat), Flow-through, Not Reported	Measured	89 (83-95) ug/L	Mortality (Mortality-Mortality, Response Site: Not reported)	NR-ZERO (89 ug/L)	Mortality	Uninformative	5899898
556-67-2	5 Day(s), (8 Day(s))	*Oncorhynchus mykiss* (Rainbow Trout), Not reported, Not Reported, Not reported (NR)	Fresh water, Aqueous (aquatic habitat), Flow-through, Not Reported	Measured	18 (14-20) ug/L / 32 (27-38) ug/L	Mortality (Mortality-Mortality, Response Site: Not reported)	NR-ZERO (32 ug/L)	Mortality	Uninformative	5899898
556-67-2	4-7 Day(s), (7 Day(s))	*Oncorhynchus mykiss* (Rainbow Trout), Not reported, Not Reported, Not reported (NR)	Fresh water, Aqueous (aquatic habitat), Flow-through, Not Reported	Measured	89 (83-95) ug/L	Mortality (Mortality-Mortality, Response Site: Not reported)	NR (89 ug/L)	Mortality	Uninformative	5899898
556-67-2	4-7 Day(s), (7 Day(s))	*Oncorhynchus mykiss* (Rainbow Trout), Not reported, Not Reported, Not reported (NR)	Fresh water, Aqueous (aquatic habitat), Flow-through, Not Reported	Measured	11 (9-13) ug/L / 41 (31-59) ug/L / 89 (56-116) ug/L	Mortality (Mortality-Mortality, Response Site: Not reported)	NR (11-89 ug/L)	Mortality	Uninformative	5899898

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Aquatic: Fish Extraction Table

CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
556-67-2	4-8 Day(s), (8 Day(s))	*Oncorhynchus mykiss* (Rainbow Trout), Not reported, Not Reported, Not reported (NR)	Fresh water, Aqueous (aquatic habitat), Flow-through, Not Reported	Measured	18 (14-20) ug/L / 32 (27-38) ug/L	Mortality (Mortality-Mortality, Response Site: Not reported)	NR (18-32 ug/L)	Mortality	Uninformative	5899898
556-67-2	38 Day(s), (38 Day(s))	*Oncorhynchus mykiss* (Rainbow Trout), Juvenile, Not Reported, Laboratory (FROM SIMON FRASER UNIVERSITY, CANADA)	Fresh water, Oral (diet, drink, gavage), Food, Not Reported	Measured	0 g/kg diet / 0.84 g/kg diet	Growth (Growth-Weight, Response Site: Whole organism)	NOEC (0.84 g/kg diet)	Development/Growth	Medium	9960764
556-67-2	2-38 Day(s), (38 Day(s))	*Oncorhynchus mykiss* (Rainbow Trout), Juvenile, Not Reported, Laboratory (FROM SIMON FRASER UNIVERSITY, CANADA)	Fresh water, Oral (diet, drink, gavage), Food, Not Reported	Measured	0 g/kg diet / 0.84 g/kg diet	Biochemical (Biochemistry-Lipid, Response Site: Tissue)	NOEC (0.84 g/kg diet)	ADME (biotransformation)	Medium	9960764
556-67-2	38 Day(s), (38 Day(s))	*Oncorhynchus mykiss* (Rainbow Trout), Juvenile, Not Reported, Laboratory (FROM SIMON FRASER UNIVERSITY, CANADA)	Fresh water, Oral (diet, drink, gavage), Food, Not Reported	Measured	0 g/kg diet / 0.84 g/kg diet	Accumulation (Accumulation-Residue, Response Site: Tissue)	BAF (0.84 g/kg diet)	ADME (biotransformation)	Medium	9960764
556-67-2	38 Day(s), (38 Day(s))	*Oncorhynchus mykiss* (Rainbow Trout), Juvenile, Not Reported, Laboratory (FROM SIMON FRASER UNIVERSITY, CANADA)	Fresh water, Oral (diet, drink, gavage), Food, Not Reported	Measured	0 g/kg diet / 0.84 g/kg diet	Accumulation (Accumulation-Residue, Response Site: Tissue)	BCF (0.84 g/kg diet)	ADME (biotransformation)	Medium	9960764

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Aquatic: Fish Extraction Table

CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
556-67-2	18 Day(s), (18 Day(s))	*Oncorhynchus mykiss* (Rainbow Trout), Not reported, Not Reported, Laboratory (OBTAINED FROM THE DOW CHEMICAL COMPANY)	Fresh water, Aqueous (aquatic habitat), Flow-through, 5-10 Organism	Measured	0 ppb / 23.2-31.2 ppb	Accumulation (Accumulation-Residue, Response Site: Whole organism)	BCF (23.2-31.2 ppb)	Other (please specify below)	High	5896903
556-67-2	5-18 Day(s), (18 Day(s))	*Oncorhynchus mykiss* (Rainbow Trout), Not reported, Not Reported, Laboratory (OBTAINED FROM THE DOW CHEMICAL COMPANY)	Fresh water, Aqueous (aquatic habitat), Flow-through, 10 Organism	Measured	0 ppb / 23.2 ppb	Accumulation (Accumulation-Residue, Response Site: Whole organism)	NR (23.2 ppb)	Other (please specify below)	High	5896903
556-67-2	18 Day(s), (18 Day(s))	*Oncorhynchus mykiss* (Rainbow Trout), Not reported, Not Reported, Laboratory (OBTAINED FROM THE DOW CHEMICAL COMPANY)	Fresh water, Aqueous (aquatic habitat), Flow-through, 10 Organism	Measured	0 ppb / 23.2 ppb	Growth (Growth-Condition index,Length,Weight, Response Site: Whole organism)	NR (23.2 ppb)	Development/Growth	High	5896903
556-67-2	18 Day(s), (18 Day(s))	*Oncorhynchus mykiss* (Rainbow Trout), Not reported, Not Reported, Laboratory (OBTAINED FROM THE DOW CHEMICAL COMPANY)	Fresh water, Aqueous (aquatic habitat), Flow-through, 5 Organism	Measured	0 ppb / 31.2 ppb	Growth (Growth-Condition index,Length,Weight, Response Site: Whole organism)	NR (31.2 ppb)	Development/Growth	High	5896903

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Aquatic: Fish Extraction Table

CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
556-67-2	18 Day(s), (18 Day(s))	*Oncorhynchus mykiss* (Rainbow Trout), Not reported, Not Reported, Laboratory (OBTAINED FROM THE DOW CHEMICAL COMPANY)	Fresh water, Aqueous (aquatic habitat), Flow-through, 4 Organism	Measured	0 ppb / 31.2 ppb	Accumulation (Accumulation-Residue, Response Site: Whole organism)	NR (31.2 ppb)	Other (please specify below)	High	5896903
556-67-2	1-18 Day(s), (18 Day(s))	*Oncorhynchus mykiss* (Rainbow Trout), Not reported, Not Reported, Laboratory (OBTAINED FROM THE DOW CHEMICAL COMPANY)	Fresh water, Aqueous (aquatic habitat), Flow-through, 10 Organism	Measured	0 ppb / 23.2 ppb	Mortality (Mortality-Survival, Response Site: Not reported)	NR (23.2 ppb)	Mortality	High	5896903
556-67-2	18 Day(s), (18 Day(s))	*Oncorhynchus mykiss* (Rainbow Trout), Not reported, Not Reported, Laboratory (OBTAINED FROM THE DOW CHEMICAL COMPANY)	Fresh water, Aqueous (aquatic habitat), Flow-through, 5 Organism	Measured	0 ppb / 31.2 ppb	Mortality (Mortality-Mortality, Response Site: Not reported)	NR-ZERO (31.2 ppb)	Mortality	High	5896903
556-67-2	>48 Hour(s), (5 Day(s))	*Oncorhynchus mykiss* (Rainbow Trout), Young, Not Reported, Laboratory (THE DOW CHEMICAL COMPANY)	Fresh water, Aqueous (aquatic habitat), Flow-through, 10 Organism	Measured	0 ppb / 17.9-20.3 ppb	Physiology (Physiology-Pigmentation, Response Site: Skin, epidermis)	NR (17.9-20.3 ppb)	Skin and Connective Tissue	High	5901767

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Aquatic: Fish Extraction Table

CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
556-67-2	>48 Hour(s), (9 Day(s))	*Oncorhynchus mykiss* (Rainbow Trout), Young, Not Reported, Laboratory (THE DOW CHEMICAL COMPANY)	Fresh water, Aqueous (aquatic habitat), Flow-through, 10 Organism	Measured	0 ppb / <15-55 ppb	Behavior (Behavior-Equilibrium,Movements, number of, Response Site: Not reported)	NR (<15-55 ppb)	Behavioral	High	5901767
556-67-2	>48 Hour(s), (9 Day(s))	*Oncorhynchus mykiss* (Rainbow Trout), Young, Not Reported, Laboratory (THE DOW CHEMICAL COMPANY)	Fresh water, Aqueous (aquatic habitat), Flow-through, 10 Organism	Measured	0 ppb / <15-55 ppb	Physiology (Physiology-Pigmentation, Response Site: Skin, epidermis)	NR (<15-55 ppb)	Skin and Connective Tissue	High	5901767
556-67-2	>48 Hour(s), (5 Day(s))	*Oncorhynchus mykiss* (Rainbow Trout), Young, Not Reported, Laboratory (THE DOW CHEMICAL COMPANY)	Fresh water, Aqueous (aquatic habitat), Flow-through, 10 Organism	Measured	0 ppb / 17.9-20.3 ppb	Behavior (Behavior-Equilibrium,Movements, number of, Response Site: Not reported)	NR (17.9-20.3 ppb)	Behavioral	High	5901767
556-67-2	3 Day(s), (9 Day(s))	*Oncorhynchus mykiss* (Rainbow Trout), Young, Not Reported, Laboratory (THE DOW CHEMICAL COMPANY)	Fresh water, Aqueous (aquatic habitat), Flow-through, 10 Organism	Measured	0 ppb / <15-55 ppb	Mortality (Mortality-Mortality, Response Site: Not reported)	NR-ZERO (<15-18.7 ppb)	Mortality	High	5901767
556-67-2	3 Day(s), (5 Day(s))	*Oncorhynchus mykiss* (Rainbow Trout), Young, Not Reported, Laboratory (THE DOW CHEMICAL COMPANY)	Fresh water, Aqueous (aquatic habitat), Flow-through, 10 Organism	Measured	0 ppb / 17.9-20.3 ppb	Mortality (Mortality-Mortality, Response Site: Not reported)	NR-ZERO (17.9-20.3 ppb)	Mortality	High	5901767

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Aquatic: Fish Extraction Table

CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
556-67-2	4-5 Day(s), (5 Day(s))	*Oncorhynchus mykiss* (Rainbow Trout), Young, Not Reported, Laboratory (THE DOW CHEMICAL COMPANY)	Fresh water, Aqueous (aquatic habitat), Flow-through, 10 Organism	Measured	0 ppb / 17.9-20.3 ppb	Accumulation (Accumulation-Residue, Response Site: Whole organism)	NR (17.9-20.3 ppb)	Other (please specify below)	High	5901767
556-67-2	5 Day(s), (5 Day(s))	*Oncorhynchus mykiss* (Rainbow Trout), Young, Not Reported, Laboratory (THE DOW CHEMICAL COMPANY)	Fresh water, Aqueous (aquatic habitat), Flow-through, 10 Organism	Measured	0 ppb / 17.9-20.3 ppb	Mortality (Mortality-Mortality, Response Site: Not reported)	NR-LETH (17.9-20.3 ppb)	Mortality	High	5901767
556-67-2	4-9 Day(s), (9 Day(s))	*Oncorhynchus mykiss* (Rainbow Trout), Young, Not Reported, Laboratory (THE DOW CHEMICAL COMPANY)	Fresh water, Aqueous (aquatic habitat), Flow-through, 10 Organism	Measured	0 ppb / <15-55 ppb	Accumulation (Accumulation-Residue, Response Site: Whole organism)	NR (<15-55 ppb)	Other (please specify below)	High	5901767
556-67-2	9 Day(s), (9 Day(s))	*Oncorhynchus mykiss* (Rainbow Trout), Young, Not Reported, Laboratory (THE DOW CHEMICAL COMPANY)	Fresh water, Aqueous (aquatic habitat), Flow-through, 10 Organism	Measured	0 ppb / <15-55 ppb	Mortality (Mortality-Mortality, Response Site: Not reported)	NR-LETH (<15-55 ppb)	Mortality	High	5901767
556-67-2	14 Day(s), (14 Day(s))	*Oncorhynchus mykiss* (Rainbow Trout), Juvenile, Not Reported, Laboratory (Thomas Fish Company, Anderson, California)	Fresh water, Aqueous (aquatic habitat), Flow-through, Not Reported	Unmeasured	0 ug/L / 0 ug/L / 1.9 ug/L / 3.4 ug/L / 6.8 ug/L / 13 ug/L / 29 ug/L	Growth (Growth-Weight, Response Site: Whole organism)	NOEC (6.8 ug/L)	Development/Growth	High	6987899

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Aquatic: Fish Extraction Table

CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
556-67-2	14 Day(s), (14 Day(s))	*Oncorhynchus mykiss* (Rainbow Trout), Juvenile, Not Reported, Laboratory (Thomas Fish Company, Anderson, California)	Fresh water, Aqueous (aquatic habitat), Flow-through, Not Reported	Unmeasured	0 ug/L / 0 ug/L / 1.9 ug/L / 3.4 ug/L / 6.8 ug/L / 13 ug/L / 29 ug/L	Mortality (Mortality-Survival, Response Site: Not reported)	NOEC (6.8 ug/L)	Mortality	High	6987899
556-67-2	1-14 Day(s), (14 Day(s))	*Oncorhynchus mykiss* (Rainbow Trout), Juvenile, Not Reported, Laboratory (Thomas Fish Company, Anderson, California)	Fresh water, Aqueous (aquatic habitat), Flow-through, Not Reported	Unmeasured	0 ug/L / 0 ug/L / 1.9 ug/L / 3.4 ug/L / 6.8 ug/L / 13 ug/L / 29 ug/L	Physiology (Physiology-Pigmentation, Response Site: Not reported)	NR (1.9-29 ug/L)	Skin and Connective Tissue	High	6987899
556-67-2	14 Day(s), (14 Day(s))	*Oncorhynchus mykiss* (Rainbow Trout), Juvenile, Not Reported, Laboratory (Thomas Fish Company, Anderson, California)	Fresh water, Aqueous (aquatic habitat), Flow-through, Not Reported	Unmeasured	0 ug/L / 0 ug/L / 1.9 ug/L / 3.4 ug/L / 6.8 ug/L / 13 ug/L / 29 ug/L	Mortality (Mortality-Mortality, Response Site: Not reported)	LC50 (17 (14-21) ug/L)	Mortality	High	6987899
556-67-2	14 Day(s), (14 Day(s))	*Oncorhynchus mykiss* (Rainbow Trout), Juvenile, Not Reported, Laboratory (Thomas Fish Company, Anderson, California)	Fresh water, Aqueous (aquatic habitat), Flow-through, Not Reported	Unmeasured	0 ug/L / 0 ug/L / 1.9 ug/L / 3.4 ug/L / 6.8 ug/L / 13 ug/L / 29 ug/L	Mortality (Mortality-Mortality, Response Site: Not reported)	NR-ZERO (6.8 ug/L)	Mortality	High	6987899
556-67-2	1-14 Day(s), (14 Day(s))	*Oncorhynchus mykiss* (Rainbow Trout), Juvenile, Not Reported, Laboratory (Thomas Fish Company, Anderson, California)	Fresh water, Aqueous (aquatic habitat), Flow-through, Not Reported	Unmeasured	0 ug/L / 0 ug/L / 1.9 ug/L / 3.4 ug/L / 6.8 ug/L / 13 ug/L / 29 ug/L	Behavior (Behavior-Activity, general,Equilibrium, Response Site: Not reported)	NR (1.9-29 ug/L)	Development/Growth	High	6987899

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Aquatic: Fish Extraction Table

CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
556-67-2	14 Day(s), (14 Day(s))	*Oncorhynchus mykiss* (Rainbow Trout), Juvenile, Not Reported, Laboratory (Thomas Fish Company, Anderson, California)	Fresh water, Aqueous (aquatic habitat), Flow-through, Not Reported	Unmeasured	0 ug/L / 0 ug/L / 1.9 ug/L / 3.4 ug/L / 6.8 ug/L / 13 ug/L / 29 ug/L	Growth (Growth-Length, Response Site: Whole organism)	NOEC (6.8 ug/L)	Development/Growth	High	6987899
556-67-2	14 Day(s), (14 Day(s))	*Oncorhynchus mykiss* (Rainbow Trout), Juvenile, Not Reported, Laboratory (Thomas Fish Company, Anderson, California)	Fresh water, Aqueous (aquatic habitat), Flow-through, Not Reported	Unmeasured	0 ug/L / 0 ug/L / 1.9 ug/L / 3.4 ug/L / 6.8 ug/L / 13 ug/L / 29 ug/L	Mortality (Mortality-Survival, Response Site: Not reported)	LOEC (13 ug/L)	Mortality	High	6987899
556-67-2	14 Day(s), (14 Day(s))	*Oncorhynchus mykiss* (Rainbow Trout), Juvenile, Not Reported, Laboratory (Thomas Fish Company, Anderson, California)	Fresh water, Aqueous (aquatic habitat), Flow-through, Not Reported	Unmeasured	0 ug/L / 0 ug/L / 1.9 ug/L / 3.4 ug/L / 6.8 ug/L / 13 ug/L / 29 ug/L	Growth (Growth-Length, Response Site: Whole organism)	LOEC (13 ug/L)	Development/Growth	High	6987899
556-67-2	14 Day(s), (14 Day(s))	*Oncorhynchus mykiss* (Rainbow Trout), Juvenile, Not Reported, Laboratory (Thomas Fish Company, Anderson, California)	Fresh water, Aqueous (aquatic habitat), Flow-through, Not Reported	Unmeasured	0 ug/L / 0 ug/L / 1.9 ug/L / 3.4 ug/L / 6.8 ug/L / 13 ug/L / 29 ug/L	Growth (Growth-Weight, Response Site: Whole organism)	LOEC (13 ug/L)	Development/Growth	High	6987899
556-67-2	45-60 Days post-hatch, (93 Day(s))	*Oncorhynchus mykiss* (Rainbow Trout), Egg, 2 Hours post fertilization (Measured in: Larvae), Not Reported, Laboratory (MOUNT LASSEN TROUT FARM, REDBLUFF, CA)	Fresh water, Aqueous (aquatic habitat), Flow-through, NA Larvae	Measured	0 ug/L / 0.25 ug/L / 0.53 ug/L / 1.1 ug/L / 1.9 ug/L / 4.4 ug/L	Mortality (Mortality-Survival, Response Site: Not reported)	NOEC (4.4 ug/L)	Mortality	High	6834101

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Aquatic: Fish Extraction Table

CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
556-67-2	0-45 Days post-hatch, (93 Day(s))	*Oncorhynchus mykiss* (Rainbow Trout), Egg, 2 Hours post fertilization (Measured in: Larvae), Not Reported, Laboratory (MOUNT LASSEN TROUT FARM, RED-BLUFF, CA)	Fresh water, Aqueous (aquatic habitat), Flow-through, NA Larvae	Measured	0 ug/L / 0.25 ug/L / 0.53 ug/L / 1.1 ug/L / 1.9 ug/L / 4.4 ug/L	Mortality (Mortality-Survival, Response Site: Not reported)	NOEC (4.4 ug/L)	Mortality	High	6834101
556-67-2	14 Day(s), (14 Day(s))	*Oncorhynchus mykiss* (Rainbow Trout), Not reported, Not Reported, Laboratory (COMMERCIAL FISH HATCHERIES)	Fresh water, Aqueous (aquatic habitat), Flow-through, Not Reported	Measured	0 ug/L / 2.9 ug/L / 4.4 ug/L / 6.9 ug/L / 12 ug/L / 22 ug/L	Mortality (Mortality-Mortality, Response Site: Not reported)	LC50 (10 (8.5-13) ug/L)	Mortality	High	6834101
556-67-2	14 Day(s), (14 Day(s))	*Oncorhynchus mykiss* (Rainbow Trout), Not reported, Not Reported, Laboratory (COMMERCIAL FISH HATCHERIES)	Fresh water, Aqueous (aquatic habitat), Flow-through, Not Reported	Measured	0 ug/L / 2.9 ug/L / 4.4 ug/L / 6.9 ug/L / 12 ug/L / 22 ug/L	Mortality (Mortality-Mortality, Response Site: Not reported)	LOEC (6.9 ug/L)	Mortality	High	6834101
556-67-2	14 Day(s), (14 Day(s))	*Oncorhynchus mykiss* (Rainbow Trout), Not reported, Not Reported, Laboratory (COMMERCIAL FISH HATCHERIES)	Fresh water, Aqueous (aquatic habitat), Flow-through, Not Reported	Measured	0 ug/L / 2.9 ug/L / 4.4 ug/L / 6.9 ug/L / 12 ug/L / 22 ug/L	Mortality (Mortality-Mortality, Response Site: Not reported)	NOEC (4.4 ug/L)	Mortality	High	6834101

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Aquatic: Fish Extraction Table

CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
556-67-2	19 Day(s), (93 Day(s))	*Oncorhynchus mykiss* (Rainbow Trout), Egg, 2 Hours post fertilization (Measured in: Embryo), Not Reported, Laboratory (MOUNT LASSEN TROUT FARM, REDBLUFF, CA)	Fresh water, Aqueous (aquatic habitat), Flow-through, NA Embryo	Measured	0 ug/L / 0.25 ug/L / 0.53 ug/L / 1.1 ug/L / 1.9 ug/L / 4.4 ug/L	Reproduction (Reproduction-Viability, Response Site: Not reported)	NR (0.25-4.4 ug/L)	Reproductive/Teratogenic	High	6834101
556-67-2	33 Day(s), (93 Day(s))	*Oncorhynchus mykiss* (Rainbow Trout), Egg, 2 Hours post fertilization (Measured in: Embryo), Not Reported, Laboratory (MOUNT LASSEN TROUT FARM, REDBLUFF, CA)	Fresh water, Aqueous (aquatic habitat), Flow-through, NA Embryo	Measured	0 ug/L / 0.25 ug/L / 0.53 ug/L / 1.1 ug/L / 1.9 ug/L / 4.4 ug/L	Mortality (Mortality-Survival, Response Site: Not reported)	NR (0.25-4.4 ug/L)	Mortality	High	6834101
556-67-2	90 Day(s), (93 Day(s))	*Oncorhynchus mykiss* (Rainbow Trout), Egg, 2 Hours post fertilization, Not Reported, Laboratory (MOUNT LASSEN TROUT FARM, REDBLUFF, CA)	Fresh water, Aqueous (aquatic habitat), Flow-through, Not Reported	Measured	0 ug/L / 0.25 ug/L / 0.53 ug/L / 1.1 ug/L / 1.9 ug/L / 4.4 ug/L	Multiple (Multiple-Multiple effects reported as one result, Response Site: Not reported)	LOEC (6.9 ug/L)	Mortality	High	6834101
556-67-2	90 Day(s), (93 Day(s))	*Oncorhynchus mykiss* (Rainbow Trout), Egg, 2 Hours post fertilization, Not Reported, Laboratory (MOUNT LASSEN TROUT FARM, REDBLUFF, CA)	Fresh water, Aqueous (aquatic habitat), Flow-through, Not Reported	Measured	0 ug/L / 0.25 ug/L / 0.53 ug/L / 1.1 ug/L / 1.9 ug/L / 4.4 ug/L	Multiple (Multiple-Multiple effects reported as one result, Response Site: Not reported)	MATC (5.5 (4.4-6.9) ug/L)	Mortality	High	6834101

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Aquatic: Fish Extraction Table

CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
556-67-2	90 Day(s), (93 Day(s))	*Oncorhynchus mykiss* (Rainbow Trout), Egg, 2 Hours post fertilization, Not Reported, Laboratory (MOUNT LASSEN TROUT FARM, REDBLUFF, CA)	Fresh water, Aqueous (aquatic habitat), Flow-through, Not Reported	Measured	0 ug/L / 0.25 ug/L / 0.53 ug/L / 1.1 ug/L / 1.9 ug/L / 4.4 ug/L	Multiple (Multiple-Multiple effects reported as one result, Response Site: Not reported)	NOEC (4.4 ug/L)	Mortality	High	6834101
556-67-2	0-93 Day(s), (93 Day(s))	*Oncorhynchus mykiss* (Rainbow Trout), Egg, 2 Hours post fertilization, Not Reported, Laboratory (MOUNT LASSEN TROUT FARM, REDBLUFF, CA)	Fresh water, Aqueous (aquatic habitat), Flow-through, Not Reported	Measured	0 ug/L / 0.25 ug/L / 0.53 ug/L / 1.1 ug/L / 1.9 ug/L / 4.4 ug/L	Growth (Development-Abnormal, Response Site: Not reported)	NR (0.25-4.4 ug/L)	Development/Growth	High	6834101
556-67-2	0-93 Day(s), (93 Day(s))	*Oncorhynchus mykiss* (Rainbow Trout), Egg, 2 Hours post fertilization, Not Reported, Laboratory (MOUNT LASSEN TROUT FARM, REDBLUFF, CA)	Fresh water, Aqueous (aquatic habitat), Flow-through, Not Reported	Measured	0 ug/L / 0.25 ug/L / 0.53 ug/L / 1.1 ug/L / 1.9 ug/L / 4.4 ug/L	Growth (Growth-Length,Weight, Response Site: Whole organism)	NR (0.25-4.4 ug/L)	Development/Growth	High	6834101
556-67-2	1-7 Day(s), (14 Day(s))	*Oncorhynchus mykiss* (Rainbow Trout), Not reported, Not Reported, Laboratory (OBTAINED FROM SPRING CREEK HATCHERY)	Fresh water, Aqueous (aquatic habitat), Flow-through, 20 Organism	Measured	0 ug/L / 2.9 ug/L / 4.4 ug/L / 6.9 ug/L / 12 ug/L / 22 ug/L	Mortality (Mortality-Mortality, Response Site: Not reported)	LC50 (>22 ug/L)	Mortality	High	5889401

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Aquatic: Fish Extraction Table

CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
556-67-2	8 Day(s), (14 Day(s))	*Oncorhynchus mykiss* (Rainbow Trout), Not reported, Not Reported, Laboratory (OBTAINED FROM SPRING CREEK HATCHERY)	Fresh water, Aqueous (aquatic habitat), Flow-through, 20 Organism	Measured	0 ug/L / 2.9 ug/L / 4.4 ug/L / 6.9 ug/L / 12 ug/L / 22 ug/L	Mortality (Mortality-Mortality, Response Site: Not reported)	LC50 (22 ug/L)	Mortality	High	5889401
556-67-2	9 Day(s), (14 Day(s))	*Oncorhynchus mykiss* (Rainbow Trout), Not reported, Not Reported, Laboratory (OBTAINED FROM SPRING CREEK HATCHERY)	Fresh water, Aqueous (aquatic habitat), Flow-through, 20 Organism	Measured	0 ug/L / 2.9 ug/L / 4.4 ug/L / 6.9 ug/L / 12 ug/L / 22 ug/L	Mortality (Mortality-Mortality, Response Site: Not reported)	LC50 (22 ug/L)	Mortality	High	5889401
556-67-2	10 Day(s), (14 Day(s))	*Oncorhynchus mykiss* (Rainbow Trout), Not reported, Not Reported, Laboratory (OBTAINED FROM SPRING CREEK HATCHERY)	Fresh water, Aqueous (aquatic habitat), Flow-through, 20 Organism	Measured	0 ug/L / 2.9 ug/L / 4.4 ug/L / 6.9 ug/L / 12 ug/L / 22 ug/L	Mortality (Mortality-Mortality, Response Site: Not reported)	LC50 (19 ug/L)	Mortality	High	5889401
556-67-2	11 Day(s), (14 Day(s))	*Oncorhynchus mykiss* (Rainbow Trout), Not reported, Not Reported, Laboratory (OBTAINED FROM SPRING CREEK HATCHERY)	Fresh water, Aqueous (aquatic habitat), Flow-through, 20 Organism	Measured	0 ug/L / 2.9 ug/L / 4.4 ug/L / 6.9 ug/L / 12 ug/L / 22 ug/L	Mortality (Mortality-Mortality, Response Site: Not reported)	LC50 (15 ug/L)	Mortality	High	5889401

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Aquatic: Fish Extraction Table

CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
556-67-2	12 Day(s), (14 Day(s))	*Oncorhynchus mykiss* (Rainbow Trout), Not reported, Not Reported, Laboratory (OBTAINED FROM SPRING CREEK HATCHERY)	Fresh water, Aqueous (aquatic habitat), Flow-through, 20 Organism	Measured	0 ug/L / 2.9 ug/L / 4.4 ug/L / 6.9 ug/L / 12 ug/L / 22 ug/L	Mortality (Mortality-Mortality, Response Site: Not reported)	LC50 (14 ug/L)	Mortality	High	5889401
556-67-2	13 Day(s), (14 Day(s))	*Oncorhynchus mykiss* (Rainbow Trout), Not reported, Not Reported, Laboratory (OBTAINED FROM SPRING CREEK HATCHERY)	Fresh water, Aqueous (aquatic habitat), Flow-through, 20 Organism	Measured	0 ug/L / 2.9 ug/L / 4.4 ug/L / 6.9 ug/L / 12 ug/L / 22 ug/L	Mortality (Mortality-Mortality, Response Site: Not reported)	LC50 (12 ug/L)	Mortality	High	5889401
556-67-2	11 Day(s), (40 Day(s))	*Oncorhynchus mykiss* (Rainbow Trout), Eyed egg or stage, eyed embryo, 20-25 Day(s) (Measured in: Embryo), Not Reported, Laboratory (MOUNT LASSEN TROUT FARMS, RED BLUFF, CALIFORNIA)	Fresh water, Aqueous (aquatic habitat), Flow-through, NA Embryo	Unmeasured	0 ug/L / 0.57 ug/L / 0.95 ug/L / 1.6 ug/L / 2.8 ug/L / 4.4 ug/L	Mortality (Mortality-Hatch, Response Site: Not reported)	NOEC (4.4 ug/L)	Mortality	High	5889407
556-67-2	19 Day(s), (93 Day(s))	*Oncorhynchus mykiss* (Rainbow Trout), Embryo, <=24 Hours post fertilization, Not Reported, Laboratory (MOUNT LASSEN TROUT FARMS, RED BLUFF, CALIFORNIA)	Fresh water, Aqueous (aquatic habitat), Flow-through, NA Embryo	Measured	<0.10-0.37 ug/L / 0.25 ug/L / 0.53 ug/L / 1.1 ug/L / 1.9 ug/L / 4.4 ug/L	Reproduction (Reproduction-Viability, Response Site: Not reported)	NOEC (4.4 ug/L)	Reproductive/Teratogenic	High	5889407

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Aquatic: Fish Extraction Table

CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
556-67-2	33 Day(s), (93 Day(s))	*Oncorhynchus mykiss* (Rainbow Trout), Embryo, <=24 Hours post fertilization, Not Reported, Laboratory (MOUNT LASSEN TROUT FARMS, RED BLUFF, CALIFORNIA)	Fresh water, Aqueous (aquatic habitat), Flow-through, NA Embryo	Measured	<0.10-0.37 ug/L / 0.25 ug/L / 0.53 ug/L / 1.1 ug/L / 1.9 ug/L / 4.4 ug/L	Mortality (Mortality-Hatch, Response Site: Not reported)	NOEC (4.4 ug/L)	Mortality	High	5889407
556-67-2	40 Day(s), (40 Day(s))	*Oncorhynchus mykiss* (Rainbow Trout), Eyed egg or stage, eyed embryo, 20-25 Day(s) (Measured in: Larvae), Not Reported, Laboratory (MOUNT LASSEN TROUT FARMS, RED BLUFF, CALIFORNIA)	Fresh water, Aqueous (aquatic habitat), Flow-through, NA Larvae	Unmeasured	0 ug/L / 0.57 ug/L / 0.95 ug/L / 1.6 ug/L / 2.8 ug/L / 4.4 ug/L	Mortality (Mortality-Survival, Response Site: Not reported)	NOEC (4.4 ug/L)	Mortality	High	5889407
556-67-2	40 Day(s), (40 Day(s))	*Oncorhynchus mykiss* (Rainbow Trout), Eyed egg or stage, eyed embryo, 20-25 Day(s) (Measured in: Larvae), Not Reported, Laboratory (MOUNT LASSEN TROUT FARMS, RED BLUFF, CALIFORNIA)	Fresh water, Aqueous (aquatic habitat), Flow-through, NA Larvae	Unmeasured	0 ug/L / 0.57 ug/L / 0.95 ug/L / 1.6 ug/L / 2.8 ug/L / 4.4 ug/L	Growth (Growth-Weight, Response Site: Whole organism)	NOEC (4.4 ug/L)	Development/Growth	High	5889407

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Aquatic: Fish Extraction Table

CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
556-67-2	33-78 Day(s), (93 Day(s))	*Oncorhynchus mykiss* (Rainbow Trout), Embryo, <=24 Hours post fertilization (Measured in: Larvae), Not Reported, Laboratory (MOUNT LASSEN TROUT FARMS, RED BLUFF, CALIFORNIA)	Fresh water, Aqueous (aquatic habitat), Flow-through, NA Larvae	Measured	<0.10-0.37 ug/L / 0.25 ug/L / 0.53 ug/L / 1.1 ug/L / 1.9 ug/L / 4.4 ug/L	Mortality (Mortality-Survival, Response Site: Not reported)	NOEC (4.4 ug/L)	Mortality	High	5889407
556-67-2	78-93 Day(s), (93 Day(s))	*Oncorhynchus mykiss* (Rainbow Trout), Embryo, <=24 Hours post fertilization (Measured in: Larvae), Not Reported, Laboratory (MOUNT LASSEN TROUT FARMS, RED BLUFF, CALIFORNIA)	Fresh water, Aqueous (aquatic habitat), Flow-through, NA Larvae	Measured	<0.10-0.37 ug/L / 0.25 ug/L / 0.53 ug/L / 1.1 ug/L / 1.9 ug/L / 4.4 ug/L	Mortality (Mortality-Survival, Response Site: Not reported)	NOEC (4.4 ug/L)	Mortality	High	5889407
556-67-2	93 Day(s), (93 Day(s))	*Oncorhynchus mykiss* (Rainbow Trout), Embryo, <=24 Hours post fertilization (Measured in: Larvae), Not Reported, Laboratory (MOUNT LASSEN TROUT FARMS, RED BLUFF, CALIFORNIA)	Fresh water, Aqueous (aquatic habitat), Flow-through, NA Larvae	Measured	<0.10-0.37 ug/L / 0.25 ug/L / 0.53 ug/L / 1.1 ug/L / 1.9 ug/L / 4.4 ug/L	Growth (Growth-Length, Response Site: Whole organism)	NOEC (4.4 ug/L)	Development/Growth	High	5889407

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Aquatic: Fish Extraction Table

CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
556-67-2	93 Day(s), (93 Day(s))	*Oncorhynchus mykiss* (Rainbow Trout), Embryo, <=24 Hours post fertilization (Measured in: Larvae), Not Reported, Laboratory (MOUNT LASSEN TROUT FARMS, RED BLUFF, CALIFORNIA)	Fresh water, Aqueous (aquatic habitat), Flow-through, NA Larvae	Measured	<0.10-0.37 ug/L / 0.25 ug/L / 0.53 ug/L / 1.1 ug/L / 1.9 ug/L / 4.4 ug/L	Growth (Growth-Weight, Response Site: Whole organism)	NOEC (4.4 ug/L)	Development/Growth	High	5889407
556-67-2	33-93 Day(s), (93 Day(s))	*Oncorhynchus mykiss* (Rainbow Trout), Embryo, <=24 Hours post fertilization (Measured in: Larvae), Not Reported, Laboratory (MOUNT LASSEN TROUT FARMS, RED BLUFF, CALIFORNIA)	Fresh water, Aqueous (aquatic habitat), Flow-through, NA Larvae	Measured	<0.10-0.37 ug/L / 0.25 ug/L / 0.53 ug/L / 1.1 ug/L / 1.9 ug/L / 4.4 ug/L	Mortality (Mortality-Survival, Response Site: Not reported)	NOEC (4.4 ug/L)	Mortality	High	5889407
556-67-2	35 Day(s), (77 Day(s))	*Oncorhynchus mykiss* (Rainbow Trout), Juvenile, Not Reported, Laboratory (THOMAS FISH COMPANY, ANDERSON, CA.)	Fresh water, Oral (diet, drink, gavage), Food, Not Reported	Measured	0 ug/g diet / 457 ug/g diet	Growth (Growth-Weight, Response Site: Whole organism)	NOEC (457 ug/g diet)	Development/Growth	High	6833850
556-67-2	1-35 Day(s), (77 Day(s))	*Oncorhynchus mykiss* (Rainbow Trout), Juvenile, Not Reported, Laboratory (THOMAS FISH COMPANY, ANDERSON, CA.)	Fresh water, Oral (diet, drink, gavage), Food, Not Reported	Measured	0 ug/g diet / 457 ug/g diet	Accumulation (Accumulation-Assimilation of test chemical,Elimination,Residue,Uptake, Response Site: Gastrointestinal tract,Whole organism)	NR (457 ug/g diet)	Other (please specify below)	High	6833850

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CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
556-67-2	35 Day(s), (77 Day(s))	*Oncorhynchus mykiss* (Rainbow Trout), Juvenile, Not Reported, Laboratory (THOMAS FISH COMPANY, ANDERSON, CA.)	Fresh water, Oral (diet, drink, gavage), Food, Not Reported	Measured	0 ug/g diet / 457 ug/g diet	Biochemical (Biochemistry-Lipid, Response Site: Whole organism)	NOEC (457 ug/g diet)	ADME (biotransformation)	High	6833850
556-67-2	1-10 Day(s), (10 Day(s))	*Pimephales promelas* (Fathead Minnow), Not reported, Not Reported, Laboratory (OBTAINED FROM COMMERCIAL HATCHERIES)	Fresh water, Aqueous (aquatic habitat), Static, Not Reported	Measured	10 ppb / ~100 ppb	Accumulation (Accumulation-Residue, Response Site: Whole organism)	NR (10-~100 ppb)	ADME (biotransformation)	Uninformative	6836346
556-67-2	1-14 Day(s), (24 Day(s))	*Pimephales promelas* (Fathead Minnow), Not reported, Not Reported, Laboratory (OBTAINED FROM COMMERCIAL HATCHERIES)	Fresh water, Aqueous (aquatic habitat), Flow-through, Not Reported	Measured	20-80 ppb	Accumulation (Accumulation-Residue, Response Site: Whole organism)	NR (20-80 ppb)	ADME (biotransformation)	Uninformative	6836346
556-67-2	16 Day(s), (16 Day(s))	*Pimephales promelas* (Fathead Minnow), Not reported, Not Reported, Laboratory (OBTAINED FROM COSPER ENVIRONMENTAL SERVICES)	Fresh water, Aqueous (aquatic habitat), Flow-through, 10 Organism	Measured	0 ppb / 30 (14-45) ppb	Mortality (Mortality-Mortality, Response Site: Not reported)	NR-ZERO (30 (14-45) ppb)	Mortality	High	5895957

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Aquatic: Fish Extraction Table

CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
556-67-2	16 Day(s), (16 Day(s))	*Pimephales promelas* (Fathead Minnow), Not reported, Not Reported, Laboratory (OBTAINED FROM COSPER ENVIRONMENTAL SERVICES)	Fresh water, Aqueous (aquatic habitat), Flow-through, 10 Organism	Measured	0 ppb / 30 (14-45) ppb	Growth (Growth-Length,Length to weight ratio,Weight, Response Site: Whole organism)	NR (30 (14-45) ppb)	Development/Growth	High	5895957
556-67-2	16 Day(s), (16 Day(s))	*Pimephales promelas* (Fathead Minnow), Not reported, Not Reported, Laboratory (OBTAINED FROM COSPER ENVIRONMENTAL SERVICES)	Fresh water, Aqueous (aquatic habitat), Flow-through, 10 Organism	Measured	0 ppb / 30 (14-45) ppb	Accumulation (Accumulation-Residue, Response Site: Not reported)	NR (30 (14-45) ppb)	Other (please specify below)	High	5895957
556-67-2	16 Day(s), (16 Day(s))	*Pimephales promelas* (Fathead Minnow), Not reported, Not Reported, Laboratory (OBTAINED FROM COSPER ENVIRONMENTAL SERVICES)	Fresh water, Aqueous (aquatic habitat), Flow-through, Not Reported	Measured	0 ppb / 30 (14-45) ppb	Accumulation (Accumulation-Residue, Response Site: Not reported)	BCF (3000-13,000)	Other (please specify below)	High	5895957
556-67-2	1 Day(s), (20 Day(s))	*Pimephales promelas* (Fathead Minnow), Sexually immature, <=6 Month(s), Not Reported, Laboratory (SPRINGBORN LABORATORIES, INC., WAREHAM, MASSACHUSETTS)	Fresh water, Aqueous (aquatic habitat), Flow-through, 2 Organism	Measured	0 ug/L / 0.51 (0.42-0.69) ug/L	Accumulation (Accumulation-Residue, Response Site: Whole organism)	BCF (0.51 (0.43-0.69) ug/L)	ADME (biotransformation)	High	6834211

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CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
556-67-2	1 Day(s), (20 Day(s))	*Pimephales promelas* (Fathead Minnow), Sexually immature, <=6 Month(s), Not Reported, Laboratory (SPRINGBORN LABORATORIES, INC., WAREHAM, MASSACHUSETTS)	Fresh water, Aqueous (aquatic habitat), Flow-through, 2 Organism	Measured	0 ug/L / 0.41 (0.27-0.49) ug/L	Accumulation (Accumulation-Residue, Response Site: Whole organism)	BCF (0.41 (0.27-0.45) ug/L)	ADME (biotransformation)	High	6834211
556-67-2	1 Day(s), (42 Day(s))	*Pimephales promelas* (Fathead Minnow), Sexually immature, <=6 Month(s), Not Reported, Laboratory (SPRINGBORN LABORATORIES, INC., WAREHAM, MASSACHUSETTS)	Fresh water, Aqueous (aquatic habitat), Flow-through, 4 Organism	Measured	<0.087 ug/L / <0.0868-0.439 ug/L	Accumulation (Accumulation-Residue, Response Site: Whole organism)	BCF (0.372-0.439 ug/L)	ADME (biotransformation)	High	6834211
556-67-2	2 Day(s), (20 Day(s))	*Pimephales promelas* (Fathead Minnow), Sexually immature, <=6 Month(s), Not Reported, Laboratory (SPRINGBORN LABORATORIES, INC., WAREHAM, MASSACHUSETTS)	Fresh water, Aqueous (aquatic habitat), Flow-through, 2 Organism	Measured	0 ug/L / 0.51 (0.42-0.69) ug/L	Accumulation (Accumulation-Residue, Response Site: Whole organism)	BCF (0.51 (0.43-0.69) ug/L)	ADME (biotransformation)	High	6834211

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CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
556-67-2	2 Day(s), (20 Day(s))	*Pimephales promelas* (Fathead Minnow), Sexually immature, <=6 Month(s), Not Reported, Laboratory (SPRINGBORN LABORATORIES, INC., WAREHAM, MASSACHUSETTS)	Fresh water, Aqueous (aquatic habitat), Flow-through, 2 Organism	Measured	0 ug/L / 0.41 (0.27-0.49) ug/L	Accumulation (Accumulation-Residue, Response Site: Whole organism)	BCF (0.41 (0.27-0.45) ug/L)	ADME (biotransformation)	High	6834211
556-67-2	3 Day(s), (42 Day(s))	*Pimephales promelas* (Fathead Minnow), Sexually immature, <=6 Month(s), Not Reported, Laboratory (SPRINGBORN LABORATORIES, INC., WAREHAM, MASSACHUSETTS)	Fresh water, Aqueous (aquatic habitat), Flow-through, 4 Organism	Measured	<0.087 ug/L / <0.0868-0.439 ug/L	Accumulation (Accumulation-Residue, Response Site: Whole organism)	BCF (0.317-0.439 ug/L)	ADME (biotransformation)	High	6834211
556-67-2	3 Day(s), (20 Day(s))	*Pimephales promelas* (Fathead Minnow), Sexually immature, <=6 Month(s), Not Reported, Laboratory (SPRINGBORN LABORATORIES, INC., WAREHAM, MASSACHUSETTS)	Fresh water, Aqueous (aquatic habitat), Flow-through, 2 Organism	Measured	0 ug/L / 0.51 (0.42-0.69) ug/L	Accumulation (Accumulation-Residue, Response Site: Whole organism)	BCF (0.51 (0.42-0.69) ug/L)	ADME (biotransformation)	High	6834211

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CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
556-67-2	3 Day(s), (20 Day(s))	*Pimephales promelas* (Fathead Minnow), Sexually immature, <=6 Month(s), Not Reported, Laboratory (SPRINGBORN LABORATORIES, INC., WAREHAM, MASSACHUSETTS)	Fresh water, Aqueous (aquatic habitat), Flow-through, 2 Organism	Measured	0 ug/L / 0.41 (0.27-0.49) ug/L	Accumulation (Accumulation-Residue, Response Site: Whole organism)	BCF (0.41 (0.27-0.45) ug/L)	ADME (biotransformation)	High	6834211
556-67-2	4 Day(s), (20 Day(s))	*Pimephales promelas* (Fathead Minnow), Sexually immature, <=6 Month(s), Not Reported, Laboratory (SPRINGBORN LABORATORIES, INC., WAREHAM, MASSACHUSETTS)	Fresh water, Aqueous (aquatic habitat), Flow-through, 2 Organism	Measured	0 ug/L / 0.41 (0.27-0.49) ug/L	Accumulation (Accumulation-Residue, Response Site: Whole organism)	BCF (0.41 (0.27-0.45) ug/L)	ADME (biotransformation)	High	6834211
556-67-2	4 Day(s), (20 Day(s))	*Pimephales promelas* (Fathead Minnow), Sexually immature, <=6 Month(s), Not Reported, Laboratory (SPRINGBORN LABORATORIES, INC., WAREHAM, MASSACHUSETTS)	Fresh water, Aqueous (aquatic habitat), Flow-through, 2 Organism	Measured	0 ug/L / 0.51 (0.42-0.69) ug/L	Accumulation (Accumulation-Residue, Response Site: Whole organism)	BCF (0.51 (0.42-0.69) ug/L)	ADME (biotransformation)	High	6834211

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CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
556-67-2	5 Day(s), (20 Day(s))	*Pimephales promelas* (Fathead Minnow), Sexually immature, <=6 Month(s), Not Reported, Laboratory (SPRINGBORN LABORATORIES, INC., WAREHAM, MASSACHUSETTS)	Fresh water, Aqueous (aquatic habitat), Flow-through, 2 Organism	Measured	0 ug/L / 0.41 (0.27-0.49) ug/L	Accumulation (Accumulation-Residue, Response Site: Whole organism)	BCF (0.41 (0.27-0.49) ug/L)	Other (please specify below)	High	6834211
556-67-2	5 Day(s), (20 Day(s))	*Pimephales promelas* (Fathead Minnow), Sexually immature, <=6 Month(s), Not Reported, Laboratory (SPRINGBORN LABORATORIES, INC., WAREHAM, MASSACHUSETTS)	Fresh water, Aqueous (aquatic habitat), Flow-through, 2 Organism	Measured	0 ug/L / 0.51 (0.42-0.69) ug/L	Accumulation (Accumulation-Residue, Response Site: Whole organism)	BCF (0.51 (0.42-0.69) ug/L)	Other (please specify below)	High	6834211
556-67-2	1-6 Day(s), (20 Day(s))	*Pimephales promelas* (Fathead Minnow), Sexually immature, <=6 Month(s), Not Reported, Laboratory (SPRINGBORN LABORATORIES, INC., WAREHAM, MASSACHUSETTS)	Fresh water, Aqueous (aquatic habitat), Flow-through, 30 Organism	Measured	0 ug/L / 0.41 (0.27-0.49) ug/L	Physiology (Injury-Injury, general, Response Site: Not reported)	NR (0.41 (0.27-0.49) ug/L)	Behavioral	Medium	6834211

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CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
556-67-2	1-6 Day(s), (20 Day(s))	*Pimephales promelas* (Fathead Minnow), Sexually immature, <=6 Month(s), Not Reported, Laboratory (SPRINGBORN LABORATORIES, INC., WAREHAM, MASSACHUSETTS)	Fresh water, Aqueous (aquatic habitat), Flow-through, 30 Organism	Measured	0 ug/L / 0.51 (0.42-0.69) ug/L	Behavior (Behavior-Displaying behavior, Response Site: Not reported)	NR (0.51 (0.42-0.69) ug/L)	Behavioral	Medium	6834211
556-67-2	6 Day(s), (20 Day(s))	*Pimephales promelas* (Fathead Minnow), Sexually immature, <=6 Month(s), Not Reported, Laboratory (SPRINGBORN LABORATORIES, INC., WAREHAM, MASSACHUSETTS)	Fresh water, Aqueous (aquatic habitat), Flow-through, 2 Organism	Measured	0 ug/L / 0.51 (0.42-0.69) ug/L	Accumulation (Accumulation-Residue, Response Site: Whole organism)	BCF (0.51 (0.42-0.69) ug/L)	Other (please specify below)	High	6834211
556-67-2	1-6 Day(s), (20 Day(s))	*Pimephales promelas* (Fathead Minnow), Sexually immature, <=6 Month(s), Not Reported, Laboratory (SPRINGBORN LABORATORIES, INC., WAREHAM, MASSACHUSETTS)	Fresh water, Aqueous (aquatic habitat), Flow-through, 30 Organism	Measured	0 ug/L / 0.41 (0.27-0.49) ug/L	Mortality (Mortality-Mortality, Response Site: Not reported)	NR-ZERO (0.41 (0.27-0.49) ug/L)	Mortality	High	6834211

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CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
556-67-2	1-6 Day(s), (20 Day(s))	*Pimephales promelas* (Fathead Minnow), Sexually immature, <=6 Month(s), Not Reported, Laboratory (SPRINGBORN LABORATORIES, INC., WAREHAM, MASSACHUSETTS)	Fresh water, Aqueous (aquatic habitat), Flow-through, 30 Organism	Measured	0 ug/L / 0.51 (0.42-0.69) ug/L	Mortality (Mortality-Mortality, Response Site: Not reported)	NR-ZERO (0.51 (0.42-0.69) ug/L)	Mortality	High	6834211
556-67-2	1-6 Day(s), (20 Day(s))	*Pimephales promelas* (Fathead Minnow), Sexually immature, <=6 Month(s), Not Reported, Laboratory (SPRINGBORN LABORATORIES, INC., WAREHAM, MASSACHUSETTS)	Fresh water, Aqueous (aquatic habitat), Flow-through, 30 Organism	Measured	0 ug/L / 0.41 (0.27-0.49) ug/L	Behavior (Behavior-Displaying behavior, Response Site: Not reported)	NR (0.41 (0.27-0.49) ug/L)	Behavioral	Medium	6834211
556-67-2	1-6 Day(s), (20 Day(s))	*Pimephales promelas* (Fathead Minnow), Sexually immature, <=6 Month(s), Not Reported, Laboratory (SPRINGBORN LABORATORIES, INC., WAREHAM, MASSACHUSETTS)	Fresh water, Aqueous (aquatic habitat), Flow-through, 30 Organism	Measured	0 ug/L / 0.51 (0.42-0.69) ug/L	Physiology (Injury-Injury, general, Response Site: Not reported)	NR (0.51 (0.42-0.69) ug/L)	Behavioral	Medium	6834211

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CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
556-67-2	6 Day(s), (20 Day(s))	*Pimephales promelas* (Fathead Minnow), Sexually immature, <=6 Month(s), Not Reported, Laboratory (SPRINGBORN LABORATORIES, INC., WAREHAM, MASSACHUSETTS)	Fresh water, Aqueous (aquatic habitat), Flow-through, 2 Organism	Measured	0 ug/L / 0.41 (0.27-0.49) ug/L	Accumulation (Accumulation-Residue, Response Site: Whole organism)	BCF (0.41 (0.27-0.49) ug/L)	Other (please specify below)	High	6834211
556-67-2	7 Day(s), (42 Day(s))	*Pimephales promelas* (Fathead Minnow), Sexually immature, <=6 Month(s), Not Reported, Laboratory (SPRINGBORN LABORATORIES, INC., WAREHAM, MASSACHUSETTS)	Fresh water, Aqueous (aquatic habitat), Flow-through, 4 Organism	Measured	<0.087 ug/L / <0.0868-0.439 ug/L	Accumulation (Accumulation-Residue, Response Site: Whole organism)	BCF (0.160-0.439 ug/L)	ADME (biotransformation)	High	6834211
556-67-2	10 Day(s), (42 Day(s))	*Pimephales promelas* (Fathead Minnow), Sexually immature, <=6 Month(s), Not Reported, Laboratory (SPRINGBORN LABORATORIES, INC., WAREHAM, MASSACHUSETTS)	Fresh water, Aqueous (aquatic habitat), Flow-through, 4 Organism	Measured	<0.087 ug/L / <0.0868-0.439 ug/L	Accumulation (Accumulation-Residue, Response Site: Whole organism)	BCF (0.160-0.439 ug/L)	ADME (biotransformation)	High	6834211

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CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
556-67-2	14 Day(s), (42 Day(s))	*Pimephales promelas* (Fathead Minnow), Sexually immature, <=6 Month(s), Not Reported, Laboratory (SPRINGBORN LABORATORIES, INC., WAREHAM, MASSACHUSETTS)	Fresh water, Aqueous (aquatic habitat), Flow-through, 4 Organism	Measured	<0.087 ug/L / <0.0868-0.439 ug/L	Accumulation (Accumulation-Residue, Response Site: Whole organism)	BCF (0.160-0.439 ug/L)	ADME (biotransformation)	High	6834211
556-67-2	18 Day(s), (42 Day(s))	*Pimephales promelas* (Fathead Minnow), Sexually immature, <=6 Month(s), Not Reported, Laboratory (SPRINGBORN LABORATORIES, INC., WAREHAM, MASSACHUSETTS)	Fresh water, Aqueous (aquatic habitat), Flow-through, 4 Organism	Measured	<0.087 ug/L / <0.0868-0.439 ug/L	Accumulation (Accumulation-Residue, Response Site: Whole organism)	BCF (<0.0868-0.439 ug/L)	ADME (biotransformation)	High	6834211
556-67-2	22 Day(s), (42 Day(s))	*Pimephales promelas* (Fathead Minnow), Sexually immature, <=6 Month(s), Not Reported, Laboratory (SPRINGBORN LABORATORIES, INC., WAREHAM, MASSACHUSETTS)	Fresh water, Aqueous (aquatic habitat), Flow-through, 4 Organism	Measured	<0.087 ug/L / <0.0868-0.439 ug/L	Accumulation (Accumulation-Residue, Response Site: Whole organism)	BCF (<0.0868-0.439 ug/L)	Other (please specify below)	High	6834211

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Aquatic: Fish Extraction Table

CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
556-67-2	1-28 Day(s), (42 Day(s))	*Pimephales promelas* (Fathead Minnow), Sexually immature, <=6 Month(s), Not Reported, Laboratory (SPRINGBORN LABORATORIES, INC., WAREHAM, MASSACHUSETTS)	Fresh water, Aqueous (aquatic habitat), Flow-through, 70 Organism	Measured	<0.087 ug/L / <0.0868-0.439 ug/L	Mortality (Mortality-Mortality, Response Site: Not reported)	NR-ZERO (<0.0868-0.439 ug/L)	Mortality	High	6834211
556-67-2	28 Day(s), (42 Day(s))	*Pimephales promelas* (Fathead Minnow), Sexually immature, <=6 Month(s), Not Reported, Laboratory (SPRINGBORN LABORATORIES, INC., WAREHAM, MASSACHUSETTS)	Fresh water, Aqueous (aquatic habitat), Flow-through, Not Reported	Measured	<0.087 ug/L / <0.0868-0.439 ug/L	Accumulation (Accumulation-Residue, Response Site: Residual, remnant, carcass,Viscera)	NR (<0.0868-0.439 ug/L)	Other (please specify below)	High	6834211
556-67-2	1-28 Day(s), (42 Day(s))	*Pimephales promelas* (Fathead Minnow), Sexually immature, <=6 Month(s), Not Reported, Laboratory (SPRINGBORN LABORATORIES, INC., WAREHAM, MASSACHUSETTS)	Fresh water, Aqueous (aquatic habitat), Flow-through, 70 Organism	Measured	<0.087 ug/L / <0.0868-0.439 ug/L	Behavior (Behavior-Displaying behavior, Response Site: Not reported)	NR (<0.0868-0.439 ug/L)	Behavioral	High	6834211

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Aquatic: Fish Extraction Table

CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
556-67-2	1-28 Day(s), (42 Day(s))	*Pimephales promelas* (Fathead Minnow), Sexually immature, <=6 Month(s), Not Reported, Laboratory (SPRINGBORN LABORATORIES, INC., WAREHAM, MASSACHUSETTS)	Fresh water, Aqueous (aquatic habitat), Flow-through, 70 Organism	Measured	<0.087 ug/L / <0.0868-0.439 ug/L	Physiology (Injury-Injury, general, Response Site: Not reported)	NR (<0.0868-0.439 ug/L)	Behavioral	High	6834211
556-67-2	28 Day(s), (42 Day(s))	*Pimephales promelas* (Fathead Minnow), Sexually immature, <=6 Month(s), Not Reported, Laboratory (SPRINGBORN LABORATORIES, INC., WAREHAM, MASSACHUSETTS)	Fresh water, Aqueous (aquatic habitat), Flow-through, 4 Organism	Measured	<0.087 ug/L / <0.0868-0.439 ug/L	Accumulation (Accumulation-Residue, Response Site: Whole organism)	BCF (<0.0868-0.439 ug/L)	Other (please specify below)	High	6834211

* If multiple extractions contained all identical information except the effect level, extraction rows were collapsed and the differing levels are listed by comma in this row.

Aquatic: Non-vascular plants Extraction Table

CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
556-67-2	3-14 Day(s), (14 Day(s))	*Anabaena flosaquae* (Blue-Green Algae), Not reported, Not Reported, Not reported	Fresh water, Aqueous (aquatic habitat), Aquatic - not reported, Not Reported	Unmeasured	0 ppm / 10 ppm / 100 ppm / 500 ppm / 1000 ppm / 2000 ppm	Population (Population-Abundance, Response Site: Not reported)	NR (10-2000 ppm)	Development/Growth	Uninformative	5900580
556-67-2	72 Hour(s), (72 Hour(s))	*Raphidocelis subcapitata* (Green Algae), Not reported, Not Reported, Not reported (NR)	Culture, Aqueous (aquatic habitat), Not reported, Not Reported	Unmeasured	0 % sat / 0 % sat / 80 % sat / 90 % sat	Population (Population-Specific growth rate, Response Site: Not reported)	NR (80-90 % sat)	Development/Growth	Medium	6834433
556-67-2	72 Hour(s), (72 Hour(s))	*Raphidocelis subcapitata* (Green Algae), Not reported, Not Reported, Not reported (NR)	Culture, Aqueous (aquatic habitat), Not reported, Not Reported	Unmeasured	0 % sat / 100 % sat	Population (Population-Specific growth rate, Response Site: Not reported)	NR (100 % sat)	Development/Growth	Medium	6834433
556-67-2	96 Hour(s), (96 Hour(s))	*Selenastrum capricornutum* (Green Algae), Not reported, Not Reported, Laboratory (SPRINGBORN LABORATORIES, ORIGINALLY OBTAINED FROM CAROLINA BIOLOGICAL SUPPLY COMPANY, BURLINGTON, NORTH CAROLINA)	Culture, Aqueous (aquatic habitat), Static, Not Reported	Measured	<1.00-1.9 ug/L / <1.00-29 ug/L	Population (Population-Abundance, Response Site: Not reported)	NOEC (<1.00-29 ug/L)	Development/Growth	High	5889483

* If multiple extractions contained all identical information except the effect level, extraction rows were collapsed and the differing levels are listed by comma in this row.

Aquatic: Worms Extraction Table

CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
556-67-2	28 Day(s), (51 Day(s))	*Lumbriculus variegatus* (Oligochaete, Worm), Not reported, Not Reported, Laboratory (ENVIRONMENTAL CONSULTING AND TESTING 1423 N 8TH ST SUITE 118 SUPERIOR, WI 54880 USA)	Fresh water, Aqueous (aquatic habitat), Sediment, Not Reported	Measured	<0.835 AI mg/kg dw sediment / 0.86 (0.594-1.07) AI mg/kg dw sediment / 4.06 (1.53-6.47) AI mg/kg dw sediment	Accumulation (Accumulation-Residue, Response Site: Tissue)	BAF (0.86 (0.594-1.07) AI mg/kg dw sediment)	Other (please specify below)	High	7002241
556-67-2	28 Day(s), (51 Day(s))	*Lumbriculus variegatus* (Oligochaete, Worm), Not reported, Not Reported, Laboratory (ENVIRONMENTAL CONSULTING AND TESTING 1423 N 8TH ST SUITE 118 SUPERIOR, WI 54880 USA)	Fresh water, Aqueous (aquatic habitat), Sediment, Not Reported	Measured	<0.835 AI mg/kg dw sediment / 0.86 (0.594-1.07) AI mg/kg dw sediment / 4.06 (1.53-6.47) AI mg/kg dw sediment	Accumulation (Accumulation-Residue, Response Site: Tissue)	BAF (4.06 (1.53-6.47) AI mg/kg dw sediment)	Other (please specify below)	High	7002241
556-67-2	28 Day(s), (51 Day(s))	*Lumbriculus variegatus* (Oligochaete, Worm), Not reported, Not Reported, Laboratory (ENVIRONMENTAL CONSULTING AND TESTING 1423 N 8TH ST SUITE 118 SUPERIOR, WI 54880 USA)	Fresh water, Aqueous (aquatic habitat), Sediment, Not Reported	Measured	<0.835 AI mg/kg dw sediment / 0.86 (0.594-1.07) AI mg/kg dw sediment / 4.06 (1.53-6.47) AI mg/kg dw sediment	Accumulation (Accumulation-Residue, Response Site: Tissue)	NR (0.594-6.47 AI mg/kg dw sediment)	Other (please specify below)	High	7002241

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Aquatic: Worms Extraction Table

CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
556-67-2	28 Day(s), (51 Day(s))	*Lumbriculus variegatus* (Oligochaete, Worm), Not reported, Not Reported, Laboratory (ENVIRONMENTAL CONSULTING AND TESTING 1423 N 8TH ST SUITE 118 SUPERIOR, WI 54880 USA)	Fresh water, Aqueous (aquatic habitat), Sediment, Not Reported	Measured	<0.835 AI mg/kg dw sediment / 0.86 (0.594-1.07) AI mg/kg dw sediment / 4.06 (1.53-6.47) AI mg/kg dw sediment	Mortality (Mortality-Mortality, Response Site: Not reported)	NR-ZERO (4.06 (1.53-6.47) AI mg/kg dw sediment)	Mortality	High	7002241
556-67-2	28 Day(s), (51 Day(s))	*Lumbriculus variegatus* (Oligochaete, Worm), Not reported, Not Reported, Laboratory (ENVIRONMENTAL CONSULTING AND TESTING 1423 N 8TH ST SUITE 118 SUPERIOR, WI 54880 USA)	Fresh water, Aqueous (aquatic habitat), Sediment, Not Reported	Measured	<0.835 AI mg/kg dw sediment / 0.86 (0.594-1.07) AI mg/kg dw sediment / 4.06 (1.53-6.47) AI mg/kg dw sediment	Behavior (Avoidance-Chemical avoidance, Response Site: Not reported)	NR (0.594-6.47 AI mg/kg dw sediment)	Behavioral	Uninformative	7002241
556-67-2	28 Day(s), (51 Day(s))	*Lumbriculus variegatus* (Oligochaete, Worm), Not reported, Not Reported, Laboratory (ENVIRONMENTAL CONSULTING AND TESTING 1423 N 8TH ST SUITE 118 SUPERIOR, WI 54880 USA)	Fresh water, Aqueous (aquatic habitat), Sediment, Not Reported	Measured	<0.835 AI mg/kg dw sediment / 0.86 (0.594-1.07) AI mg/kg dw sediment / 4.06 (1.53-6.47) AI mg/kg dw sediment	Biochemical (Biochemistry-Lipid, Response Site: Tissue)	NR (0.594-6.47 AI mg/kg dw sediment)	Nutritional and Metabolic	Uninformative	7002241

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Aquatic: Worms Extraction Table

CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
556-67-2	28 Day(s), (28 Day(s))	*Lumbriculus variegatus* (Oligochaete, Worm), Adult, Not Reported, Laboratory (FROM ENVIRONMENTAL CONSULTING AND TESTING, SUPERIOR, WISCONSIN)	Fresh water, Aqueous (aquatic habitat), Sediment, Not Reported	Measured	<0.510 mg/kg dw sediment / 0.73 (0.390-1.00) mg/kg dw sediment / 1.5 (0.620-2.66) mg/kg dw sediment / 3.1 (2.24-3.95) mg/kg dw sediment / 5.8 (5.24-6.99) mg/kg dw sediment / 11 (9.62-11.9) mg/kg dw sediment / 38 (34.4-45.1) mg/kg dw sediment	Growth (Growth-Weight, Response Site: Whole organism)	LOEC (>38 mg/kg dw sediment)	Development/Growth	High	7002243
556-67-2	28 Day(s), (28 Day(s))	*Lumbriculus variegatus* (Oligochaete, Worm), Adult, Not Reported, Laboratory (FROM ENVIRONMENTAL CONSULTING AND TESTING, SUPERIOR, WISCONSIN)	Fresh water, Aqueous (aquatic habitat), Sediment, Not Reported	Measured	<0.510 mg/kg dw sediment / 0.73 (0.390-1.00) mg/kg dw sediment / 1.5 (0.620-2.66) mg/kg dw sediment / 3.1 (2.24-3.95) mg/kg dw sediment / 5.8 (5.24-6.99) mg/kg dw sediment / 11 (9.62-11.9) mg/kg dw sediment / 38 (34.4-45.1) mg/kg dw sediment	Growth (Growth-Weight, Response Site: Whole organism)	NOEC (38 (34.4-45.1) mg/kg dw sediment)	Development/Growth	High	7002243

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Aquatic: Worms Extraction Table

CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
556-67-2	28 Day(s), (28 Day(s))	*Lumbriculus variegatus* (Oligochaete, Worm), Adult, Not Reported, Laboratory (FROM ENVIRONMENTAL CONSULTING AND TESTING, SUPERIOR, WISCONSIN)	Fresh water, Aqueous (aquatic habitat), Sediment, Not Reported	Measured	<0.510 mg/kg dw sediment / 0.73 (0.390-1.00) mg/kg dw sediment / 1.5 (0.620-2.66) mg/kg dw sediment / 3.1 (2.24-3.95) mg/kg dw sediment / 5.8 (5.24-6.99) mg/kg dw sediment / 11 (9.62-11.9) mg/kg dw sediment / 38 (34.4-45.1) mg/kg dw sediment	Multiple (Multiple-Multiple effects reported as one result, Response Site: Not reported)	EC50 (9.32 (4.38-25.4) mg/kg dw sediment)	Reproductive/Teratogenic	High	7002243
556-67-2	28 Day(s), (28 Day(s))	*Lumbriculus variegatus* (Oligochaete, Worm), Adult, Not Reported, Laboratory (FROM ENVIRONMENTAL CONSULTING AND TESTING, SUPERIOR, WISCONSIN)	Fresh water, Aqueous (aquatic habitat), Sediment, Not Reported	Measured	<0.510 mg/kg dw sediment / 0.73 (0.390-1.00) mg/kg dw sediment / 1.5 (0.620-2.66) mg/kg dw sediment / 3.1 (2.24-3.95) mg/kg dw sediment / 5.8 (5.24-6.99) mg/kg dw sediment / 11 (9.62-11.9) mg/kg dw sediment / 38 (34.4-45.1) mg/kg dw sediment	Multiple (Multiple-Multiple effects reported as one result, Response Site: Not reported)	LOEC (0.73 (0.390-1.00) mg/kg dw sediment)	Reproductive/Teratogenic	High	7002243

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Aquatic: Worms Extraction Table

CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
556-67-2	28 Day(s), (28 Day(s))	*Lumbriculus variegatus* (Oligochaete, Worm), Adult, Not Reported, Laboratory (FROM ENVIRONMENTAL CONSULTING AND TESTING, SUPERIOR, WISCONSIN)	Fresh water, Aqueous (aquatic habitat), Sediment, Not Reported	Measured	<0.510 mg/kg dw sediment / 0.73 (0.390-1.00) mg/kg dw sediment / 1.5 (0.620-2.66) mg/kg dw sediment / 3.1 (2.24-3.95) mg/kg dw sediment / 5.8 (5.24-6.99) mg/kg dw sediment / 11 (9.62-11.9) mg/kg dw sediment / 38 (34.4-45.1) mg/kg dw sediment	Multiple (Multiple-Multiple effects reported as one result, Response Site: Not reported)	NOEC (<0.73 mg/kg dw sediment)	Reproductive/Teratogenic	High	7002243
556-67-2	28 Day(s), (28 Day(s))	*Lumbriculus variegatus* (Oligochaete, Worm), Not reported, Not Reported, Laboratory (FROM MAIN LABORATORY CULTURES MAINTAINED AT SPRINGBORN SMITHERS LABORATORIES, WAREHAM, MASSACHUSETTS, USA)	Fresh water, Aqueous (aquatic habitat), Sediment, Not Reported	Unmeasured	0 AI mg/kg dw sediment / 0 AI mg/kg dw sediment / 0.050 AI mg/kg dw sediment / 0.50 AI mg/kg dw sediment / 5.0 AI mg/kg dw sediment / 50 AI mg/kg dw sediment / 500 AI mg/kg dw sediment	Population (Population-Biomass, Response Site: Not reported)	LOEC (500 AI mg/kg dw sediment)	Development/Growth	High	7309671

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Aquatic: Worms Extraction Table

CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
556-67-2	28 Day(s), (28 Day(s))	*Lumbriculus variegatus* (Oligochaete, Worm), Not reported, Not Reported, Laboratory (FROM MAIN LABORATORY CULTURES MAINTAINED AT SPRINGBORN SMITHERS LABORATORIES, WAREHAM, MASSACHUSETTS, USA)	Fresh water, Aqueous (aquatic habitat), Sediment, Not Reported	Unmeasured	0 AI mg/kg dw sediment / 0 AI mg/kg dw sediment / 0.050 AI mg/kg dw sediment / 0.50 AI mg/kg dw sediment / 5.0 AI mg/kg dw sediment / 50 AI mg/kg dw sediment / 500 AI mg/kg dw sediment	Population (Population-Biomass, Response Site: Not reported)	NOEC (50 AI mg/kg dw sediment)	Development/Growth	High	7309671
556-67-2	28 Day(s), (28 Day(s))	*Lumbriculus variegatus* (Oligochaete, Worm), Not reported, Not Reported, Laboratory (FROM MAIN LABORATORY CULTURES MAINTAINED AT SPRINGBORN SMITHERS LABORATORIES, WAREHAM, MASSACHUSETTS, USA)	Fresh water, Aqueous (aquatic habitat), Sediment, Not Reported	Measured	<0.60 AI mg/kg dw sediment / <0.60 AI mg/kg dw sediment / 1.2 (0.92-1.6) AI mg/kg dw sediment / 3.2 (2.3-3.7) AI mg/kg dw sediment / 8.8 (6.9-13) AI mg/kg dw sediment / 13 (8.3-18) AI mg/kg dw sediment / 19 (15-24) AI mg/kg dw sediment / 32 (29-39) AI mg/kg dw sediment	Population (Population-Biomass, Response Site: Not reported)	NOEC (32 (29-39) AI mg/kg dw sediment)	Development/Growth	High	7309671

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Aquatic: Worms Extraction Table

CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
556-67-2	28 Day(s), (28 Day(s))	*Lumbriculus variegatus* (Oligochaete, Worm), Not reported, Not Reported, Laboratory (FROM MAIN LABORATORY CULTURES MAINTAINED AT SPRINGBORN SMITHERS LABORATORIES, WAREHAM, MASSACHUSETTS, USA)	Fresh water, Aqueous (aquatic habitat), Sediment, Not Reported	Measured	<0.60 AI mg/kg dw sediment / <0.60 AI mg/kg dw sediment / 1.2 (0.92-1.6) AI mg/kg dw sediment / 3.2 (2.3-3.7) AI mg/kg dw sediment / 8.8 (6.9-13) AI mg/kg dw sediment / 13 (8.3-18) AI mg/kg dw sediment / 19 (15-24) AI mg/kg dw sediment / 32 (29-39) AI mg/kg dw sediment	Growth (Growth-Limb/ body part regeneration, Response Site: Not reported)	NR (0.92-39 AI mg/kg dw sediment)	Development/Growth	High	7309671

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Aquatic: Worms Extraction Table

CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
556-67-2	28 Day(s), (28 Day(s))	*Lumbriculus variegatus* (Oligochaete, Worm), Not reported, Not Reported, Laboratory (FROM MAIN LABORATORY CULTURES MAINTAINED AT SPRINGBORN SMITHERS LABORATORIES, WAREHAM, MASSACHUSETTS, USA)	Fresh water, Aqueous (aquatic habitat), Sediment, Not Reported	Measured	<0.60 AI mg/kg dw sediment / <0.60 AI mg/kg dw sediment / 1.2 (0.92-1.6) AI mg/kg dw sediment / 3.2 (2.3-3.7) AI mg/kg dw sediment / 8.8 (6.9-13) AI mg/kg dw sediment / 13 (8.3-18) AI mg/kg dw sediment / 19 (15-24) AI mg/kg dw sediment / 32 (29-39) AI mg/kg dw sediment	Reproduction (Reproduction-Reproduction, general, Response Site: Not reported)	NR (0.92-39 AI mg/kg dw sediment)	Reproductive/Teratogenic	High	7309671
556-67-2	28 Day(s), (28 Day(s))	*Lumbriculus variegatus* (Oligochaete, Worm), Not reported, Not Reported, Laboratory (FROM MAIN LABORATORY CULTURES MAINTAINED AT SPRINGBORN SMITHERS LABORATORIES, WAREHAM, MASSACHUSETTS, USA)	Fresh water, Aqueous (aquatic habitat), Sediment, Not Reported	Unmeasured	0 AI mg/kg dw sediment / 0 AI mg/kg dw sediment / 0.050 AI mg/kg dw sediment / 0.50 AI mg/kg dw sediment / 5.0 AI mg/kg dw sediment / 50 AI mg/kg dw sediment / 500 AI mg/kg dw sediment	Mortality (Mortality-Survival, Response Site: Not reported)	LOEC (50 AI mg/kg dw sediment)	Mortality	High	7309671

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Aquatic: Worms Extraction Table

CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
556-67-2	28 Day(s), (28 Day(s))	*Lumbriculus variegatus* (Oligochaete, Worm), Not reported, Not Reported, Laboratory (FROM MAIN LABORATORY CULTURES MAINTAINED AT SPRINGBORN SMITHERS LABORATORIES, WAREHAM, MASSACHUSETTS, USA)	Fresh water, Aqueous (aquatic habitat), Sediment, Not Reported	Unmeasured	0 AI mg/kg dw sediment / 0 AI mg/kg dw sediment / 0.050 AI mg/kg dw sediment / 0.50 AI mg/kg dw sediment / 5.0 AI mg/kg dw sediment / 50 AI mg/kg dw sediment / 500 AI mg/kg dw sediment	Mortality (Mortality-Survival, Response Site: Not reported)	NOEC (5.0 AI mg/kg dw sediment)	Mortality	High	7309671
556-67-2	28 Day(s), (28 Day(s))	*Lumbriculus variegatus* (Oligochaete, Worm), Not reported, Not Reported, Laboratory (FROM MAIN LABORATORY CULTURES MAINTAINED AT SPRINGBORN SMITHERS LABORATORIES, WAREHAM, MASSACHUSETTS, USA)	Fresh water, Aqueous (aquatic habitat), Sediment, Not Reported	Measured	<0.60 AI mg/kg dw sediment / <0.60 AI mg/kg dw sediment / 1.2 (0.92-1.6) AI mg/kg dw sediment / 3.2 (2.3-3.7) AI mg/kg dw sediment / 8.8 (6.9-13) AI mg/kg dw sediment / 13 (8.3-18) AI mg/kg dw sediment / 19 (15-24) AI mg/kg dw sediment / 32 (29-39) AI mg/kg dw sediment	Multiple (Multiple-Multiple effects reported as one result, Response Site: Not reported)	EC50 (>32 AI mg/kg dw sediment)	Mortality	High	7309671

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Aquatic: Worms Extraction Table

CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
556-67-2	28 Day(s), (28 Day(s))	*Lumbriculus variegatus* (Oligochaete, Worm), Not reported, Not Reported, Laboratory (FROM MAIN LABORATORY CULTURES MAINTAINED AT SPRINGBORN SMITHERS LABORATORIES, WAREHAM, MASSACHUSETTS, USA)	Fresh water, Aqueous (aquatic habitat), Sediment, Not Reported	Measured	<0.60 AI mg/kg dw sediment / <0.60 AI mg/kg dw sediment / 1.2 (0.92-1.6) AI mg/kg dw sediment / 3.2 (2.3-3.7) AI mg/kg dw sediment / 8.8 (6.9-13) AI mg/kg dw sediment / 13 (8.3-18) AI mg/kg dw sediment / 19 (15-24) AI mg/kg dw sediment / 32 (29-39) AI mg/kg dw sediment	Mortality (Mortality-Survival, Response Site: Not reported)	LOEC (19 (15-24) AI mg/kg dw sediment)	Mortality	High	7309671

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Aquatic: Worms Extraction Table

CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
556-67-2	28 Day(s), (28 Day(s))	*Lumbriculus variegatus* (Oligochaete, Worm), Not reported, Not Reported, Laboratory (FROM MAIN LABORATORY CULTURES MAINTAINED AT SPRINGBORN SMITHERS LABORATORIES, WAREHAM, MASSACHUSETTS, USA)	Fresh water, Aqueous (aquatic habitat), Sediment, Not Reported	Measured	<0.60 AI mg/kg dw sediment / <0.60 AI mg/kg dw sediment / 1.2 (0.92-1.6) AI mg/kg dw sediment / 3.2 (2.3-3.7) AI mg/kg dw sediment / 8.8 (6.9-13) AI mg/kg dw sediment / 13 (8.3-18) AI mg/kg dw sediment / 19 (15-24) AI mg/kg dw sediment / 32 (29-39) AI mg/kg dw sediment	Mortality (Mortality-Survival, Response Site: Not reported)	NOEC (13 (8.3-18) AI mg/kg dw sediment)	Mortality	High	7309671

* If multiple extractions contained all identical information except the effect level, extraction rows were collapsed and the differing levels are listed by comma in this row.

Terrestrial: Arthropods Extraction Table

CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
556-67-2	48 Hour(s), (48 Hour(s))	*Acyrthosiphon pisum ssp. pisum* (Pea Aphid), Adult, Not Reported, Laboratory (NR)	Litter, Exposures that include multiple exposure groups, Multiple routes between application groups, Not Reported	Unmeasured	1000 ppm	Mortality (Mortality-Mortality, Response Site: Not reported)	NR-ZERO (1000 ppm)	Mortality	Uninformative	5885944
556-67-2	5 Day(s), (5 Day(s))	*Acyrthosiphon pisum ssp. pisum* (Pea Aphid), Adult, Not Reported, Laboratory (NR)	Litter, Exposures that include multiple exposure groups, Multiple routes between application groups, Not Reported	Unmeasured	100 ppm	Mortality (Mortality-Mortality, Response Site: Not reported)	NR-ZERO (100 ppm)	Mortality	Uninformative	5885944
556-67-2	1 Minute(s), (1 Minute(s))	*Bovicola bovis* (Red Louse), Adult, Not Reported, Laboratory (FROM A NATURALLY INFECTED CALF HELD AT THE COLLEGE OF VETERINARY MEDICINE, MICHIGAN STATE UNIVERSITY)	Filter paper, Topical, Dermal, 5 Organism	Unmeasured	0 % v/v / 100 % v/v	Mortality (Mortality-Mortality, Response Site: Not reported)	NR-LETH (100 % v/v)	Mortality	Uninformative	7310461
556-67-2	1 Minute(s), (1 Minute(s))	*Bovicola bovis* (Red Louse), Adult, Not Reported, Laboratory (FROM A NATURALLY INFECTED CALF HELD AT THE COLLEGE OF VETERINARY MEDICINE, MICHIGAN STATE UNIVERSITY)	No substrate, Topical, Immersion, 5 Organism	Unmeasured	0 % v/v / 100 % v/v	Mortality (Mortality-Mortality, Response Site: Not reported)	NR-LETH (100 % v/v)	Mortality	Uninformative	7310461

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Terrestrial: Arthropods Extraction Table

CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
556-67-2	0.5 Minute(s), (1 Minute(s))	*Bovicola bovis* (Red Louse), Adult, Not Reported, Laboratory (FROM A NATURALLY INFECTED CALF HELD AT THE COLLEGE OF VETERINARY MEDICINE, MICHIGAN STATE UNIVERSITY)	Filter paper, Topical, Dermal, 5 Organism	Unmeasured	0 % v/v / 100 % v/v	Mortality (Mortality-Mortality, Response Site: Not reported)	NR-ZERO (100 % v/v)	Mortality	Uninformative	7310461
556-67-2	0.5 Minute(s), (1 Minute(s))	*Bovicola bovis* (Red Louse), Adult, Not Reported, Laboratory (FROM A NATURALLY INFECTED CALF HELD AT THE COLLEGE OF VETERINARY MEDICINE, MICHIGAN STATE UNIVERSITY)	No substrate, Topical, Immersion, 5 Organism	Unmeasured	0 % v/v / 100 % v/v	Mortality (Mortality-Mortality, Response Site: Not reported)	NR-ZERO (100 % v/v)	Mortality	Uninformative	7310461
556-67-2	1-14 Hour(s), (14 Hour(s))	*Bovicola bovis* (Red Louse), Adult, Not Reported, Laboratory (FROM A NATURALLY INFECTED CALF HELD AT THE COLLEGE OF VETERINARY MEDICINE, MICHIGAN STATE UNIVERSITY)	No substrate, Environmental, Spray, unspecified, Not Reported	Unmeasured	0 % v/v / 100 % v/v	Mortality (Mortality-Mortality, Response Site: Not reported)	NR (100 % v/v)	Mortality	Uninformative	7310461

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Terrestrial: Arthropods Extraction Table

CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
556-67-2	48 Hour(s), (48 Hour(s))	*Epilachna varivestis* (Mexican Bean Beetle), Larva, Not Reported, Laboratory (NR)	Litter, Oral (diet, drink, gavage), Food, Not Reported	Unmeasured	1000 ppm diet	Mortality (Mortality-Mortality, Response Site: Not reported)	NR-ZERO (1000 ppm diet)	Mortality	Uninformative	5885944
556-67-2	24 Hour(s), (24 Hour(s))	*Gromphadorhina portentosa* (Madagascar Giant Hissing Cockroach), Adult, Both, Not reported (NR)	No substrate, Topical, Dermal, Not Reported	Unmeasured	0 ul/g / 0.5 ul/g / NR / 9 ul/g	Physiology (Intoxication-Immobile, Response Site: Not reported)	ED50 (1691 (1045-2194) mg/kg bdwt)	Immobilization	Uninformative	7307184
556-67-2	24 Hour(s), (24 Hour(s))	*Gromphadorhina portentosa* (Madagascar Giant Hissing Cockroach), Adult, Both, Not reported (NR)	No substrate, Topical, Dermal, Not Reported	Unmeasured	0 ul/g / 0.5 ul/g / NR / 9 ul/g	Mortality (Mortality-Knockdown, Response Site: Not reported)	LD50 (2736 (2213-3363) mg/kg bdwt)	Mortality	Uninformative	7307184
556-67-2	24 Hour(s), (24 Hour(s))	*Musca domestica* (House Fly), Adult, Not Reported, Laboratory (NR)	No substrate, Topical, Dermal, Not Reported	Unmeasured	1000 ppm	Mortality (Mortality-Mortality, Response Site: Not reported)	NR-ZERO (1000 ppm)	Mortality	Uninformative	5885944
556-67-2	48 Hour(s), (48 Hour(s))	*Persectania ewingii* (Southern Armyworm), Larva, Not Reported, Laboratory (NR)	Litter, Oral (diet, drink, gavage), Food, Not Reported	Unmeasured	1000 ppm diet	Mortality (Mortality-Mortality, Response Site: Not reported)	NR-ZERO (1000 ppm diet)	Mortality	Uninformative	5885944
556-67-2	5 Day(s), (5 Day(s))	*Tetranychus sp.* (Mite), Adult (Measured in: Egg), Not Reported, Laboratory (NR)	Litter, Exposures that include multiple exposure groups, Multiple routes between application groups, NA Egg	Unmeasured	1000 ppm	Mortality (Mortality-Mortality, Response Site: Not reported)	NR (1000 ppm)	Mortality	Uninformative	5885944

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Terrestrial: Arthropods Extraction Table

CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
556-67-2	5 Day(s), (5 Day(s))	*Tetranychus sp.* (Mite), Adult, Not Reported, Laboratory (NR)	Litter, Exposures that include multiple exposure groups, Multiple routes between application groups, NA Adult	Unmeasured	1000 ppm	Mortality (Mortality-Mortality, Response Site: Not reported)	NR-ZERO (1000 ppm)	Mortality	Uninformative	5885944

* If multiple extractions contained all identical information except the effect level, extraction rows were collapsed and the differing levels are listed by comma in this row.

Terrestrial: Worms Extraction Table

CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
556-67-2	28 Day(s), (56 Day(s))	*Eisenia fetida* (Earthworm), Mature, 3-5 Month(s) (Measured in: F0 generation), Not Reported, Laboratory (SMITHERS)	Natural soil, Environmental, Culture medium, 41 F0 generation	Measured	<0.20 mg/kg dry soil / 8.3 (1.7-19) mg/kg dry soil / 14 (2.2-40) mg/kg dry soil / 33 (7.3-79) mg/kg dry soil / 75 (12-190) mg/kg dry soil / 130 (35-300) mg/kg dry soil	Growth (Growth-Weight, Response Site: Whole organism)	EC50 (>130 mg/kg dry soil)	Development/Growth	High	10706155
556-67-2	28 Day(s), (56 Day(s))	*Eisenia fetida* (Earthworm), Mature, 3-5 Month(s) (Measured in: F0 generation), Not Reported, Laboratory (SMITHERS)	Natural soil, Environmental, Culture medium, 41 F0 generation	Measured	<0.20 mg/kg dry soil / 8.3 (1.7-19) mg/kg dry soil / 14 (2.2-40) mg/kg dry soil / 33 (7.3-79) mg/kg dry soil / 75 (12-190) mg/kg dry soil / 130 (35-300) mg/kg dry soil	Mortality (Mortality-Survival, Response Site: Not reported)	LC50 (>130 mg/kg dry soil)	Mortality	High	10706155
556-67-2	28 Day(s), (56 Day(s))	*Eisenia fetida* (Earthworm), Mature, 3-5 Month(s) (Measured in: F0 generation), Not Reported, Laboratory (SMITHERS)	Natural soil, Environmental, Culture medium, 41 F0 generation	Measured	<0.20 mg/kg dry soil / 8.3 (1.7-19) mg/kg dry soil / 14 (2.2-40) mg/kg dry soil / 33 (7.3-79) mg/kg dry soil / 75 (12-190) mg/kg dry soil / 130 (35-300) mg/kg dry soil	Growth (Growth-Weight, Response Site: Whole organism)	LOEL (>130 mg/kg dry soil)	Development/Growth	High	10706155

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Terrestrial: Worms Extraction Table

CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
556-67-2	28 Day(s), (56 Day(s))	*Eisenia fetida* (Earthworm), Mature, 3-5 Month(s) (Measured in: F0 generation), Not Reported, Laboratory (SMITHERS)	Natural soil, Environmental, Culture medium, 41 F0 generation	Measured	<0.20 mg/kg dry soil / 8.3 (1.7-19) mg/kg dry soil / 14 (2.2-40) mg/kg dry soil / 33 (7.3-79) mg/kg dry soil / 75 (12-190) mg/kg dry soil / 130 (35-300) mg/kg dry soil	Mortality (Mortality-Survival, Response Site: Not reported)	LOEL (>130 mg/kg dry soil)	Mortality	High	10706155
556-67-2	28 Day(s), (56 Day(s))	*Eisenia fetida* (Earthworm), Mature, 3-5 Month(s) (Measured in: F0 generation), Not Reported, Laboratory (SMITHERS)	Natural soil, Environmental, Culture medium, 41 F0 generation	Measured	<0.20 mg/kg dry soil / 8.3 (1.7-19) mg/kg dry soil / 14 (2.2-40) mg/kg dry soil / 33 (7.3-79) mg/kg dry soil / 75 (12-190) mg/kg dry soil / 130 (35-300) mg/kg dry soil	Growth (Growth-Weight, Response Site: Whole organism)	NOEL (130 (49-300) mg/kg dry soil)	Development/Growth	High	10706155
556-67-2	28 Day(s), (56 Day(s))	*Eisenia fetida* (Earthworm), Mature, 3-5 Month(s) (Measured in: F0 generation), Not Reported, Laboratory (SMITHERS)	Natural soil, Environmental, Culture medium, 41 F0 generation	Measured	<0.20 mg/kg dry soil / 8.3 (1.7-19) mg/kg dry soil / 14 (2.2-40) mg/kg dry soil / 33 (7.3-79) mg/kg dry soil / 75 (12-190) mg/kg dry soil / 130 (35-300) mg/kg dry soil	Mortality (Mortality-Survival, Response Site: Not reported)	NOEL (130 (49-300) mg/kg dry soil)	Mortality	High	10706155

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Terrestrial: Worms Extraction Table

CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
556-67-2	28 Day(s), (56 Day(s))	*Eisenia fetida* (Earthworm), Mature, 3-5 Month(s) (Measured in: F0 generation), Not Reported, Laboratory (SMITHERS)	Natural soil, Environmental, Culture medium, 41 F0 generation	Measured	<0.20 mg/kg dry soil / 8.3 (1.7-19) mg/kg dry soil / 14 (2.2-40) mg/kg dry soil / 33 (7.3-79) mg/kg dry soil / 75 (12-190) mg/kg dry soil / 130 (35-300) mg/kg dry soil	Mortality (Mortality-Mortality, Response Site: Not reported)	NR-ZERO (130 (49-300) mg/kg dry soil)	Mortality	High	10706155
556-67-2	56 Day(s), (56 Day(s))	*Eisenia fetida* (Earthworm), Mature, 3-5 Month(s) (Measured in: F0 generation), Not Reported, Laboratory (SMITHERS)	Natural soil, Environmental, Culture medium, NA F0 generation	Measured	<0.20 mg/kg dry soil / 8.3 (1.7-19) mg/kg dry soil / 14 (2.2-40) mg/kg dry soil / 33 (7.3-79) mg/kg dry soil / 75 (12-190) mg/kg dry soil / 130 (35-300) mg/kg dry soil	Reproduction (Reproduction-Progeny counts/numbers, Response Site: Not reported)	EC50 (>130 mg/kg dry soil)	Reproductive/Teratogenic	High	10706155
556-67-2	56 Day(s), (56 Day(s))	*Eisenia fetida* (Earthworm), Mature, 3-5 Month(s) (Measured in: F0 generation), Not Reported, Laboratory (SMITHERS)	Natural soil, Environmental, Culture medium, NA F0 generation	Measured	<0.20 mg/kg dry soil / 8.3 (1.7-19) mg/kg dry soil / 14 (2.2-40) mg/kg dry soil / 33 (7.3-79) mg/kg dry soil / 75 (12-190) mg/kg dry soil / 130 (35-300) mg/kg dry soil	Reproduction (Reproduction-Progeny counts/numbers, Response Site: Not reported)	LOEL (130 (35-300) mg/kg dry soil)	Reproductive/Teratogenic	High	10706155

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Terrestrial: Worms Extraction Table

CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
556-67-2	56 Day(s), (56 Day(s))	*Eisenia fetida* (Earthworm), Mature, 3-5 Month(s) (Measured in: F0 generation), Not Reported, Laboratory (SMITHERS)	Natural soil, Environmental, Culture medium, NA F0 generation	Measured	<0.20 mg/kg dry soil / 8.3 (1.7-19) mg/kg dry soil / 14 (2.2-40) mg/kg dry soil / 33 (7.3-79) mg/kg dry soil / 75 (12-190) mg/kg dry soil / 130 (35-300) mg/kg dry soil	Reproduction (Reproduction-Progeny counts/numbers, Response Site: Not reported)	NOEL (75 (12-190) mg/kg dry soil)	Reproductive/Teratogenic	High	10706155

* If multiple extractions contained all identical information except the effect level, extraction rows were collapsed and the differing levels are listed by comma in this row.

Aquatic: Arthropods Extraction Table

CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
1066-42-8	24 Hour(s), (24 Hour(s))	*Aedes aegypti* (Yellow Fever Mosquito), Larva, 4 Instar, Not Reported, Laboratory (NR)	Fresh water, Aqueous (aquatic habitat), Static, Not Reported	Unmeasured	10 ppm	Mortality (Mortality-Mortality, Response Site: Not reported)	NR-ZERO (10 ppm)	Mortality	Uninformative	5885944
1066-42-8	24 Hour(s), (48 Hour(s))	*Daphnia magna* (Water Flea), Neonate, <24 Hour(s), Not Reported, Laboratory (ORIGINAL BROOD STOCK FROM AQUATIC BIOSYSTEMS, FORT COLLINS, COLORADO, THEN CULTURED IN-HOUSE)	Fresh water, Aqueous (aquatic habitat), Static, 10 Organism	Measured	<11.2 mg/L / 117 (115-119) mg/L	Mortality (Mortality-Mortality, Response Site: Not reported)	EC50 (>117 mg/L)	Immobilization	High	9731652
1066-42-8	48 Hour(s), (48 Hour(s))	*Daphnia magna* (Water Flea), Neonate, <24 Hour(s), Not Reported, Laboratory (ORIGINAL BROOD STOCK FROM AQUATIC BIOSYSTEMS, FORT COLLINS, COLORADO, THEN CULTURED IN-HOUSE)	Fresh water, Aqueous (aquatic habitat), Static, 10 Organism	Measured	<11.2 mg/L / 117 (115-119) mg/L	Mortality (Mortality-Mortality, Response Site: Not reported)	EC50 (>117 mg/L)	Mortality	High	9731652

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Aquatic: Arthropods Extraction Table

CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
1066-42-8	24-48 Hour(s), (48 Hour(s))	*Daphnia magna* (Water Flea), Neonate, <24 Hour(s), Not Reported, Laboratory (ORIGINAL BROOD STOCK FROM AQUATIC BIOSYSTEMS, FORT COLLINS, COLORADO, THEN CULTURED IN-HOUSE)	Fresh water, Aqueous (aquatic habitat), Static, 10 Organism	Measured	<11.2 mg/L / 117 (115-119) mg/L	Behavior (Behavior-Swimming, Response Site: Not reported)	NR (117 (115-119) mg/L)	Behavioral	High	9731652
1066-42-8	48 Hour(s), (48 Hour(s))	*Daphnia magna* (Water Flea), Neonate, <24 Hour(s), Not Reported, Laboratory (ORIGINAL BROOD STOCK FROM AQUATIC BIOSYSTEMS, FORT COLLINS, COLORADO, THEN CULTURED IN-HOUSE)	Fresh water, Aqueous (aquatic habitat), Static, 10 Organism	Measured	<11.2 mg/L / 117 (115-119) mg/L	Mortality (Mortality-Mortality, Response Site: Not reported)	NR-ZERO (117 (115-119) mg/L)	Mortality	High	9731652
1066-42-8	8-12 Day(s), (21 Day(s))	*Daphnia magna* (Water Flea), Neonate, <24 Hour(s) (Measured in: F0 generation), Not Reported, Laboratory (INITIALLY OBTAINED FROM AQUATIC BIOSYSTEMS, INC., FORT COLLINS, COLORADO, THEN CULTURED IN-HOUSE)	Fresh water, Aqueous (aquatic habitat), Renewal, 9 F0 generation	Measured	<1.00 mg/L / 12.6 (11.6-13.1) mg/L	Reproduction (Reproduction-Time to first progeny, Response Site: Not reported)	NR (12.6 (12.5-13.1) mg/L)	Reproductive/Teratogenic	High	9644538

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Aquatic: Arthropods Extraction Table

CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
1066-42-8	18 Day(s), (21 Day(s))	*Daphnia magna* (Water Flea), Neonate, <24 Hour(s) (Measured in: F0 generation), Not Reported, Laboratory (INITIALLY OBTAINED FROM AQUATIC BIOSYSTEMS, INC., FORT COLLINS, COLORADO, THEN CULTURED IN-HOUSE)	Fresh water, Aqueous (aquatic habitat), Renewal, 10 F0 generation	Measured	<1.00 mg/L / 12.6 (11.6-13.1) mg/L	Mortality (Mortality-Mortality, Response Site: Not reported)	NR-ZERO (12.6 (11.6-13.1) mg/L)	Mortality	High	9644538
1066-42-8	21 Day(s), (21 Day(s))	*Daphnia magna* (Water Flea), Neonate, <24 Hour(s) (Measured in: F0 generation), Not Reported, Laboratory (INITIALLY OBTAINED FROM AQUATIC BIOSYSTEMS, INC., FORT COLLINS, COLORADO, THEN CULTURED IN-HOUSE)	Fresh water, Aqueous (aquatic habitat), Renewal, 9 F0 generation	Measured	<1.00 mg/L / 12.6 (11.6-13.1) mg/L	Reproduction (Reproduction-Progeny counts/numbers, Response Site: Not reported)	NOEC (12.6 (11.6-13.1) mg/L)	Reproductive/Teratogenic	High	9644538

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Aquatic: Arthropods Extraction Table

CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
1066-42-8	21 Day(s), (21 Day(s))	*Daphnia magna* (Water Flea), Neonate, <24 Hour(s) (Measured in: F0 generation), Not Reported, Laboratory (INITIALLY OBTAINED FROM AQUATIC BIOSYSTEMS, INC., FORT COLLINS, COLORADO, THEN CULTURED IN-HOUSE)	Fresh water, Aqueous (aquatic habitat), Renewal, 9 F0 generation	Measured	<1.00 mg/L / 12.6 (11.6-13.1) mg/L	Mortality (Mortality-Survival, Response Site: Not reported)	NOEC (12.6 (11.6-13.1) mg/L)	Mortality	High	9644538
1066-42-8	21 Day(s), (21 Day(s))	*Daphnia magna* (Water Flea), Neonate, <24 Hour(s) (Measured in: F0 generation), Not Reported, Laboratory (INITIALLY OBTAINED FROM AQUATIC BIOSYSTEMS, INC., FORT COLLINS, COLORADO, THEN CULTURED IN-HOUSE)	Fresh water, Aqueous (aquatic habitat), Renewal, 9 F0 generation	Measured	<1.00 mg/L / 12.6 (11.6-13.1) mg/L	Growth (Growth-Length, Response Site: Whole organism)	NOEC (12.6 (11.6-13.1) mg/L)	Development/Growth	High	9644538

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Aquatic: Arthropods Extraction Table

CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
1066-42-8	21 Day(s), (21 Day(s))	*Daphnia magna* (Water Flea), Neonate, <24 Hour(s) (Measured in: F0 generation), Not Reported, Laboratory (INITIALLY OBTAINED FROM AQUATIC BIOSYSTEMS, INC., FORT COLLINS, COLORADO, THEN CULTURED IN-HOUSE)	Fresh water, Aqueous (aquatic habitat), Renewal, 9 F0 generation	Measured	<1.00 mg/L / 12.6 (11.6-13.1) mg/L	Reproduction (Reproduction-Progeny counts/numbers, Response Site: Not reported)	MATC (>12.6 mg/L)	Reproductive/Teratogenic	High	9644538
1066-42-8	21 Day(s), (21 Day(s))	*Daphnia magna* (Water Flea), Neonate, <24 Hour(s) (Measured in: F0 generation), Not Reported, Laboratory (INITIALLY OBTAINED FROM AQUATIC BIOSYSTEMS, INC., FORT COLLINS, COLORADO, THEN CULTURED IN-HOUSE)	Fresh water, Aqueous (aquatic habitat), Renewal, 9 F0 generation	Measured	<1.00 mg/L / 12.6 (11.6-13.1) mg/L	Mortality (Mortality-Survival, Response Site: Not reported)	MATC (>12.6 mg/L)	Mortality	High	9644538

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Aquatic: Arthropods Extraction Table

CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
1066-42-8	21 Day(s), (21 Day(s))	*Daphnia magna* (Water Flea), Neonate, <24 Hour(s) (Measured in: F0 generation), Not Reported, Laboratory (INITIALLY OBTAINED FROM AQUATIC BIOSYSTEMS, INC., FORT COLLINS, COLORADO, THEN CULTURED IN-HOUSE)	Fresh water, Aqueous (aquatic habitat), Renewal, 9 F0 generation	Measured	<1.00 mg/L / 12.6 (11.6-13.1) mg/L	Growth (Growth-Length, Response Site: Whole organism)	MATC (>12.6 mg/L)	Development/Growth	High	9644538
1066-42-8	21 Day(s), (21 Day(s))	*Daphnia magna* (Water Flea), Neonate, <24 Hour(s) (Measured in: F0 generation), Not Reported, Laboratory (INITIALLY OBTAINED FROM AQUATIC BIOSYSTEMS, INC., FORT COLLINS, COLORADO, THEN CULTURED IN-HOUSE)	Fresh water, Aqueous (aquatic habitat), Renewal, 8 F0 generation	Measured	<1.00 mg/L / 12.6 (11.6-13.1) mg/L	Growth (Growth-Weight, Response Site: Whole organism)	MATC (>12.6 mg/L)	Development/Growth	High	9644538

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Aquatic: Arthropods Extraction Table

CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
1066-42-8	21 Day(s), (21 Day(s))	*Daphnia magna* (Water Flea), Neonate, <24 Hour(s) (Measured in: F0 generation), Not Reported, Laboratory (INITIALLY OBTAINED FROM AQUATIC BIOSYSTEMS, INC., FORT COLLINS, COLORADO, THEN CULTURED IN-HOUSE)	Fresh water, Aqueous (aquatic habitat), Renewal, 9 F0 generation	Measured	<1.00 mg/L / 12.6 (11.6-13.1) mg/L	Reproduction (Reproduction-Progeny counts/numbers, Response Site: Not reported)	LOEC (>12.6 mg/L)	Reproductive/Teratogenic	High	9644538
1066-42-8	21 Day(s), (21 Day(s))	*Daphnia magna* (Water Flea), Neonate, <24 Hour(s) (Measured in: F0 generation), Not Reported, Laboratory (INITIALLY OBTAINED FROM AQUATIC BIOSYSTEMS, INC., FORT COLLINS, COLORADO, THEN CULTURED IN-HOUSE)	Fresh water, Aqueous (aquatic habitat), Renewal, 9 F0 generation	Measured	<1.00 mg/L / 12.6 (11.6-13.1) mg/L	Mortality (Mortality-Survival, Response Site: Not reported)	LOEC (>12.6 mg/L)	Mortality	High	9644538

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Aquatic: Arthropods Extraction Table

CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
1066-42-8	21 Day(s), (21 Day(s))	*Daphnia magna* (Water Flea), Neonate, <24 Hour(s) (Measured in: F0 generation), Not Reported, Laboratory (INITIALLY OBTAINED FROM AQUATIC BIOSYSTEMS, INC., FORT COLLINS, COLORADO, THEN CULTURED IN-HOUSE)	Fresh water, Aqueous (aquatic habitat), Renewal, 9 F0 generation	Measured	<1.00 mg/L / 12.6 (11.6-13.1) mg/L	Growth (Growth-Length, Response Site: Whole organism)	LOEC (>12.6 mg/L)	Development/Growth	High	9644538
1066-42-8	21 Day(s), (21 Day(s))	*Daphnia magna* (Water Flea), Neonate, <24 Hour(s) (Measured in: F0 generation), Not Reported, Laboratory (INITIALLY OBTAINED FROM AQUATIC BIOSYSTEMS, INC., FORT COLLINS, COLORADO, THEN CULTURED IN-HOUSE)	Fresh water, Aqueous (aquatic habitat), Renewal, 8 F0 generation	Measured	<1.00 mg/L / 12.6 (11.6-13.1) mg/L	Growth (Growth-Weight, Response Site: Whole organism)	LOEC (>12.6 mg/L)	Development/Growth	High	9644538

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Aquatic: Arthropods Extraction Table

CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
1066-42-8	21 Day(s), (21 Day(s))	*Daphnia magna* (Water Flea), Neonate, <24 Hour(s) (Measured in: F0 generation), Not Reported, Laboratory (INITIALLY OBTAINED FROM AQUATIC BIOSYSTEMS, INC., FORT COLLINS, COLORADO, THEN CULTURED IN-HOUSE)	Fresh water, Aqueous (aquatic habitat), Renewal, 8 F0 generation	Measured	<1.00 mg/L / 12.6 (11.6-13.1) mg/L	Growth (Growth-Weight, Response Site: Whole organism)	NOEC (12.6 (11.6-13.1) mg/L)	Development/Growth	High	9644538

* If multiple extractions contained all identical information except the effect level, extraction rows were collapsed and the differing levels are listed by comma in this row.

Aquatic: Fish Extraction Table

CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
1066-42-8	24 Hour(s), (96 Hour(s))	*Oncorhynchus mykiss* (Rainbow Trout), Not reported, Not Reported, Laboratory (THOMAS FISH COMPANY, ANDERSON, CALIFORNIA)	Fresh water, Aqueous (aquatic habitat), Static, 30 Organism	Measured	<11.2 mg/L / 126 (120-131) mg/L	Mortality (Mortality-Mortality, Response Site: Not reported)	LC50 (>126 mg/L)	Mortality	High	9644536
1066-42-8	48 Hour(s), (96 Hour(s))	*Oncorhynchus mykiss* (Rainbow Trout), Not reported, Not Reported, Laboratory (THOMAS FISH COMPANY, ANDERSON, CALIFORNIA)	Fresh water, Aqueous (aquatic habitat), Static, 30 Organism	Measured	<11.2 mg/L / 126 (120-131) mg/L	Mortality (Mortality-Mortality, Response Site: Not reported)	LC50 (>126 mg/L)	Mortality	High	9644536
1066-42-8	72 Hour(s), (96 Hour(s))	*Oncorhynchus mykiss* (Rainbow Trout), Not reported, Not Reported, Laboratory (THOMAS FISH COMPANY, ANDERSON, CALIFORNIA)	Fresh water, Aqueous (aquatic habitat), Static, 30 Organism	Measured	<11.2 mg/L / 126 (120-131) mg/L	Mortality (Mortality-Mortality, Response Site: Not reported)	LC50 (>126 mg/L)	Mortality	High	9644536
1066-42-8	96 Hour(s), (96 Hour(s))	*Oncorhynchus mykiss* (Rainbow Trout), Not reported, Not Reported, Laboratory (THOMAS FISH COMPANY, ANDERSON, CALIFORNIA)	Fresh water, Aqueous (aquatic habitat), Static, 30 Organism	Measured	<11.2 mg/L / 126 (120-131) mg/L	Mortality (Mortality-Mortality, Response Site: Not reported)	LC50 (>126 mg/L)	Mortality	High	9644536

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Aquatic: Fish Extraction Table

CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
1066-42-8	96 Hour(s), (96 Hour(s))	*Oncorhynchus mykiss* (Rainbow Trout), Not reported, Not Reported, Laboratory (THOMAS FISH COMPANY, ANDERSON, CALIFORNIA)	Fresh water, Aqueous (aquatic habitat), Static, 30 Organism	Measured	<11.2 mg/L / 126 (120-131) mg/L	Mortality (Mortality-Mortality, Response Site: Not reported)	NR-ZERO (126 (120-131) mg/L)	Mortality	High	9644536
1066-42-8	96 Hour(s), (96 Hour(s))	*Oncorhynchus mykiss* (Rainbow Trout), Not reported, Not Reported, Laboratory (THOMAS FISH COMPANY, ANDERSON, CALIFORNIA)	Fresh water, Aqueous (aquatic habitat), Static, 30 Organism	Measured	<11.2 mg/L / 126 (120-131) mg/L	Growth (Morphology-Normal, Response Site: Not reported)	NR (126 (120-131) mg/L)	Behavioral	High	9644536
1066-42-8	4 Day(s), (32 Day(s))	*Pimephales promelas* (Fathead Minnow), Embryo, 6-24 Hours post fertilization (Measured in: Larvae), Not Reported, Laboratory (OBTAINED FROM BROOD STOCK MAINTAINED AT SMITHERS)	Fresh water, Aqueous (aquatic habitat), Renewal, NA Larvae	Measured	<0.10 mg/L / 0.78 (0.63-0.91) mg/L / 1.5 (1.2-1.7) mg/L / 3.0 (2.5-3.4) mg/L / 6.2 (4.9-7.4) mg/L / 12 (10-14) mg/L	Growth (Development-Normal, Response Site: Not reported)	NOEC (12 (10-14) mg/L)	Development/Growth	High	9644537
1066-42-8	4 Day(s), (32 Day(s))	*Pimephales promelas* (Fathead Minnow), Embryo, 6-24 Hours post fertilization, Not Reported, Laboratory (OBTAINED FROM BROOD STOCK MAINTAINED AT SMITHERS)	Fresh water, Aqueous (aquatic habitat), Renewal, NA Embryo	Measured	<0.10 mg/L / 0.78 (0.63-0.91) mg/L / 1.5 (1.2-1.7) mg/L / 3.0 (2.5-3.4) mg/L / 6.2 (4.9-7.4) mg/L / 12 (10-14) mg/L	Mortality (Mortality-Hatch, Response Site: Not reported)	NOEC (12 (10-14) mg/L)	Mortality	High	9644537

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Aquatic: Fish Extraction Table

CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
1066-42-8	4 Day(s), (32 Day(s))	*Pimephales promelas* (Fathead Minnow), Embryo, 6-24 Hours post fertilization (Measured in: Larvae), Not Reported, Laboratory (OBTAINED FROM BROOD STOCK MAINTAINED AT SMITHERS)	Fresh water, Aqueous (aquatic habitat), Renewal, NA Larvae	Measured	<0.10 mg/L / 0.78 (0.63-0.91) mg/L / 1.5 (1.2-1.7) mg/L / 3.0 (2.5-3.4) mg/L / 6.2 (4.9-7.4) mg/L / 12 (10-14) mg/L	Growth (Development-Normal, Response Site: Not reported)	EC20 (>12 (10-14) mg/L)	Development/Growth	High	9644537
1066-42-8	4 Day(s), (32 Day(s))	*Pimephales promelas* (Fathead Minnow), Embryo, 6-24 Hours post fertilization, Not Reported, Laboratory (OBTAINED FROM BROOD STOCK MAINTAINED AT SMITHERS)	Fresh water, Aqueous (aquatic habitat), Renewal, NA Embryo	Measured	<0.10 mg/L / 0.78 (0.63-0.91) mg/L / 1.5 (1.2-1.7) mg/L / 3.0 (2.5-3.4) mg/L / 6.2 (4.9-7.4) mg/L / 12 (10-14) mg/L	Mortality (Mortality-Hatch, Response Site: Not reported)	LC50 (>12 (10-14) mg/L)	Mortality	High	9644537
1066-42-8	4 Day(s), (32 Day(s))	*Pimephales promelas* (Fathead Minnow), Embryo, 6-24 Hours post fertilization (Measured in: Larvae), Not Reported, Laboratory (OBTAINED FROM BROOD STOCK MAINTAINED AT SMITHERS)	Fresh water, Aqueous (aquatic habitat), Renewal, NA Larvae	Measured	<0.10 mg/L / 0.78 (0.63-0.91) mg/L / 1.5 (1.2-1.7) mg/L / 3.0 (2.5-3.4) mg/L / 6.2 (4.9-7.4) mg/L / 12 (10-14) mg/L	Growth (Development-Normal, Response Site: Not reported)	EC50 (>12 (10-14) mg/L)	Development/Growth	High	9644537

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Aquatic: Fish Extraction Table

CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
1066-42-8	4 Day(s), (32 Day(s))	*Pimephales promelas* (Fathead Minnow), Embryo, 6-24 Hours post fertilization, Not Reported, Laboratory (OBTAINED FROM BROOD STOCK MAINTAINED AT SMITHERS)	Fresh water, Aqueous (aquatic habitat), Renewal, NA Embryo	Measured	<0.10 mg/L / 0.78 (0.63-0.91) mg/L / 1.5 (1.2-1.7) mg/L / 3.0 (2.5-3.4) mg/L / 6.2 (4.9-7.4) mg/L / 12 (10-14) mg/L	Mortality (Mortality-Hatch, Response Site: Not reported)	LC20 (>12 (10-14) mg/L)	Mortality	High	9644537
1066-42-8	4 Day(s), (32 Day(s))	*Pimephales promelas* (Fathead Minnow), Embryo, 6-24 Hours post fertilization (Measured in: Larvae), Not Reported, Laboratory (OBTAINED FROM BROOD STOCK MAINTAINED AT SMITHERS)	Fresh water, Aqueous (aquatic habitat), Renewal, NA Larvae	Measured	<0.10 mg/L / 0.78 (0.63-0.91) mg/L / 1.5 (1.2-1.7) mg/L / 3.0 (2.5-3.4) mg/L / 6.2 (4.9-7.4) mg/L / 12 (10-14) mg/L	Growth (Development-Normal, Response Site: Not reported)	EC10 (>12 (10-14) mg/L)	Development/Growth	High	9644537
1066-42-8	4 Day(s), (19 Day(s))	*Pimephales promelas* (Fathead Minnow), Embryo, 6-24 Hours post fertilization (Measured in: Larvae), Not Reported, Laboratory (OBTAINED FROM BROOD STOCK MAINTAINED AT SMITHERS)	Fresh water, Aqueous (aquatic habitat), Renewal, NA Larvae	Unmeasured	0 mg/L / 0.75 mg/L / 1.5 mg/L / 3.0 mg/L / 6.0 mg/L / 12 mg/L	Growth (Development-Normal, Response Site: Not reported)	NR (0.75-12 mg/L)	Development/Growth	Medium	9644537

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Aquatic: Fish Extraction Table

CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
1066-42-8	4 Day(s), (19 Day(s))	*Pimephales promelas* (Fathead Minnow), Embryo, 6-24 Hours post fertilization, Not Reported, Laboratory (OBTAINED FROM BROOD STOCK MAINTAINED AT SMITHERS)	Fresh water, Aqueous (aquatic habitat), Renewal, NA Embryo	Unmeasured	0 mg/L / 0.75 mg/L / 1.5 mg/L / 3.0 mg/L / 6.0 mg/L / 12 mg/L	Mortality (Mortality-Hatch, Response Site: Not reported)	NR (0.75-12 mg/L)	Mortality	Medium	9644537
1066-42-8	4 Day(s), (32 Day(s))	*Pimephales promelas* (Fathead Minnow), Embryo, 6-24 Hours post fertilization, Not Reported, Laboratory (OBTAINED FROM BROOD STOCK MAINTAINED AT SMITHERS)	Fresh water, Aqueous (aquatic habitat), Renewal, NA Embryo	Measured	<0.10 mg/L / 0.78 (0.63-0.91) mg/L / 1.5 (1.2-1.7) mg/L / 3.0 (2.5-3.4) mg/L / 6.2 (4.9-7.4) mg/L / 12 (10-14) mg/L	Mortality (Mortality-Hatch, Response Site: Not reported)	LC10 (>12 (10-14) mg/L)	Mortality	High	9644537
1066-42-8	19 Day(s), (19 Day(s))	*Pimephales promelas* (Fathead Minnow), Embryo, 6-24 Hours post fertilization (Measured in: Larvae), Not Reported, Laboratory (OBTAINED FROM BROOD STOCK MAINTAINED AT SMITHERS)	Fresh water, Aqueous (aquatic habitat), Renewal, NA Larvae	Unmeasured	0 mg/L / 0.75 mg/L / 1.5 mg/L / 3.0 mg/L / 6.0 mg/L / 12 mg/L	Growth (Growth-Weight, Response Site: Whole organism)	NR (0.75-12 mg/L)	Development/Growth	Medium	9644537

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Aquatic: Fish Extraction Table

CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
1066-42-8	19 Day(s), (19 Day(s))	*Pimephales promelas* (Fathead Minnow), Embryo, 6-24 Hours post fertilization (Measured in: Larvae), Not Reported, Laboratory (OBTAINED FROM BROOD STOCK MAINTAINED AT SMITHERS)	Fresh water, Aqueous (aquatic habitat), Renewal, NA Larvae	Unmeasured	0 mg/L / 0.75 mg/L / 1.5 mg/L / 3.0 mg/L / 6.0 mg/L / 12 mg/L	Mortality (Mortality-Survival, Response Site: Not reported)	NR (0.75-12 mg/L)	Mortality	Medium	9644537
1066-42-8	19 Day(s), (19 Day(s))	*Pimephales promelas* (Fathead Minnow), Embryo, 6-24 Hours post fertilization (Measured in: Larvae), Not Reported, Laboratory (OBTAINED FROM BROOD STOCK MAINTAINED AT SMITHERS)	Fresh water, Aqueous (aquatic habitat), Renewal, NA Larvae	Unmeasured	0 mg/L / 0.75 mg/L / 1.5 mg/L / 3.0 mg/L / 6.0 mg/L / 12 mg/L	Growth (Growth-Length, Response Site: Whole organism)	NR (0.75-12 mg/L)	Development/Growth	Medium	9644537
1066-42-8	32 Day(s), (32 Day(s))	*Pimephales promelas* (Fathead Minnow), Embryo, 6-24 Hours post fertilization (Measured in: Larvae), Not Reported, Laboratory (OBTAINED FROM BROOD STOCK MAINTAINED AT SMITHERS)	Fresh water, Aqueous (aquatic habitat), Renewal, NA Larvae	Measured	<0.10 mg/L / 0.78 (0.63-0.91) mg/L / 1.5 (1.2-1.7) mg/L / 3.0 (2.5-3.4) mg/L / 6.2 (4.9-7.4) mg/L / 12 (10-14) mg/L	Growth (Growth-Length, Response Site: Whole organism)	EC20 (>12 (10-14) mg/L)	Development/Growth	High	9644537

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Aquatic: Fish Extraction Table

CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
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1066-42-8	32 Day(s), (32 Day(s))	*Pimephales promelas* (Fathead Minnow), Embryo, 6-24 Hours post fertilization (Measured in: Larvae), Not Reported, Laboratory (OBTAINED FROM BROOD STOCK MAINTAINED AT SMITHERS)	Fresh water, Aqueous (aquatic habitat), Renewal, NA Larvae	Measured	<0.10 mg/L / 0.78 (0.63-0.91) mg/L / 1.5 (1.2-1.7) mg/L / 3.0 (2.5-3.4) mg/L / 6.2 (4.9-7.4) mg/L / 12 (10-14) mg/L	Growth (Growth-Weight, Response Site: Whole organism)	EC10 (>12 (10-14) mg/L)	Development/Growth	High	9644537
1066-42-8	32 Day(s), (32 Day(s))	*Pimephales promelas* (Fathead Minnow), Embryo, 6-24 Hours post fertilization (Measured in: Larvae), Not Reported, Laboratory (OBTAINED FROM BROOD STOCK MAINTAINED AT SMITHERS)	Fresh water, Aqueous (aquatic habitat), Renewal, NA Larvae	Measured	<0.10 mg/L / 0.78 (0.63-0.91) mg/L / 1.5 (1.2-1.7) mg/L / 3.0 (2.5-3.4) mg/L / 6.2 (4.9-7.4) mg/L / 12 (10-14) mg/L	Growth (Growth-Weight, Response Site: Whole organism)	EC20 (>12 (10-14) mg/L)	Development/Growth	High	9644537

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Aquatic: Fish Extraction Table

CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
1066-42-8	32 Day(s), (32 Day(s))	*Pimephales promelas* (Fathead Minnow), Embryo, 6-24 Hours post fertilization (Measured in: Larvae), Not Reported, Laboratory (OBTAINED FROM BROOD STOCK MAINTAINED AT SMITHERS)	Fresh water, Aqueous (aquatic habitat), Renewal, NA Larvae	Measured	<0.10 mg/L / 0.78 (0.63-0.91) mg/L / 1.5 (1.2-1.7) mg/L / 3.0 (2.5-3.4) mg/L / 6.2 (4.9-7.4) mg/L / 12 (10-14) mg/L	Mortality (Mortality-Survival, Response Site: Not reported)	NOEC (12 (10-14) mg/L)	Mortality	High	9644537
1066-42-8	32 Day(s), (32 Day(s))	*Pimephales promelas* (Fathead Minnow), Embryo, 6-24 Hours post fertilization (Measured in: Larvae), Not Reported, Laboratory (OBTAINED FROM BROOD STOCK MAINTAINED AT SMITHERS)	Fresh water, Aqueous (aquatic habitat), Renewal, NA Larvae	Measured	<0.10 mg/L / 0.78 (0.63-0.91) mg/L / 1.5 (1.2-1.7) mg/L / 3.0 (2.5-3.4) mg/L / 6.2 (4.9-7.4) mg/L / 12 (10-14) mg/L	Growth (Growth-Weight, Response Site: Whole organism)	EC50 (>12 (10-14) mg/L)	Development/Growth	High	9644537
1066-42-8	32 Day(s), (32 Day(s))	*Pimephales promelas* (Fathead Minnow), Embryo, 6-24 Hours post fertilization (Measured in: Larvae), Not Reported, Laboratory (OBTAINED FROM BROOD STOCK MAINTAINED AT SMITHERS)	Fresh water, Aqueous (aquatic habitat), Renewal, NA Larvae	Measured	<0.10 mg/L / 0.78 (0.63-0.91) mg/L / 1.5 (1.2-1.7) mg/L / 3.0 (2.5-3.4) mg/L / 6.2 (4.9-7.4) mg/L / 12 (10-14) mg/L	Mortality (Mortality-Survival, Response Site: Not reported)	LC20 (>12 (10-14) mg/L)	Mortality	High	9644537

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Aquatic: Fish Extraction Table

CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
1066-42-8	32 Day(s), (32 Day(s))	*Pimephales promelas* (Fathead Minnow), Embryo, 6-24 Hours post fertilization (Measured in: Larvae), Not Reported, Laboratory (OBTAINED FROM BROOD STOCK MAINTAINED AT SMITHERS)	Fresh water, Aqueous (aquatic habitat), Renewal, NA Larvae	Measured	<0.10 mg/L / 0.78 (0.63-0.91) mg/L / 1.5 (1.2-1.7) mg/L / 3.0 (2.5-3.4) mg/L / 6.2 (4.9-7.4) mg/L / 12 (10-14) mg/L	Mortality (Mortality-Survival, Response Site: Not reported)	LC50 (>12 (10-14) mg/L)	Mortality	High	9644537
1066-42-8	32 Day(s), (32 Day(s))	*Pimephales promelas* (Fathead Minnow), Embryo, 6-24 Hours post fertilization (Measured in: Larvae), Not Reported, Laboratory (OBTAINED FROM BROOD STOCK MAINTAINED AT SMITHERS)	Fresh water, Aqueous (aquatic habitat), Renewal, NA Larvae	Measured	<0.10 mg/L / 0.78 (0.63-0.91) mg/L / 1.5 (1.2-1.7) mg/L / 3.0 (2.5-3.4) mg/L / 6.2 (4.9-7.4) mg/L / 12 (10-14) mg/L	Growth (Growth-Length, Response Site: Whole organism)	NOEC (12 (10-14) mg/L)	Development/Growth	High	9644537
1066-42-8	32 Day(s), (32 Day(s))	*Pimephales promelas* (Fathead Minnow), Embryo, 6-24 Hours post fertilization (Measured in: Larvae), Not Reported, Laboratory (OBTAINED FROM BROOD STOCK MAINTAINED AT SMITHERS)	Fresh water, Aqueous (aquatic habitat), Renewal, NA Larvae	Measured	<0.10 mg/L / 0.78 (0.63-0.91) mg/L / 1.5 (1.2-1.7) mg/L / 3.0 (2.5-3.4) mg/L / 6.2 (4.9-7.4) mg/L / 12 (10-14) mg/L	Growth (Growth-Weight, Response Site: Whole organism)	NOEC (12 (10-14) mg/L)	Development/Growth	High	9644537

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Aquatic: Fish Extraction Table

CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
1066-42-8	32 Day(s), (32 Day(s))	*Pimephales promelas* (Fathead Minnow), Embryo, 6-24 Hours post fertilization (Measured in: Larvae), Not Reported, Laboratory (OBTAINED FROM BROOD STOCK MAINTAINED AT SMITHERS)	Fresh water, Aqueous (aquatic habitat), Renewal, NA Larvae	Measured	<0.10 mg/L / 0.78 (0.63-0.91) mg/L / 1.5 (1.2-1.7) mg/L / 3.0 (2.5-3.4) mg/L / 6.2 (4.9-7.4) mg/L / 12 (10-14) mg/L	Growth (Morphology-Abnormal, Response Site: Not reported)	NR (0.78-12 mg/L)	Development/Growth	High	9644537
1066-42-8	32 Day(s), (32 Day(s))	*Pimephales promelas* (Fathead Minnow), Embryo, 6-24 Hours post fertilization (Measured in: Larvae), Not Reported, Laboratory (OBTAINED FROM BROOD STOCK MAINTAINED AT SMITHERS)	Fresh water, Aqueous (aquatic habitat), Renewal, NA Larvae	Measured	<0.10 mg/L / 0.78 (0.63-0.91) mg/L / 1.5 (1.2-1.7) mg/L / 3.0 (2.5-3.4) mg/L / 6.2 (4.9-7.4) mg/L / 12 (10-14) mg/L	Growth (Growth-Length, Response Site: Whole organism)	EC50 (>12 (10-14) mg/L)	Development/Growth	High	9644537
1066-42-8	32 Day(s), (32 Day(s))	*Pimephales promelas* (Fathead Minnow), Embryo, 6-24 Hours post fertilization (Measured in: Larvae), Not Reported, Laboratory (OBTAINED FROM BROOD STOCK MAINTAINED AT SMITHERS)	Fresh water, Aqueous (aquatic habitat), Renewal, NA Larvae	Measured	<0.10 mg/L / 0.78 (0.63-0.91) mg/L / 1.5 (1.2-1.7) mg/L / 3.0 (2.5-3.4) mg/L / 6.2 (4.9-7.4) mg/L / 12 (10-14) mg/L	Mortality (Mortality-Survival, Response Site: Not reported)	LC10 (>12 (10-14) mg/L)	Mortality	High	9644537

* If multiple extractions contained all identical information except the effect level, extraction rows were collapsed and the differing levels are listed by comma in this row.

Terrestrial: Arthropods Extraction Table

CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
1066-42-8	48 Hour(s), (48 Hour(s))	*Acyrthosiphon pisum ssp. pisum* (Pea Aphid), Adult, Not Reported, Laboratory (NR)	Litter, Exposures that include multiple exposure groups, Multiple routes between application groups, Not Reported	Unmeasured	1000 ppm	Mortality (Mortality-Mortality, Response Site: Not reported)	NR-ZERO (1000 ppm)	Mortality	Uninformative	5885944
1066-42-8	5 Day(s), (5 Day(s))	*Acyrthosiphon pisum ssp. pisum* (Pea Aphid), Adult, Not Reported, Laboratory (NR)	Litter, Exposures that include multiple exposure groups, Multiple routes between application groups, Not Reported	Unmeasured	100 ppm	Mortality (Mortality-Mortality, Response Site: Not reported)	NR-ZERO (100 ppm)	Mortality	Uninformative	5885944
1066-42-8	48 Hour(s), (48 Hour(s))	*Epilachna varivestis* (Mexican Bean Beetle), Larva, Not Reported, Laboratory (NR)	Litter, Oral (diet, drink, gavage), Food, Not Reported	Unmeasured	1000 ppm diet	Mortality (Mortality-Mortality, Response Site: Not reported)	NR-ZERO (1000 ppm diet)	Mortality	Uninformative	5885944
1066-42-8	24 Hour(s), (24 Hour(s))	*Musca domestica* (House Fly), Adult, Not Reported, Laboratory (NR)	No substrate, Topical, Dermal, Not Reported	Unmeasured	1000 ppm	Mortality (Mortality-Mortality, Response Site: Not reported)	NR-ZERO (1000 ppm)	Mortality	Uninformative	5885944
1066-42-8	48 Hour(s), (48 Hour(s))	*Persectania ewingii* (Southern Armyworm), Larva, Not Reported, Laboratory (NR)	Litter, Oral (diet, drink, gavage), Food, Not Reported	Unmeasured	1000 ppm diet	Mortality (Mortality-Mortality, Response Site: Not reported)	NR-ZERO (1000 ppm diet)	Mortality	Uninformative	5885944
1066-42-8	5 Day(s), (5 Day(s))	*Tetranychus sp.* (Mite), Adult (Measured in: Egg), Not Reported, Laboratory (NR)	Litter, Exposures that include multiple exposure groups, Multiple routes between application groups, NA Egg	Unmeasured	1000 ppm	Mortality (Mortality-Mortality, Response Site: Not reported)	NR (1000 ppm)	Mortality	Uninformative	5885944

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Terrestrial: Arthropods Extraction Table

CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
1066-42-8	5 Day(s), (5 Day(s))	*Tetranychus sp.* (Mite), Adult, Not Reported, Laboratory (NR)	Litter, Exposures that include multiple exposure groups, Multiple routes between application groups, NA Adult	Unmeasured	1000 ppm	Mortality (Mortality-Mortality, Response Site: Not reported)	NR-ZERO (1000 ppm)	Mortality	Uninformative	5885944

* If multiple extractions contained all identical information except the effect level, extraction rows were collapsed and the differing levels are listed by comma in this row.

Terrestrial: Vascular plants Extraction Table

CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
1066-42-8	14 Day(s), (14 Day(s))	*Allium cepa* (Common Onion), Seed, Not Reported, Laboratory (FROM JOHNNY'S SELECTED SEEDS, WINSLOW, MAINE, USA)	Natural soil, Environmental, Soil slurry, Not Reported	Unmeasured	0 AI mg/kg dry soil / 0.050 AI mg/kg dry soil / 0.50 AI mg/kg dry soil / 5.0 AI mg/kg dry soil	Growth (Morphology-Abnormal, Response Site: Not reported)	NR (0.050-5.0 AI mg/kg dry soil)	Development/Growth	High	9644539
1066-42-8	14 Day(s), (14 Day(s))	*Allium cepa* (Common Onion), Seed, Not Reported, Laboratory (FROM JOHNNY'S SELECTED SEEDS, WINSLOW, MAINE, USA)	Natural soil, Environmental, Soil slurry, Not Reported	Unmeasured	0 AI mg/kg dry soil / 0.050 AI mg/kg dry soil / 0.50 AI mg/kg dry soil / 5.0 AI mg/kg dry soil	Growth (Development-Emergence, Response Site: Not reported)	NR (0.050-5.0 AI mg/kg dry soil)	Development/Growth	High	9644539
1066-42-8	14 Day(s), (14 Day(s))	*Allium cepa* (Common Onion), Seed, Not Reported, Laboratory (FROM JOHNNY'S SELECTED SEEDS, WINSLOW, MAINE, USA)	Natural soil, Environmental, Soil slurry, Not Reported	Measured	<1.00 AI mg/kg dry soil / 2.8 (1.2-4.3) AI mg/kg dry soil	Mortality (Mortality-Survival, Response Site: Not reported)	NOEL (>=2.8 AI mg/kg dry soil)	Mortality	High	9644539
1066-42-8	14 Day(s), (14 Day(s))	*Allium cepa* (Common Onion), Seed, Not Reported, Laboratory (FROM JOHNNY'S SELECTED SEEDS, WINSLOW, MAINE, USA)	Natural soil, Environmental, Soil slurry, Not Reported	Unmeasured	0 AI mg/kg dry soil / 0.050 AI mg/kg dry soil / 0.50 AI mg/kg dry soil / 5.0 AI mg/kg dry soil	Mortality (Mortality-Mortality, Response Site: Not reported)	NR-ZERO (5.0 AI mg/kg dry soil)	Mortality	High	9644539

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Terrestrial: Vascular plants Extraction Table

CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
1066-42-8	14 Day(s), (14 Day(s))	*Allium cepa* (Common Onion), Seed, Not Reported, Laboratory (FROM JOHNNY'S SELECTED SEEDS, WINSLOW, MAINE, USA)	Natural soil, Environmental, Soil slurry, Not Reported	Measured	<1.00 AI mg/kg dry soil / 2.8 (1.2-4.3) AI mg/kg dry soil	Growth (Development-Emergence, Response Site: Not reported)	NOEL (>=2.8 AI mg/kg dry soil)	Development/Growth	High	9644539
1066-42-8	14 Day(s), (14 Day(s))	*Allium cepa* (Common Onion), Seed, Not Reported, Laboratory (FROM JOHNNY'S SELECTED SEEDS, WINSLOW, MAINE, USA)	Natural soil, Environmental, Soil slurry, Not Reported	Measured	<1.00 AI mg/kg dry soil / 2.8 (1.2-4.3) AI mg/kg dry soil	Growth (Growth-Biomass, Response Site: Shoot)	NOEL (>=2.8 AI mg/kg dry soil)	Development/Growth	High	9644539
1066-42-8	14 Day(s), (14 Day(s))	*Allium cepa* (Common Onion), Seed, Not Reported, Laboratory (FROM JOHNNY'S SELECTED SEEDS, WINSLOW, MAINE, USA)	Natural soil, Environmental, Soil slurry, Not Reported	Unmeasured	0 AI mg/kg dry soil / 0.050 AI mg/kg dry soil / 0.50 AI mg/kg dry soil / 5.0 AI mg/kg dry soil	Growth (Growth-Biomass, Response Site: Shoot)	NR (0.050-5.0 AI mg/kg dry soil)	Development/Growth	High	9644539
1066-42-8	14 Day(s), (14 Day(s))	*Avena sativa* (Common Oat), Seed, Not Reported, Laboratory (FROM GRANITE SEED COMPANY, LEHI, UTAH, USA)	Natural soil, Environmental, Soil slurry, Not Reported	Unmeasured	0 AI mg/kg dry soil / 0.050 AI mg/kg dry soil / 0.50 AI mg/kg dry soil / 5.0 AI mg/kg dry soil	Growth (Morphology-Abnormal, Response Site: Not reported)	NR (0.050-5.0 AI mg/kg dry soil)	Development/Growth	High	9644539

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Terrestrial: Vascular plants Extraction Table

CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
1066-42-8	14 Day(s), (14 Day(s))	*Avena sativa* (Common Oat), Seed, Not Reported, Laboratory (FROM GRANITE SEED COMPANY, LEHI, UTAH, USA)	Natural soil, Environmental, Soil slurry, Not Reported	Unmeasured	0 AI mg/kg dry soil / 0.050 AI mg/kg dry soil / 0.50 AI mg/kg dry soil / 5.0 AI mg/kg dry soil	Mortality (Mortality-Mortality, Response Site: Not reported)	NR-ZERO (5.0 AI mg/kg dry soil)	Mortality	High	9644539
1066-42-8	14 Day(s), (14 Day(s))	*Avena sativa* (Common Oat), Seed, Not Reported, Laboratory (FROM GRANITE SEED COMPANY, LEHI, UTAH, USA)	Natural soil, Environmental, Soil slurry, Not Reported	Measured	<1.00 AI mg/kg dry soil / 2.8 (1.2-4.3) AI mg/kg dry soil	Growth (Development-Emergence, Response Site: Not reported)	NOEL (>=2.8 AI mg/kg dry soil)	Development/Growth	High	9644539
1066-42-8	14 Day(s), (14 Day(s))	*Avena sativa* (Common Oat), Seed, Not Reported, Laboratory (FROM GRANITE SEED COMPANY, LEHI, UTAH, USA)	Natural soil, Environmental, Soil slurry, Not Reported	Unmeasured	0 AI mg/kg dry soil / 0.050 AI mg/kg dry soil / 0.50 AI mg/kg dry soil / 5.0 AI mg/kg dry soil	Growth (Growth-Biomass, Response Site: Shoot)	NR (0.050-5.0 AI mg/kg dry soil)	Development/Growth	High	9644539
1066-42-8	14 Day(s), (14 Day(s))	*Avena sativa* (Common Oat), Seed, Not Reported, Laboratory (FROM GRANITE SEED COMPANY, LEHI, UTAH, USA)	Natural soil, Environmental, Soil slurry, Not Reported	Measured	<1.00 AI mg/kg dry soil / 2.8 (1.2-4.3) AI mg/kg dry soil	Mortality (Mortality-Survival, Response Site: Not reported)	NOEL (>=2.8 AI mg/kg dry soil)	Mortality	High	9644539

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Terrestrial: Vascular plants Extraction Table

CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
1066-42-8	14 Day(s), (14 Day(s))	*Avena sativa* (Common Oat), Seed, Not Reported, Laboratory (FROM GRANITE SEED COMPANY, LEHI, UTAH, USA)	Natural soil, Environmental, Soil slurry, Not Reported	Unmeasured	0 AI mg/kg dry soil / 0.050 AI mg/kg dry soil / 0.50 AI mg/kg dry soil / 5.0 AI mg/kg dry soil	Growth (Development-Emergence, Response Site: Not reported)	NR (0.050-5.0 AI mg/kg dry soil)	Development/Growth	High	9644539
1066-42-8	14 Day(s), (14 Day(s))	*Avena sativa* (Common Oat), Seed, Not Reported, Laboratory (FROM GRANITE SEED COMPANY, LEHI, UTAH, USA)	Natural soil, Environmental, Soil slurry, Not Reported	Measured	<1.00 AI mg/kg dry soil / 2.8 (1.2-4.3) AI mg/kg dry soil	Growth (Growth-Biomass, Response Site: Shoot)	NOEL (>=2.8 AI mg/kg dry soil)	Development/Growth	High	9644539
1066-42-8	14 Day(s), (14 Day(s))	*Brassica oleracea* (Cabbage), Seed, Not Reported, Laboratory (FROM PARK SEED COMPANY, HODGES, SOUTH CAROLINA, USA)	Natural soil, Environmental, Soil slurry, Not Reported	Unmeasured	0 AI mg/kg dry soil / 0.050 AI mg/kg dry soil / 0.50 AI mg/kg dry soil / 5.0 AI mg/kg dry soil	Growth (Morphology-Abnormal, Response Site: Not reported)	NR (0.050-5.0 AI mg/kg dry soil)	Development/Growth	High	9644539
1066-42-8	14 Day(s), (14 Day(s))	*Brassica oleracea* (Cabbage), Seed, Not Reported, Laboratory (FROM PARK SEED COMPANY, HODGES, SOUTH CAROLINA, USA)	Natural soil, Environmental, Soil slurry, Not Reported	Measured	<1.00 AI mg/kg dry soil / 2.8 (1.2-4.3) AI mg/kg dry soil	Growth (Development-Emergence, Response Site: Not reported)	NOEL (>=2.8 AI mg/kg dry soil)	Development/Growth	High	9644539

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Terrestrial: Vascular plants Extraction Table

CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
1066-42-8	14 Day(s), (14 Day(s))	*Brassica oleracea* (Cabbage), Seed, Not Reported, Laboratory (FROM PARK SEED COMPANY, HODGES, SOUTH CAROLINA, USA)	Natural soil, Environmental, Soil slurry, Not Reported	Unmeasured	0 AI mg/kg dry soil / 0.050 AI mg/kg dry soil / 0.50 AI mg/kg dry soil / 5.0 AI mg/kg dry soil	Growth (Development-Emergence, Response Site: Not reported)	NR (0.050-5.0 AI mg/kg dry soil)	Development/Growth	High	9644539
1066-42-8	14 Day(s), (14 Day(s))	*Brassica oleracea* (Cabbage), Seed, Not Reported, Laboratory (FROM PARK SEED COMPANY, HODGES, SOUTH CAROLINA, USA)	Natural soil, Environmental, Soil slurry, Not Reported	Measured	<1.00 AI mg/kg dry soil / 2.8 (1.2-4.3) AI mg/kg dry soil	Growth (Growth-Biomass, Response Site: Shoot)	NOEL (>=2.8 AI mg/kg dry soil)	Development/Growth	High	9644539
1066-42-8	14 Day(s), (14 Day(s))	*Brassica oleracea* (Cabbage), Seed, Not Reported, Laboratory (FROM PARK SEED COMPANY, HODGES, SOUTH CAROLINA, USA)	Natural soil, Environmental, Soil slurry, Not Reported	Unmeasured	0 AI mg/kg dry soil / 0.050 AI mg/kg dry soil / 0.50 AI mg/kg dry soil / 5.0 AI mg/kg dry soil	Mortality (Mortality-Mortality, Response Site: Not reported)	NR-ZERO (5.0 AI mg/kg dry soil)	Mortality	High	9644539
1066-42-8	14 Day(s), (14 Day(s))	*Brassica oleracea* (Cabbage), Seed, Not Reported, Laboratory (FROM PARK SEED COMPANY, HODGES, SOUTH CAROLINA, USA)	Natural soil, Environmental, Soil slurry, Not Reported	Unmeasured	0 AI mg/kg dry soil / 0.050 AI mg/kg dry soil / 0.50 AI mg/kg dry soil / 5.0 AI mg/kg dry soil	Growth (Growth-Biomass, Response Site: Shoot)	NR (0.050-5.0 AI mg/kg dry soil)	Development/Growth	High	9644539

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Terrestrial: Vascular plants Extraction Table

CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
1066-42-8	14 Day(s), (14 Day(s))	*Brassica oleracea* (Cabbage), Seed, Not Reported, Laboratory (FROM PARK SEED COMPANY, HODGES, SOUTH CAROLINA, USA)	Natural soil, Environmental, Soil slurry, Not Reported	Measured	<1.00 AI mg/kg dry soil / 2.8 (1.2-4.3) AI mg/kg dry soil	Mortality (Mortality-Survival, Response Site: Not reported)	NOEL (>=2.8 AI mg/kg dry soil)	Mortality	High	9644539
1066-42-8	14 Day(s), (14 Day(s))	*Cucumis sativus* (Cucumber), Seed, Not Reported, Laboratory (FROM JOHNNY'S SELECTED SEEDS, WINSLOW, MAINE, USA)	Natural soil, Environmental, Soil slurry, Not Reported	Measured	<1.00 AI mg/kg dry soil / 2.8 (1.2-4.3) AI mg/kg dry soil	Growth (Development-Emergence, Response Site: Not reported)	NOEL (>=2.8 AI mg/kg dry soil)	Development/Growth	High	9644539
1066-42-8	14 Day(s), (14 Day(s))	*Cucumis sativus* (Cucumber), Seed, Not Reported, Laboratory (FROM JOHNNY'S SELECTED SEEDS, WINSLOW, MAINE, USA)	Natural soil, Environmental, Soil slurry, Not Reported	Measured	<1.00 AI mg/kg dry soil / 2.8 (1.2-4.3) AI mg/kg dry soil	Growth (Growth-Biomass, Response Site: Shoot)	NOEL (>=2.8 AI mg/kg dry soil)	Development/Growth	High	9644539
1066-42-8	14 Day(s), (14 Day(s))	*Cucumis sativus* (Cucumber), Seed, Not Reported, Laboratory (FROM JOHNNY'S SELECTED SEEDS, WINSLOW, MAINE, USA)	Natural soil, Environmental, Soil slurry, Not Reported	Measured	<1.00 AI mg/kg dry soil / 2.8 (1.2-4.3) AI mg/kg dry soil	Mortality (Mortality-Survival, Response Site: Not reported)	NOEL (>=2.8 AI mg/kg dry soil)	Mortality	High	9644539

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Terrestrial: Vascular plants Extraction Table

CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
1066-42-8	14 Day(s), (14 Day(s))	*Cucumis sativus* (Cucumber), Seed, Not Reported, Laboratory (FROM JOHNNY'S SELECTED SEEDS, WINSLOW, MAINE, USA)	Natural soil, Environmental, Soil slurry, Not Reported	Unmeasured	0 AI mg/kg dry soil / 0.050 AI mg/kg dry soil / 0.50 AI mg/kg dry soil / 5.0 AI mg/kg dry soil	Mortality (Mortality-Mortality, Response Site: Not reported)	NR-ZERO (5.0 AI mg/kg dry soil)	Mortality	High	9644539
1066-42-8	14 Day(s), (14 Day(s))	*Cucumis sativus* (Cucumber), Seed, Not Reported, Laboratory (FROM JOHNNY'S SELECTED SEEDS, WINSLOW, MAINE, USA)	Natural soil, Environmental, Soil slurry, Not Reported	Unmeasured	0 AI mg/kg dry soil / 0.050 AI mg/kg dry soil / 0.50 AI mg/kg dry soil / 5.0 AI mg/kg dry soil	Growth (Development-Emergence, Response Site: Not reported)	NR (0.050-5.0 AI mg/kg dry soil)	Development/Growth	High	9644539
1066-42-8	14 Day(s), (14 Day(s))	*Cucumis sativus* (Cucumber), Seed, Not Reported, Laboratory (FROM JOHNNY'S SELECTED SEEDS, WINSLOW, MAINE, USA)	Natural soil, Environmental, Soil slurry, Not Reported	Unmeasured	0 AI mg/kg dry soil / 0.050 AI mg/kg dry soil / 0.50 AI mg/kg dry soil / 5.0 AI mg/kg dry soil	Growth (Growth-Biomass, Response Site: Shoot)	NR (0.050-5.0 AI mg/kg dry soil)	Development/Growth	High	9644539
1066-42-8	14 Day(s), (14 Day(s))	*Cucumis sativus* (Cucumber), Seed, Not Reported, Laboratory (FROM JOHNNY'S SELECTED SEEDS, WINSLOW, MAINE, USA)	Natural soil, Environmental, Soil slurry, Not Reported	Unmeasured	0 AI mg/kg dry soil / 0.050 AI mg/kg dry soil / 0.50 AI mg/kg dry soil / 5.0 AI mg/kg dry soil	Growth (Morphology-Abnormal, Response Site: Not reported)	NR (0.050-5.0 AI mg/kg dry soil)	Development/Growth	High	9644539

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Terrestrial: Vascular plants Extraction Table

CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
1066-42-8	14 Day(s), (14 Day(s))	*Glycine max* (Soybean), Seed, Not Reported, Laboratory (FROM NORTH CAROLINA FOUNDATION SEED PRODUCERS INC, ZEBULON, NORTH CAROLINA, USA)	Natural soil, Environmental, Soil slurry, Not Reported	Measured	<1.00 AI mg/kg dry soil / 2.8 (1.2-4.3) AI mg/kg dry soil	Mortality (Mortality-Survival, Response Site: Not reported)	NOEL (>=2.8 AI mg/kg dry soil)	Mortality	High	9644539
1066-42-8	14 Day(s), (14 Day(s))	*Glycine max* (Soybean), Seed, Not Reported, Laboratory (FROM NORTH CAROLINA FOUNDATION SEED PRODUCERS INC, ZEBULON, NORTH CAROLINA, USA)	Natural soil, Environmental, Soil slurry, Not Reported	Measured	<1.00 AI mg/kg dry soil / 2.8 (1.2-4.3) AI mg/kg dry soil	Growth (Growth-Biomass, Response Site: Shoot)	NOEL (>=2.8 AI mg/kg dry soil)	Development/Growth	High	9644539
1066-42-8	14 Day(s), (14 Day(s))	*Glycine max* (Soybean), Seed, Not Reported, Laboratory (FROM NORTH CAROLINA FOUNDATION SEED PRODUCERS INC, ZEBULON, NORTH CAROLINA, USA)	Natural soil, Environmental, Soil slurry, Not Reported	Unmeasured	0 AI mg/kg dry soil / 0.050 AI mg/kg dry soil / 0.50 AI mg/kg dry soil / 5.0 AI mg/kg dry soil	Growth (Development-Emergence, Response Site: Not reported)	NR (0.050-5.0 AI mg/kg dry soil)	Development/Growth	High	9644539

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Terrestrial: Vascular plants Extraction Table

CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
1066-42-8	14 Day(s), (14 Day(s))	*Glycine max* (Soybean), Seed, Not Reported, Laboratory (FROM NORTH CAROLINA FOUNDATION SEED PRODUCERS INC, ZEBULON, NORTH CAROLINA, USA)	Natural soil, Environmental, Soil slurry, Not Reported	Unmeasured	0 AI mg/kg dry soil / 0.050 AI mg/kg dry soil / 0.50 AI mg/kg dry soil / 5.0 AI mg/kg dry soil	Growth (Morphology-Abnormal, Response Site: Not reported)	NR (0.050-5.0 AI mg/kg dry soil)	Development/Growth	High	9644539
1066-42-8	14 Day(s), (14 Day(s))	*Glycine max* (Soybean), Seed, Not Reported, Laboratory (FROM NORTH CAROLINA FOUNDATION SEED PRODUCERS INC, ZEBULON, NORTH CAROLINA, USA)	Natural soil, Environmental, Soil slurry, Not Reported	Unmeasured	0 AI mg/kg dry soil / 0.050 AI mg/kg dry soil / 0.50 AI mg/kg dry soil / 5.0 AI mg/kg dry soil	Mortality (Mortality-Mortality, Response Site: Not reported)	NR-ZERO (5.0 AI mg/kg dry soil)	Mortality	High	9644539
1066-42-8	14 Day(s), (14 Day(s))	*Glycine max* (Soybean), Seed, Not Reported, Laboratory (FROM NORTH CAROLINA FOUNDATION SEED PRODUCERS INC, ZEBULON, NORTH CAROLINA, USA)	Natural soil, Environmental, Soil slurry, Not Reported	Unmeasured	0 AI mg/kg dry soil / 0.050 AI mg/kg dry soil / 0.50 AI mg/kg dry soil / 5.0 AI mg/kg dry soil	Growth (Growth-Biomass, Response Site: Shoot)	NR (0.050-5.0 AI mg/kg dry soil)	Development/Growth	High	9644539

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Terrestrial: Vascular plants Extraction Table

CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
1066-42-8	14 Day(s), (14 Day(s))	*Glycine max* (Soybean), Seed, Not Reported, Laboratory (FROM NORTH CAROLINA FOUNDATION SEED PRODUCERS INC, ZEBULON, NORTH CAROLINA, USA)	Natural soil, Environmental, Soil slurry, Not Reported	Measured	<1.00 AI mg/kg dry soil / 2.8 (1.2-4.3) AI mg/kg dry soil	Growth (Development-Emergence, Response Site: Not reported)	NOEL (>=2.8 AI mg/kg dry soil)	Development/Growth	High	9644539
1066-42-8	14 Day(s), (14 Day(s))	*Helianthus annuus* (Common Annual Sunflower), Seed, Not Reported, Laboratory (FROM JOHNNY'S SELECTED SEEDS, WINSLOW, MAINE, USA)	Natural soil, Environmental, Soil slurry, Not Reported	Measured	<1.00 AI mg/kg dry soil / 2.8 (1.2-4.3) AI mg/kg dry soil	Growth (Development-Emergence, Response Site: Not reported)	NOEL (>=2.8 AI mg/kg dry soil)	Development/Growth	High	9644539
1066-42-8	14 Day(s), (14 Day(s))	*Helianthus annuus* (Common Annual Sunflower), Seed, Not Reported, Laboratory (FROM JOHNNY'S SELECTED SEEDS, WINSLOW, MAINE, USA)	Natural soil, Environmental, Soil slurry, Not Reported	Measured	<1.00 AI mg/kg dry soil / 2.8 (1.2-4.3) AI mg/kg dry soil	Growth (Growth-Biomass, Response Site: Shoot)	NOEL (>=2.8 AI mg/kg dry soil)	Development/Growth	High	9644539
1066-42-8	14 Day(s), (14 Day(s))	*Helianthus annuus* (Common Annual Sunflower), Seed, Not Reported, Laboratory (FROM JOHNNY'S SELECTED SEEDS, WINSLOW, MAINE, USA)	Natural soil, Environmental, Soil slurry, Not Reported	Unmeasured	0 AI mg/kg dry soil / 0.050 AI mg/kg dry soil / 0.50 AI mg/kg dry soil / 5.0 AI mg/kg dry soil	Growth (Morphology-Abnormal, Response Site: Not reported)	NR (0.050-5.0 AI mg/kg dry soil)	Development/Growth	High	9644539

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Terrestrial: Vascular plants Extraction Table

CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
1066-42-8	14 Day(s), (14 Day(s))	*Helianthus annuus* (Common Annual Sunflower), Seed, Not Reported, Laboratory (FROM JOHNNY'S SELECTED SEEDS, WINSLOW, MAINE, USA)	Natural soil, Environmental, Soil slurry, Not Reported	Measured	<1.00 AI mg/kg dry soil / 2.8 (1.2-4.3) AI mg/kg dry soil	Mortality (Mortality-Survival, Response Site: Not reported)	NOEL (>=2.8 AI mg/kg dry soil)	Mortality	High	9644539
1066-42-8	14 Day(s), (14 Day(s))	*Helianthus annuus* (Common Annual Sunflower), Seed, Not Reported, Laboratory (FROM JOHNNY'S SELECTED SEEDS, WINSLOW, MAINE, USA)	Natural soil, Environmental, Soil slurry, Not Reported	Unmeasured	0 AI mg/kg dry soil / 0.050 AI mg/kg dry soil / 0.50 AI mg/kg dry soil / 5.0 AI mg/kg dry soil	Growth (Development-Emergence, Response Site: Not reported)	NR (0.050-5.0 AI mg/kg dry soil)	Development/Growth	High	9644539
1066-42-8	14 Day(s), (14 Day(s))	*Helianthus annuus* (Common Annual Sunflower), Seed, Not Reported, Laboratory (FROM JOHNNY'S SELECTED SEEDS, WINSLOW, MAINE, USA)	Natural soil, Environmental, Soil slurry, Not Reported	Unmeasured	0 AI mg/kg dry soil / 0.050 AI mg/kg dry soil / 0.50 AI mg/kg dry soil / 5.0 AI mg/kg dry soil	Mortality (Mortality-Mortality, Response Site: Not reported)	NR-ZERO (5.0 AI mg/kg dry soil)	Mortality	High	9644539
1066-42-8	14 Day(s), (14 Day(s))	*Helianthus annuus* (Common Annual Sunflower), Seed, Not Reported, Laboratory (FROM JOHNNY'S SELECTED SEEDS, WINSLOW, MAINE, USA)	Natural soil, Environmental, Soil slurry, Not Reported	Unmeasured	0 AI mg/kg dry soil / 0.050 AI mg/kg dry soil / 0.50 AI mg/kg dry soil / 5.0 AI mg/kg dry soil	Growth (Growth-Biomass, Response Site: Shoot)	NR (0.050-5.0 AI mg/kg dry soil)	Development/Growth	High	9644539

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Terrestrial: Vascular plants Extraction Table

CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
1066-42-8	14 Day(s), (14 Day(s))	*Lolium perenne* (Perennial Ryegrass), Seed, Not Reported, Laboratory (FROM GRANITE SEED COMPANY, LEHI, UTAH, USA)	Natural soil, Environmental, Soil slurry, Not Reported	Unmeasured	0 AI mg/kg dry soil / 0.050 AI mg/kg dry soil / 0.50 AI mg/kg dry soil / 5.0 AI mg/kg dry soil	Growth (Growth-Biomass, Response Site: Shoot)	NR (0.050-5.0 AI mg/kg dry soil)	Development/Growth	High	9644539
1066-42-8	14 Day(s), (14 Day(s))	*Lolium perenne* (Perennial Ryegrass), Seed, Not Reported, Laboratory (FROM GRANITE SEED COMPANY, LEHI, UTAH, USA)	Natural soil, Environmental, Soil slurry, Not Reported	Measured	<1.00 AI mg/kg dry soil / 2.8 (1.2-4.3) AI mg/kg dry soil	Growth (Growth-Biomass, Response Site: Shoot)	NOEL (>=2.8 AI mg/kg dry soil)	Development/Growth	High	9644539
1066-42-8	14 Day(s), (14 Day(s))	*Lolium perenne* (Perennial Ryegrass), Seed, Not Reported, Laboratory (FROM GRANITE SEED COMPANY, LEHI, UTAH, USA)	Natural soil, Environmental, Soil slurry, Not Reported	Measured	<1.00 AI mg/kg dry soil / 2.8 (1.2-4.3) AI mg/kg dry soil	Mortality (Mortality-Survival, Response Site: Not reported)	NOEL (>=2.8 AI mg/kg dry soil)	Mortality	High	9644539
1066-42-8	14 Day(s), (14 Day(s))	*Lolium perenne* (Perennial Ryegrass), Seed, Not Reported, Laboratory (FROM GRANITE SEED COMPANY, LEHI, UTAH, USA)	Natural soil, Environmental, Soil slurry, Not Reported	Unmeasured	0 AI mg/kg dry soil / 0.050 AI mg/kg dry soil / 0.50 AI mg/kg dry soil / 5.0 AI mg/kg dry soil	Growth (Development-Emergence, Response Site: Not reported)	NR (0.050-5.0 AI mg/kg dry soil)	Development/Growth	High	9644539

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Terrestrial: Vascular plants Extraction Table

CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
1066-42-8	14 Day(s), (14 Day(s))	*Lolium perenne* (Perennial Ryegrass), Seed, Not Reported, Laboratory (FROM GRANITE SEED COMPANY, LEHI, UTAH, USA)	Natural soil, Environmental, Soil slurry, Not Reported	Unmeasured	0 AI mg/kg dry soil / 0.050 AI mg/kg dry soil / 0.50 AI mg/kg dry soil / 5.0 AI mg/kg dry soil	Mortality (Mortality-Mortality, Response Site: Not reported)	NR-ZERO (5.0 AI mg/kg dry soil)	Mortality	High	9644539
1066-42-8	14 Day(s), (14 Day(s))	*Lolium perenne* (Perennial Ryegrass), Seed, Not Reported, Laboratory (FROM GRANITE SEED COMPANY, LEHI, UTAH, USA)	Natural soil, Environmental, Soil slurry, Not Reported	Unmeasured	0 AI mg/kg dry soil / 0.050 AI mg/kg dry soil / 0.50 AI mg/kg dry soil / 5.0 AI mg/kg dry soil	Growth (Morphology-Abnormal, Response Site: Not reported)	NR (0.050-5.0 AI mg/kg dry soil)	Development/Growth	High	9644539
1066-42-8	14 Day(s), (14 Day(s))	*Lolium perenne* (Perennial Ryegrass), Seed, Not Reported, Laboratory (FROM GRANITE SEED COMPANY, LEHI, UTAH, USA)	Natural soil, Environmental, Soil slurry, Not Reported	Measured	<1.00 AI mg/kg dry soil / 2.8 (1.2-4.3) AI mg/kg dry soil	Growth (Development-Emergence, Response Site: Not reported)	NOEL (>=2.8 AI mg/kg dry soil)	Development/Growth	High	9644539
1066-42-8	14 Day(s), (14 Day(s))	*Raphanus sativus* (Radish), Seed, Not Reported, Laboratory (FROM JOHNNY'S SELECTED SEEDS, WINSLOW, MAINE, USA)	Natural soil, Environmental, Soil slurry, Not Reported	Unmeasured	0 AI mg/kg dry soil / 0.050 AI mg/kg dry soil / 0.50 AI mg/kg dry soil / 5.0 AI mg/kg dry soil	Growth (Growth-Biomass, Response Site: Shoot)	NR (0.050-5.0 AI mg/kg dry soil)	Development/Growth	High	9644539

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CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
1066-42-8	14 Day(s), (14 Day(s))	*Raphanus sativus* (Radish), Seed, Not Reported, Laboratory (FROM JOHNNY'S SELECTED SEEDS, WINSLOW, MAINE, USA)	Natural soil, Environmental, Soil slurry, Not Reported	Measured	<1.00 AI mg/kg dry soil / 2.8 (1.2-4.3) AI mg/kg dry soil	Growth (Development-Emergence, Response Site: Not reported)	NOEL (>=2.8 AI mg/kg dry soil)	Development/Growth	High	9644539
1066-42-8	14 Day(s), (14 Day(s))	*Raphanus sativus* (Radish), Seed, Not Reported, Laboratory (FROM JOHNNY'S SELECTED SEEDS, WINSLOW, MAINE, USA)	Natural soil, Environmental, Soil slurry, Not Reported	Unmeasured	0 AI mg/kg dry soil / 0.050 AI mg/kg dry soil / 0.50 AI mg/kg dry soil / 5.0 AI mg/kg dry soil	Mortality (Mortality-Mortality, Response Site: Not reported)	NR-ZERO (5.0 AI mg/kg dry soil)	Mortality	High	9644539
1066-42-8	14 Day(s), (14 Day(s))	*Raphanus sativus* (Radish), Seed, Not Reported, Laboratory (FROM JOHNNY'S SELECTED SEEDS, WINSLOW, MAINE, USA)	Natural soil, Environmental, Soil slurry, Not Reported	Measured	<1.00 AI mg/kg dry soil / 2.8 (1.2-4.3) AI mg/kg dry soil	Mortality (Mortality-Survival, Response Site: Not reported)	NOEL (>=2.8 AI mg/kg dry soil)	Mortality	High	9644539
1066-42-8	14 Day(s), (14 Day(s))	*Raphanus sativus* (Radish), Seed, Not Reported, Laboratory (FROM JOHNNY'S SELECTED SEEDS, WINSLOW, MAINE, USA)	Natural soil, Environmental, Soil slurry, Not Reported	Unmeasured	0 AI mg/kg dry soil / 0.050 AI mg/kg dry soil / 0.50 AI mg/kg dry soil / 5.0 AI mg/kg dry soil	Growth (Development-Emergence, Response Site: Not reported)	NR (0.050-5.0 AI mg/kg dry soil)	Development/Growth	High	9644539

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CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
1066-42-8	14 Day(s), (14 Day(s))	*Raphanus sativus* (Radish), Seed, Not Reported, Laboratory (FROM JOHNNY'S SELECTED SEEDS, WINSLOW, MAINE, USA)	Natural soil, Environmental, Soil slurry, Not Reported	Unmeasured	0 AI mg/kg dry soil / 0.050 AI mg/kg dry soil / 0.50 AI mg/kg dry soil / 5.0 AI mg/kg dry soil	Growth (Morphology-Abnormal, Response Site: Not reported)	NR (0.050-5.0 AI mg/kg dry soil)	Development/Growth	High	9644539
1066-42-8	14 Day(s), (14 Day(s))	*Raphanus sativus* (Radish), Seed, Not Reported, Laboratory (FROM JOHNNY'S SELECTED SEEDS, WINSLOW, MAINE, USA)	Natural soil, Environmental, Soil slurry, Not Reported	Measured	<1.00 AI mg/kg dry soil / 2.8 (1.2-4.3) AI mg/kg dry soil	Growth (Growth-Biomass, Response Site: Shoot)	NOEL (>=2.8 AI mg/kg dry soil)	Development/Growth	High	9644539
1066-42-8	14 Day(s), (14 Day(s))	*Solanum lycopersicum var. lycopersicum* (Tomato), Seed, Not Reported, Laboratory (FROM JOHNNY'S SELECTED SEEDS, WINSLOW, MAINE, USA)	Natural soil, Environmental, Soil slurry, Not Reported	Measured	<1.00 AI mg/kg dry soil / 2.8 (1.2-4.3) AI mg/kg dry soil	Mortality (Mortality-Survival, Response Site: Not reported)	NOEL (>=2.8 AI mg/kg dry soil)	Mortality	High	9644539
1066-42-8	14 Day(s), (14 Day(s))	*Solanum lycopersicum var. lycopersicum* (Tomato), Seed, Not Reported, Laboratory (FROM JOHNNY'S SELECTED SEEDS, WINSLOW, MAINE, USA)	Natural soil, Environmental, Soil slurry, Not Reported	Measured	<1.00 AI mg/kg dry soil / 2.8 (1.2-4.3) AI mg/kg dry soil	Growth (Development-Emergence, Response Site: Not reported)	NOEL (>=2.8 AI mg/kg dry soil)	Development/Growth	High	9644539

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Terrestrial: Vascular plants Extraction Table

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1066-42-8	14 Day(s), (14 Day(s))	*Solanum lycopersicum var. lycopersicum* (Tomato), Seed, Not Reported, Laboratory (FROM JOHNNY'S SELECTED SEEDS, WINSLOW, MAINE, USA)	Natural soil, Environmental, Soil slurry, Not Reported	Unmeasured	0 AI mg/kg dry soil / 0.050 AI mg/kg dry soil / 0.50 AI mg/kg dry soil / 5.0 AI mg/kg dry soil	Growth (Development-Emergence, Response Site: Not reported)	NR (0.050-5.0 AI mg/kg dry soil)	Development/Growth	High	9644539
1066-42-8	14 Day(s), (14 Day(s))	*Solanum lycopersicum var. lycopersicum* (Tomato), Seed, Not Reported, Laboratory (FROM JOHNNY'S SELECTED SEEDS, WINSLOW, MAINE, USA)	Natural soil, Environmental, Soil slurry, Not Reported	Unmeasured	0 AI mg/kg dry soil / 0.050 AI mg/kg dry soil / 0.50 AI mg/kg dry soil / 5.0 AI mg/kg dry soil	Growth (Growth-Biomass, Response Site: Shoot)	NR (0.050-5.0 AI mg/kg dry soil)	Development/Growth	High	9644539
1066-42-8	14 Day(s), (14 Day(s))	*Solanum lycopersicum var. lycopersicum* (Tomato), Seed, Not Reported, Laboratory (FROM JOHNNY'S SELECTED SEEDS, WINSLOW, MAINE, USA)	Natural soil, Environmental, Soil slurry, Not Reported	Unmeasured	0 AI mg/kg dry soil / 0.050 AI mg/kg dry soil / 0.50 AI mg/kg dry soil / 5.0 AI mg/kg dry soil	Mortality (Mortality-Mortality, Response Site: Not reported)	NR-ZERO (5.0 AI mg/kg dry soil)	Mortality	High	9644539
1066-42-8	14 Day(s), (14 Day(s))	*Solanum lycopersicum var. lycopersicum* (Tomato), Seed, Not Reported, Laboratory (FROM JOHNNY'S SELECTED SEEDS, WINSLOW, MAINE, USA)	Natural soil, Environmental, Soil slurry, Not Reported	Unmeasured	0 AI mg/kg dry soil / 0.050 AI mg/kg dry soil / 0.50 AI mg/kg dry soil / 5.0 AI mg/kg dry soil	Growth (Morphology-Abnormal, Response Site: Not reported)	NR (0.050-5.0 AI mg/kg dry soil)	Development/Growth	High	9644539

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Terrestrial: Vascular plants Extraction Table

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1066-42-8	14 Day(s), (14 Day(s))	*Solanum lycopersicum var. lycopersicum* (Tomato), Seed, Not Reported, Laboratory (FROM JOHNNY'S SELECTED SEEDS, WINSLOW, MAINE, USA)	Natural soil, Environmental, Soil slurry, Not Reported	Measured	<1.00 AI mg/kg dry soil / 2.8 (1.2-4.3) AI mg/kg dry soil	Growth (Growth-Biomass, Response Site: Shoot)	NOEL (>=2.8 AI mg/kg dry soil)	Development/Growth	High	9644539
1066-42-8	14 Day(s), (14 Day(s))	*Zea mays* (Corn), Seed, Not Reported, Laboratory (FROM CAROLINA BIOLOGICAL SUPPLY COMPANY, BURLINGTON, NORTH CAROLINA, USA)	Natural soil, Environmental, Soil slurry, Not Reported	Unmeasured	0 AI mg/kg dry soil / 0.050 AI mg/kg dry soil / 0.50 AI mg/kg dry soil / 5.0 AI mg/kg dry soil	Growth (Growth-Biomass, Response Site: Shoot)	NR (0.050-5.0 AI mg/kg dry soil)	Development/Growth	High	9644539
1066-42-8	14 Day(s), (14 Day(s))	*Zea mays* (Corn), Seed, Not Reported, Laboratory (FROM CAROLINA BIOLOGICAL SUPPLY COMPANY, BURLINGTON, NORTH CAROLINA, USA)	Natural soil, Environmental, Soil slurry, Not Reported	Measured	<1.00 AI mg/kg dry soil / 2.8 (1.2-4.3) AI mg/kg dry soil	Mortality (Mortality-Survival, Response Site: Not reported)	NOEL (>=2.8 AI mg/kg dry soil)	Mortality	High	9644539
1066-42-8	14 Day(s), (14 Day(s))	*Zea mays* (Corn), Seed, Not Reported, Laboratory (FROM CAROLINA BIOLOGICAL SUPPLY COMPANY, BURLINGTON, NORTH CAROLINA, USA)	Natural soil, Environmental, Soil slurry, Not Reported	Measured	<1.00 AI mg/kg dry soil / 2.8 (1.2-4.3) AI mg/kg dry soil	Growth (Growth-Biomass, Response Site: Shoot)	NOEL (>=2.8 AI mg/kg dry soil)	Development/Growth	High	9644539

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Terrestrial: Vascular plants Extraction Table

CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
1066-42-8	14 Day(s), (14 Day(s))	*Zea mays* (Corn), Seed, Not Reported, Laboratory (FROM CAROLINA BIOLOGICAL SUPPLY COMPANY, BURLINGTON, NORTH CAROLINA, USA)	Natural soil, Environmental, Soil slurry, Not Reported	Measured	<1.00 AI mg/kg dry soil / 2.8 (1.2-4.3) AI mg/kg dry soil	Growth (Development-Emergence, Response Site: Not reported)	NOEL (>=2.8 AI mg/kg dry soil)	Development/Growth	High	9644539
1066-42-8	14 Day(s), (14 Day(s))	*Zea mays* (Corn), Seed, Not Reported, Laboratory (FROM CAROLINA BIOLOGICAL SUPPLY COMPANY, BURLINGTON, NORTH CAROLINA, USA)	Natural soil, Environmental, Soil slurry, Not Reported	Unmeasured	0 AI mg/kg dry soil / 0.050 AI mg/kg dry soil / 0.50 AI mg/kg dry soil / 5.0 AI mg/kg dry soil	Growth (Morphology-Abnormal, Response Site: Not reported)	NR (0.050-5.0 AI mg/kg dry soil)	Development/Growth	High	9644539
1066-42-8	14 Day(s), (14 Day(s))	*Zea mays* (Corn), Seed, Not Reported, Laboratory (FROM CAROLINA BIOLOGICAL SUPPLY COMPANY, BURLINGTON, NORTH CAROLINA, USA)	Natural soil, Environmental, Soil slurry, Not Reported	Unmeasured	0 AI mg/kg dry soil / 0.050 AI mg/kg dry soil / 0.50 AI mg/kg dry soil / 5.0 AI mg/kg dry soil	Mortality (Mortality-Mortality, Response Site: Not reported)	NR-ZERO (5.0 AI mg/kg dry soil)	Mortality	High	9644539
1066-42-8	14 Day(s), (14 Day(s))	*Zea mays* (Corn), Seed, Not Reported, Laboratory (FROM CAROLINA BIOLOGICAL SUPPLY COMPANY, BURLINGTON, NORTH CAROLINA, USA)	Natural soil, Environmental, Soil slurry, Not Reported	Unmeasured	0 AI mg/kg dry soil / 0.050 AI mg/kg dry soil / 0.50 AI mg/kg dry soil / 5.0 AI mg/kg dry soil	Growth (Development-Emergence, Response Site: Not reported)	NR (0.050-5.0 AI mg/kg dry soil)	Development/Growth	High	9644539

* If multiple extractions contained all identical information except the effect level, extraction rows were collapsed and the differing levels are listed by comma in this row.

Terrestrial: Worms Extraction Table

CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
1066-42-8	28 Day(s), (56 Day(s))	*Eisenia fetida* (Earthworm), Mature, 3-5 Month(s) (Measured in: F0 generation), Not Reported, Laboratory (ORIGINAL ADULTS FROM CAROLINA BIOLOGICAL SUPPLY COMPANY, BURLINGTON, NORTH CAROLINA, THEN CULTURED AT SMITHERS)	Artificial soil, Environmental, Culture medium, 78 F0 generation	Measured	<0.50 mg/kg dry soil / 3.8 (2.6-5.3) mg/kg dry soil	Growth (Growth-Weight, Response Site: Whole organism)	EC50 (>3.8 mg/kg dry soil)	Development/Growth	High	10706154
1066-42-8	28 Day(s), (56 Day(s))	*Eisenia fetida* (Earthworm), Mature, 3-5 Month(s) (Measured in: F0 generation), Not Reported, Laboratory (ORIGINAL ADULTS FROM CAROLINA BIOLOGICAL SUPPLY COMPANY, BURLINGTON, NORTH CAROLINA, THEN CULTURED AT SMITHERS)	Artificial soil, Environmental, Culture medium, 78 F0 generation	Measured	<0.50 mg/kg dry soil / 3.8 (2.6-5.3) mg/kg dry soil	Mortality (Mortality-Survival, Response Site: Not reported)	LC50 (>3.8 mg/kg dry soil)	Mortality	High	10706154

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Terrestrial: Worms Extraction Table

CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
1066-42-8	28 Day(s), (56 Day(s))	*Eisenia fetida* (Earthworm), Mature, 3-5 Month(s) (Measured in: F0 generation), Not Reported, Laboratory (ORIGINAL ADULTS FROM CAROLINA BIOLOGICAL SUPPLY COMPANY, BURLINGTON, NORTH CAROLINA, THEN CULTURED AT SMITHERS)	Artificial soil, Environmental, Culture medium, 78 F0 generation	Measured	<0.50 mg/kg dry soil / 3.8 (2.6-5.3) mg/kg dry soil	Growth (Growth-Weight, Response Site: Whole organism)	LOEL (>3.8 mg/kg dry soil)	Development/Growth	High	10706154
1066-42-8	28 Day(s), (56 Day(s))	*Eisenia fetida* (Earthworm), Mature, 3-5 Month(s) (Measured in: F0 generation), Not Reported, Laboratory (ORIGINAL ADULTS FROM CAROLINA BIOLOGICAL SUPPLY COMPANY, BURLINGTON, NORTH CAROLINA, THEN CULTURED AT SMITHERS)	Artificial soil, Environmental, Culture medium, 78 F0 generation	Measured	<0.50 mg/kg dry soil / 3.8 (2.6-5.3) mg/kg dry soil	Mortality (Mortality-Survival, Response Site: Not reported)	LOEL (>3.8 mg/kg dry soil)	Mortality	High	10706154

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Terrestrial: Worms Extraction Table

CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
1066-42-8	28 Day(s), (56 Day(s))	*Eisenia fetida* (Earthworm), Mature, 3-5 Month(s) (Measured in: F0 generation), Not Reported, Laboratory (ORIGINAL ADULTS FROM CAROLINA BIOLOGICAL SUPPLY COMPANY, BURLINGTON, NORTH CAROLINA, THEN CULTURED AT SMITHERS)	Artificial soil, Environmental, Culture medium, 78 F0 generation	Measured	<0.50 mg/kg dry soil / 3.8 (2.6-5.3) mg/kg dry soil	Growth (Growth-Weight, Response Site: Whole organism)	NOEL (3.8 (3.6-5.3) mg/kg dry soil)	Development/Growth	High	10706154
1066-42-8	28 Day(s), (56 Day(s))	*Eisenia fetida* (Earthworm), Mature, 3-5 Month(s) (Measured in: F0 generation), Not Reported, Laboratory (ORIGINAL ADULTS FROM CAROLINA BIOLOGICAL SUPPLY COMPANY, BURLINGTON, NORTH CAROLINA, THEN CULTURED AT SMITHERS)	Artificial soil, Environmental, Culture medium, 78 F0 generation	Measured	<0.50 mg/kg dry soil / 3.8 (2.6-5.3) mg/kg dry soil	Mortality (Mortality-Survival, Response Site: Not reported)	NOEL (3.8 (3.6-5.3) mg/kg dry soil)	Mortality	High	10706154

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Terrestrial: Worms Extraction Table

CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
1066-42-8	56 Day(s), (56 Day(s))	*Eisenia fetida* (Earthworm), Mature, 3-5 Month(s) (Measured in: F0 generation), Not Reported, Laboratory (ORIGINAL ADULTS FROM CAROLINA BIOLOGICAL SUPPLY COMPANY, BURLINGTON, NORTH CAROLINA, THEN CULTURED AT SMITHERS)	Artificial soil, Environmental, Culture medium, 78 F0 generation	Measured	<0.50 mg/kg dry soil / 3.8 (2.6-5.3) mg/kg dry soil	Reproduction (Reproduction-Progeny counts/numbers, Response Site: Not reported)	EC10 (>3.8 mg/kg dry soil)	Reproductive/Teratogenic	High	10706154
1066-42-8	56 Day(s), (56 Day(s))	*Eisenia fetida* (Earthworm), Mature, 3-5 Month(s) (Measured in: F0 generation), Not Reported, Laboratory (ORIGINAL ADULTS FROM CAROLINA BIOLOGICAL SUPPLY COMPANY, BURLINGTON, NORTH CAROLINA, THEN CULTURED AT SMITHERS)	Artificial soil, Environmental, Culture medium, 78 F0 generation	Measured	<0.50 mg/kg dry soil / 3.8 (2.6-5.3) mg/kg dry soil	Reproduction (Reproduction-Progeny counts/numbers, Response Site: Not reported)	EC50 (>3.8 mg/kg dry soil)	Reproductive/Teratogenic	High	10706154

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Terrestrial: Worms Extraction Table

CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
1066-42-8	56 Day(s), (56 Day(s))	*Eisenia fetida* (Earthworm), Mature, 3-5 Month(s) (Measured in: F0 generation), Not Reported, Laboratory (ORIGINAL ADULTS FROM CAROLINA BIOLOGICAL SUPPLY COMPANY, BURLINGTON, NORTH CAROLINA, THEN CULTURED AT SMITHERS)	Artificial soil, Environmental, Culture medium, 78 F0 generation	Measured	<0.50 mg/kg dry soil / 3.8 (2.6-5.3) mg/kg dry soil	Reproduction (Reproduction-Progeny counts/numbers, Response Site: Not reported)	LOEL (>3.8 mg/kg dry soil)	Reproductive/Teratogenic	High	10706154
1066-42-8	56 Day(s), (56 Day(s))	*Eisenia fetida* (Earthworm), Mature, 3-5 Month(s) (Measured in: F0 generation), Not Reported, Laboratory (ORIGINAL ADULTS FROM CAROLINA BIOLOGICAL SUPPLY COMPANY, BURLINGTON, NORTH CAROLINA, THEN CULTURED AT SMITHERS)	Artificial soil, Environmental, Culture medium, 78 F0 generation	Measured	<0.50 mg/kg dry soil / 3.8 (2.6-5.3) mg/kg dry soil	Reproduction (Reproduction-Progeny counts/numbers, Response Site: Not reported)	NOEL (3.8 (2.6-5.3) mg/kg dry soil)	Reproductive/Teratogenic	High	10706154

* If multiple extractions contained all identical information except the effect level, extraction rows were collapsed and the differing levels are listed by comma in this row.

Data Extraction of Rodent Data for the Application of Environmental Hazard

CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Strain	Exposure Type	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Hazard Effect/ Hazard Level	Effect Level as reported by the Study Author(s)	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
556-67-2	2 weeks, (2 weeks)	Rat (Rattus norvegicus), Sampling Age: Juvenile Exposure Age: Juvenile, M, F, Sprague-Dawley	Gavage	unmeasured	0/25/100/400/1600	1600	LOAEL	Growth	Medium	5900289
556-67-2	8 days, (8 days)	Rat (Rattus norvegicus), Sampling Age: Gestational Exposure Age: Gestational, F, Sprague-Dawley	Gavage	unmeasured	0/5/20/100	100	LOAEL	Reproduction	Medium	99288
556-67-2	13 days, (13 days)	Rabbit (Oryctolagus cuniculus), Sampling Age: Gestational Exposure Age: Gestational, F, New Zealand White	Gavage	measured	0/51.3/101.4/489/987	101.4	LOAEL	Reproduction	High	5889449
556-67-2	4 days, (4 days)	Rat (Rattus norvegicus), Sampling Age: Juvenile Exposure Age: Juvenile, F, Sprague-Dawley	Gavage	unmeasured but verified	0/10/50/100/250/500/1000	500	LOAEL	Growth	High	5887187
556-67-2	4 days, (4 days)	Rat (Rattus norvegicus), Sampling Age: Juvenile Exposure Age: Juvenile, F, Fischer 344	Gavage	unmeasured but verified	0/10/50/100/250/500/1000	250	LOAEL	Growth	High	5887187

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Data Extraction of Rodent Data for the Application of Environmental Hazard

CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Strain	Exposure Type	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Hazard Effect/ Hazard Level	Effect Level as reported by the Study Author(s)	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
556-67-2	28 days, (28 days)	Rat (Rattus norvegicus), Sampling Age: Juvenile Exposure Age: Juvenile, M, Fischer 344	Gavage	unmeasured but verified	0/10/30/100/ 300	300	LOAEL	Growth	High	5887620

Octamethylcyclotetrasiloxane (D4)- Parent compound - Acute (less than or equal to 24 hr)

Guideline and Animal Species, Strain, Sex	Exposure Route and Exposure Duration	Study-wide POD and Dose/ Concentration(s)	Summary	Major Limitations	Principal Target Organs/Systems and OQD*	HERO ID
No guideline or adherence to GLP conditions was specified. Rat-Wistar - [rat]-Male	Oral-Gavage-Duration: Acute (less than or equal to 24 hr) Single exposure. Single gavage	**POD: mL/kg (LD50) -LD50 >64.0 mL/kg** n= 5 Dose= 64, mL/kg	In an acute oral lethality study, five male Wistar-derived albino rats were exposed via gavage to Octamethylcyclotetrasiloxane (D4, also referred to as Silicone Y-7202) (purity not reported) at an oral dose volume of 64 ml/kg. Rats were checked for mortality, weight changes, and clinical signs during the 14-day observation period. The animals were then sacrificed and assessed for gross pathological changes. No rats died during the study. The study authors note that the rats weighed 203 to 227 grams at the start of the study. In the data table, it is shown that weight change was 91 to 119. However, it is unclear whether this indicates weight gain or weight loss. The clinical signs that were observed for dosed rats included sluggish behavior, heavy breathing, and piloerection. There were no gross lesions observed in any of the animals. The study authors report that an oral dose of 64 ml/kg in rats is not toxic by the Federal Hazardous Substances Act (FHSA) definition. The reported LD50 was >64.0 mg/L	This study has significant reporting deficiencies, including missing information about the test substance and animal husbandry. A dose in mg/kg was not provided.	Mortality-Mortality- Neurological/Behavioral-CNS-related clinical signs; Medium	Carnegie Mellon University, 1972 5895941

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Octamethylcyclotetrasiloxane (D4)- Parent compound - Acute (less than or equal to 24 hr)

Guideline and Animal Species, Strain, Sex	Exposure Route and Exposure Duration	Study-wide POD and Dose/ Concentration(s)	Summary	Major Limitations	Principal Target Organs/Systems and OQD*	HERO ID
No guideline or adherence to GLP conditions was specified. Rabbit-Not specified-Male	Dermal-Duration: Acute (less than or equal to 24 hr) Single exposure. single application - 24 hrs under occlusion	**POD: mL/kg (LD50) -Rabbit dermal LD50 >16.0 mL/kg** n= 4 Dose= 16, mL/kg	In an acute dermal lethality study, the clipped skin the trunks of male albino rabbits (2 with abraded skin, 2 with unabraded skin) was exposed to Octamethylcyclotetrasiloxane (D4, also referred to as Silicone Y-7202) (purity not reported) at a dose volume of 16 ml/kg under occlusive conditions for 24 hours. Rabbits were checked for mortality, weight changes, and clinical signs during a 14-day observation period. The animals were the sacrificed and assessed for gross pathological changes. No rabbits died during the study and no clinical signs or symptoms were observed. The study authors note that the rabbits weighed 2345 to 2815 grams at the start of the study. In the data table, it is shown that weight changes were 177, 132, -50, and -62; however, it was not specified which values were for rabbits with abraded or unabraded skin. The study authors note that erythema was observed in the skin of the animals, but again did not specify whether this was in the rabbits with abraded or unabraded skin. There were no gross lesions observed in any of the animals.The study authors report that dermal dose of 16 ml/kg in rabbits is not toxic by the Federal Hazardous Substances Act (FHSA) definition and the reported LD50 was >16 mL/kg.	This study has significant reporting deficiencies, including missing information about the test substance and animal husbandry. A dose in mg/kg was not provided.	Mortality-Mortality-Irritation-Skin irritation; eye irritation; Medium	Carnegie Mellon University, 1972 5895941
No guideline or adherence to GLP conditions was specified. Rat-Wistar - [rat]-Male	Inhalation-Vapor-Duration: Acute (less than or equal to 24 hr) Single exposure. Single Inhalation exposures for 1 or 8 hours	**POD: Not provided (Other) -** n= 6 , Not provided	See footnotes for full summary [1]	This study has significant reporting deficiencies, including missing information about the test substance, and animal husbandry. There are concerns about the exposure administration including the potential for the formation of aerosols. The actual exposure concentration was not reported.	Mortality-Mortality-Neurological/Behavioral-CNS-related clinical signs-Irritation-Skin irritation; eye irritation-Other (please specify below) (Clinical signs)-pus from nose-Lung/Respiratory-Clinical signs - heavy breathing, gross pathology-Gastrointestinal-Gross necropsy; Uninformative	Carnegie Mellon University, 1972 5895941

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Octamethylcyclotetrasiloxane (D4)- Parent compound - Acute (less than or equal to 24 hr)

Guideline and Animal Species, Strain, Sex	Exposure Route and Exposure Duration	Study-wide POD and Dose/ Concentration(s)	Summary	Major Limitations	Principal Target Organs/Systems and OQD*	HERO ID
No guideline or adherence to GLP conditions was specified. Rat-Other (Hilltop Wistar)-Female	Oral-Gavage-Duration: Acute (less than or equal to 24 hr) Single exposure. Single gavage	**POD: mL/kg (LD50) -LD50 >64 mL/kg** mL/kg	In an acute lethality study, Hilltop-Wistar female rats (number not specified) were administered octamethylcyclotetrasiloxane (D4, purity not reported), also referred to as volatile silicone 7207, at unspecified doses differing by a factor of 2 in a geometric series, via a single gavage. The vehicle and gavage volume were not reported, although it was specified that samples were "dosed undiluted unless toxicity was too great to determine without dilution." Animals were weighed before dosing and were observed for 14-days. No further methodological details were provided. The reported rat oral LD50 was >64.0 mL/kg.	This study was limited by reporting deficiencies, including a lack of details on the test substance, test model, and exposure administration.	Mortality-Mortality; Low	Carnegie Mellon University, 1978 7310549
This study was conducted under conditions of good laboratory practice. The study was conducted in a manner that was similar to OECD 403. Rat-Other (Cpb;WU, Wistar random)-Both	Inhalation-Aerosol-Duration: Acute (less than or equal to 24 hr)-4 Single exposure. Animals were observed for 2 weeks after exposure.	**POD: 6,500 mg/m^3 (NOAEC) -An absence of any treatment-related changes.** n= 10 Dose= 6,500, mg/m^3	In an acute inhalation toxicity study, male and female (Cpb;WU, Wistar random) rats (5 rats/sex/group) were exposed whole-body to Octamethylcyclotetrasiloxane (D4) at a concentration of 6,500 mg/m^3 of air. Animals were exposed to D4 one single time for a period of 4 hours. The animals were then held for a two-week observation period. During the exposure and observation periods, the rats were monitored for mortality and "controlled for reactions to treatment daily" (presumed to be clinical signs). Body weights were recorded just prior to exposure and on days 1, 2, 4, 7, and 14 of the observation period. After the observation period, all animals were sacrificed and examined for gross pathological changes. There were no clinical signs observed in treated rats during the exposure period. In addition, no rats died during the exposure or observation periods. There were no noted reactions to treatment from handling the rats. In the first 18 hours after exposure, males and females gained hardly or lost some weight, however, these changes did not appear to be significant. As the observation period continued, the rats "gained weight in a normal way" as stated by the study authors. No gross abnormalities were observed.The authors reported a NOAEC of 6,500 mg/m^3 air for D4 in male and female rats based on the absence of any treatment-related changes. Based on the lack of mortality, the LC50 appears to be <6,500 mg/m3	No major limitations were identified. The study had some minor reporting limitations, including the purity of the test substance.	nan; High	Civo Institute Tno, nan 7310567

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Octamethylcyclotetrasiloxane (D4)- Parent compound - Acute (less than or equal to 24 hr)

Guideline and Animal Species, Strain, Sex	Exposure Route and Exposure Duration	Study-wide POD and Dose/ Concentration(s)	Summary	Major Limitations	Principal Target Organs/Systems and OQD*	HERO ID
The authors cite: 58 FR 28511 (May 14, 1993) [OPPTS-82040; FRL-4182-1] Health and Safety Data Reporting; 40 CFR Part 716 ITC 30-Listed Siloxanes and Silicones Mouse-Not specified-Male	Oral-Gavage-Duration: Acute (less than or equal to 24 hr) Single exposure. (interferon assay)	**POD: mL (Other) -** n= 5 Dose= 0, n= 5 Dose= 0.1, n= 5 Dose= 0.5, n= 10 Dose= 0.6, mL	To study effects of oral administration of octamethylcyclotetrasiloxane (D4) on the reticuloendothelial system (RES) authors performed an interferon assay and in vivo carbon clearance assay.In a preliminary study, male mice (5/group, strain not stated) were pretreated with a single dose of 0, 0.1, 0.5 or 0.6 mL of D4 via oral gavage (vehicle not specified). Animals were then treated with 125 μg of bacterial endotoxin via intravenous or intraperitoneal administration and following 2 hours of inoculation, animals were bled by cardiac puncture. Serum interferon titers were measured using plaque assay.The authors noted that animals treated with D4 and endotoxin yielded a ”detectable response” in the serum interferon titer assay. Author reported mean values for serum interferon titers were 80, 80, 320 and 160 50% plaque reduction units (PR5) (at doses of 0, 0.1, 0.5 and 0.6 mL respectively) in animals treated with endotoxin via i.v. administration. The mean serum interferon titer for animals exposed to 0.6 mL and endotoxin via i.p. exposure was 80 PR5. As no statistical analysis was conducted and author provided data is not sufficient to conduct an independent statistical analysis, this study is marked uninformative, and no toxicity values could be determined.	This study is marked uninformative due to lacking an author reported statistical analysis and data sufficient to conduct and independent statistical analysis was not provided. Other limitations include no reporting of important study details (animal housing conditions, strain, animal allocation into groups, details on test substance purity and storage conditions, information on oral gavage vehicle).	Immune/Hematological-Reticuloendothelial system (RES): Endotoxin-induced serum interferon titer and in vivo carbon clearance assay; Uninformative	Dow Corning, 1975 5883902

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Octamethylcyclotetrasiloxane (D4)- Parent compound - Acute (less than or equal to 24 hr)

Guideline and Animal Species, Strain, Sex	Exposure Route and Exposure Duration	Study-wide POD and Dose/ Concentration(s)	Summary	Major Limitations	Principal Target Organs/Systems and OQD*	HERO ID
This study was conducted in compliance with the following good laboratory practices: 1) United States Environmental Protection Agency, (TSCA), Title 40 Code of Federal Regulations Part 792, Federal Register, 29 November 1983 and subsequent amendment Federal Register 17 August, 1989; 2) OECD Principles of Good Laboratory Practice (as revised in 1997), ENVIMC/CHEM(98)17; 3) The United Kingdom Good Laboratory Practice Regulations 1997 ((Statutory Instrument No 654); and 4) EC Council Directive 87/18/EEC of 18 December 1986 (Official Journal No L 15/29). Rabbit-New Zealand White - [rabbit]-Male	Ocular/ Eye-Duration: Acute (less than or equal to 24 hr) Single exposure. Rabbit eyes were instilled with the test substance one time.	**POD: ml (Dichotomous (P/N)) -Classified as a non-irritating based on European Economic Community guideline (93/21/EEC).** n= 6 Dose= 0.1, ml	In an acute eye irritation study, male New Zealand White rabbits (n=6) were administered 0.1 ml of undiluted Dow Corning® 344 Fluid (octamethylcyclotetrasiloxane [D4]) into the lower everted lid of one eye. The untreated eye served as the control. Rabbits were observed twice daily for mortality, morbidity, and clinical signs. Eyes were examined 1 hour and 1, 2, and 3 days after instillation for any evidence of ocular irritation. One rabbit was observed at day 4. Assessment was based on Draize score and included assessing and scoring the cornea (for opacity), iris (for appearance), and conjunctivae (for redness, chemosis, and discharge). At the conclusion of the observation period, all animals were sacrificed and discarded without necropsy. No rabbits died during the study and there were no clinical signs of systemic reaction to treatment observed. Slight redness of the conjunctivae was seen in 5 treated eyes and diffuse crimson coloration of the conjunctivae was seen in one eye one hour after instillation. The ocular irritation had completely resolved in all animals by one or two days after instillation. Mean total ocular reaction scores were 2.3, 0.3, 0, 0, and 0 at 1 hour, 1, 2, 3, and 4 days, respectively. The cornea and iris appeared normal for all animals throughout the study (score of 0). The study does not report any information on the untreated eye. The test substance elicited very slight to well-defined conjunctival irritation (diffuse crimson coloration) and is classified as a non-irritating based on European Economic Community guideline (93/21/EEC).	The major limitations of this study included missing quantitative/qualitative data for the untreated eyes, missing purity information for the test substance, and missing analytical confirmation of the chemical concentration of the dosing solution.	Irritation-Eye irritation; High	Huntingdon Life Sciences, 1999 5887283

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Octamethylcyclotetrasiloxane (D4)- Parent compound - Acute (less than or equal to 24 hr)

Guideline and Animal Species, Strain, Sex	Exposure Route and Exposure Duration	Study-wide POD and Dose/ Concentration(s)	Summary	Major Limitations	Principal Target Organs/Systems and OQD*	HERO ID
No guideline or adherence to GLP conditions was specified; however, the study was conducted in a manner similar to OECD TG. 402. Rat-Sprague-Dawley - [rat]-Both	Dermal-Duration: Acute (less than or equal to 24 hr) Single exposure. Single percutaneous application	**POD: mg/kg (LD50) -LD50 >2,000 mg/kg; no mortality observed** n= 10 Dose= 0, n= 4 Dose= 1,000, n= 14 Dose= 2,000, mg/kg	In a standard acute toxicity study, octamethylcyclotetrasiloxane (D4) (purity not reported) was applied as a single 2,000 mg/kg dose percutaneously, to the clipped dorsal skin of Sprague-Dawley rats (5/sex/group) under occlusive conditions. A control group was treated in the same manner but without exposure to the test substance. After 24-hours, the bandage was removed and the site was examined for cutaneous lesions. The skin remained unwashed, and animals were monitored for 14 days. The definitive test was preceded by a preliminary test, conducted in the same manner where rats, 2/sex/dose, were treated with 1, 000, or 2,000 mg/kg (no control). Endpoints evaluated included observations for mortality and behavioral changes immediately after administration, at 1, 2, and 6 hours, and then daily through 14 days. Body weights were measured at study initiation, and at 1, 2, 4, 7, and 15 days (definitive test only). No necropsy was conducted. No deaths occurred in the preliminary or definitive tests. No behavioral changes, body weight changes, or cutaneous lesions were observed.No author-reported toxicity value was provided. Based on the available data, the 24-hr dermal LD50 in rats is >2,000 mg/kg.	Test material purity and source were not reported.	nan; Medium	IFREB, 1994 5888580
No guideline or adherence to GLP was specified. Rabbit-Not specified-Unknown	Dermal-Duration: Acute (less than or equal to 24 hr)-1-24-24-hour(s) 24 hours/day 1 days/week 24 hour(s) The test substance was applied via a dermal patch for 24 hrs.	**POD: mL (Other) -** n= 6 Dose= 0.5, mL	A 0.5mL volume of the undiluted test material was applied under occlusion to intact or abraded skin of six albino rabbits (strain and sex not specified) for 24 hours. The skin was examined 24 and 72 hours after application using the Draize technique. Observation was extended by 3 days if effects were observed. No reactions were observed on intact skin. When applied to abraded skin, scaling was noted after 72 hours. The effect was reversed after three more days. No irritation scores were provided. The study authors reported that there was “nearly no irritating action to the skin.”	A significant amount of details were missing from this study including details of the test material, animal model, husbandry conditions, and a clear description of outcome assessment methods. The results were insufficiently reported making the study uninformative.	Irritation-Skin irritation; Uninformative	Rhone-Poulenc Inc, 1971 5888536

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Octamethylcyclotetrasiloxane (D4)- Parent compound - Acute (less than or equal to 24 hr)

Guideline and Animal Species, Strain, Sex	Exposure Route and Exposure Duration	Study-wide POD and Dose/ Concentration(s)	Summary	Major Limitations	Principal Target Organs/Systems and OQD*	HERO ID
The study was GLP compliant. Specific guidelines were not reported; however, this study mostly followed OECD 404 guidelines for dermal irritation studies. Rabbit-New Zealand White - [rabbit]-Both	Dermal-Duration: Acute (less than or equal to 24 hr) Single exposure. Test substance was in contact with skin for 24 hours before being washed off	**POD: 172 mg/kg (Dichotomous (P/N)) -Non-irritating to the skin** n= 6 Dose= 172, mg/kg	New Zealand white rabbits (3/sex) were used in this dermal irritation study. The skin on the truck of each animal was clipped free of hair. One application site remained intact, while another was abraded by making minor incisions through the stratum corneum (derma was not disturbed; cuts were not deep enough to elicit bleeding). 0.5 ml of octamethylcyclotetrasiloxane (D4) (calculated by this reviewer to be approximately 172 mg/kg) was applied to the skin, covered with a gauze patch and secured with Vetrap bandaging to intact and abraded skin. After 24 hours the skin was wiped and rinsed with USP water. Animals were evaluated for mortality, body weight and body weight gain (initial and 72 hours), and clinical signs of toxicity (24, 48, and 72 hours). Irritation of abraded and intact skin was assessed 24 and 72 hours after application of the test substance. Erythema, edema, and eschar formation were evaluated; a Draize score was obtained. All animals survived the study duration. No overt clinical signs of toxicity were observed. All animals gained body weight over the 3 days (approximately 1%). No signs of erythema or edema were seen in the intact or abraded skin at 24 or 72 hours. A Draize score of 0 was obtained. D4 was considered non-irritating to the skin of rabbits.The density of D4 is 0.956 g/ml. The study authors applied 0.5 ml to the skin of rabbits weighing an average of 2.87 kg (reported by study authors). The dose was calculated as (956 mg/ml * 0.5 ml) / 2.87 kg = 172 mg/kg	Skin was not examined at 48 hours.	Irritation-Dermal irritation; Medium	Toxikon Corp, 1990 5895948

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Octamethylcyclotetrasiloxane (D4)- Parent compound - Acute (less than or equal to 24 hr)

Guideline and Animal Species, Strain, Sex	Exposure Route and Exposure Duration	Study-wide POD and Dose/ Concentration(s)	Summary	Major Limitations	Principal Target Organs/Systems and OQD*	HERO ID
The authors cite section 8d of US EPA TSCA and was GLP compliant. The study design is also similar to what is described in OECD TG 405. Rabbit-New Zealand White - [rabbit]-Both	Ocular/ Eye-Duration: Acute (less than or equal to 24 hr) Single exposure.	**POD: 0.1 mL (Dichotomous (P/N)) -Negative for eye irritation.** n= 6 Dose= 0.1, mL	In an acute eye irritation study, New Zealand white albino rabbits (3/sex/group) were exposed to a single instillation of 0.1 mL of octamethylcyclotetrasiloxane (D4) (80-99% purity) to the left eye. The right eye was not treated and served as a control. No washout was performed for the exposed left eye. Animals were weighed at the start of the experiment and at 72 hours post exposure. Animals were monitored for clinical signs of toxicity and behavioral observations (lethargy, altered coordination, staggering, paralysis). At 1, 24, 48 and 72 hours post exposure, eyes were examined for irritation via Draize scoring in the cornea, iris and conjunctiva, as well as fluorescein staining to measure eye lesions.No animals died over the course of the study, all animals gained weight and no clinical clinical signs of toxicity were observed. No irritation nor fluorescein-stained lesions were observed over the study (the scores for all indices in all animals were 0) and the authors reported that D4 is not an ocular irritant.	The authors could have described more details about how animals were selected for the study and could also have better characterized the test substance purity.	Irritation-Ocular irritation (Draize scoring for cornea, iris, conjuctiva for opacity, area, values, redness, chemosis and discharge)-Ocular/Sensory-Ocular fluorescein staining intensity and area; High	Toxikon Corp, 1990 5895967
No guidelines or adherence to GLP conditions were reported. Rat-Wistar - [rat]-Male	Oral-Gavage-Duration: Acute (less than or equal to 24 hr) Single exposure. Single gavage studies	**POD: 2.5 mg/kg (LD50) -LD50 = 2.5 mg/kg.** n= 4 Dose= 1.25, n= 6 Dose= 2.5, n= 4 Dose= 5, n= 2 Dose= 10, n= 4 , mg/kg	See footnotes for full summary [2]	No test substance details were provided (source, purity). Except for food and water availability, no animal husbandry details were reported. Some gavage volumes were excessive.	Mortality-Mortality, and signs of toxicity related to death-Renal/Kidney-Gross pathology-Gastrointestinal-Gross pathology-Hepatic/Liver-Gross pathology-Lung/Respiratory-Gross pathology-Immune/Hematological-Gross pathology (spleen); Medium	Union Carbide, 1993 5895928

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Octamethylcyclotetrasiloxane (D4)- Parent compound - Acute (less than or equal to 24 hr)

Guideline and Animal Species, Strain, Sex	Exposure Route and Exposure Duration	Study-wide POD and Dose/ Concentration(s)	Summary	Major Limitations	Principal Target Organs/Systems and OQD*	HERO ID
No guidelines or adherence to GLP conditions were specified. Rabbit-Other (Albino rabbits)-Male	Dermal-Duration: Acute (less than or equal to 24 hr) Single exposure. 4-hr dermal exposure	**POD: 0.794 mL/kg (LD50) -24-hr dermal LD50 = 0.794 mL/kg (~759 mg/kg)** n= 4 Dose= 0.5, n= 4 Dose= 1, n= 2 Dose= 2, mL/kg	In an acute dermal toxicity study, octamethylcyclotetrasiloxane (D4 purity and composition not reported), also referred to as volatile silicone 7207, was applied "as received" at 0.5, 1.0, or 2.0 mL/kg to the intact skin on the trunk of male albino rabbits (2-4/group) for 24-hours under occluded conditions. After exposure, excess fluid was removed to prevent ingestion. Animals were observed for mortality, clinical signs, body weight change, and skin irritation for 14 days. Gross necropsy was conducted at the end of the study. Deaths occurred in 0/4, 3/4, and 2/2 animals in the 0.5, 1.0, and 2.0 mL/kg groups, respectively. All deaths occurred within 1-3 days. Body weight change was reported in the surviving rabbits in the 0.5 ml group (27, 60, 100, 210) and 1.0 ml/kg group (45), however units are not reported; it is unclear if this is percent or grams. No skin irritation was observed, but staining was mentioned at the highest dose. No clinical signs of toxicity were observed. Gross examinations identified an orange-brown color in "many organs." Kidneys were black and there was blood in the urine. The 24-hour Dermal LD50 in rabbits was 0.794 (0.486 to 1.30) mL/kg. It is unclear if this value accounts for purity. Based on a D4 density of 0.956, this is ~759 mg/kg. No additional details were provided.	No test substance details were provided (source, purity). Except for food and water availability, no animal husbandry details were reported. The source of the animals was not specified.	Mortality-Mortality, and signs of toxicity related to death-Renal/Kidney-Gross pathology; Medium	Union Carbide, 1993 5895928

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Octamethylcyclotetrasiloxane (D4)- Parent compound - Acute (less than or equal to 24 hr)

Guideline and Animal Species, Strain, Sex	Exposure Route and Exposure Duration	Study-wide POD and Dose/ Concentration(s)	Summary	Major Limitations	Principal Target Organs/Systems and OQD*	HERO ID
No guideline or adherence to GLP conditions was reported. Rat-Not specified-Male	Dermal-Duration: Acute (less than or equal to 24 hr) Single exposure. 4-hr dermal exposure	**POD: 1770 mg/kg (LD50) -4-hr dermal LD50 values were: >10,000 mg/kg (dry); >6,400 mg/kg (moistened), and 1,770 (lowest value) – 3,540 ("as received").** n= 4 Dose= 1250, n= 4 Dose= 2500, n= 4 Dose= 5000, mg/kg	See footnotes for full summary [3]	No details on the test substance purity or composition, or the form of the "as received" test substance were provided. Except for food and water availability, no animal husbandry details were reported.	Mortality-Mortality, and signs of toxicity related to death-Renal/Kidney-Gross pathology-Gastrointestinal-Gross pathology-Hepatic/Liver-Gross pathology-Lung/Respiratory-Gross pathology-Immune/Hematological-Gross pathology (spleen)-Neurological/Behavioral-clinical observations (tremors)-Other (please specify below) (Endocrine)-Gross pathology - adrenals; Low	Union Carbide, 1993 5895928
No guideline or adherence to GLP conditions was reported. Rat-Wistar - [rat]-Male	Inhalation-Aerosol-Duration: Acute (less than or equal to 24 hr)-8 Single exposure. Rats were exposed to a single 4 or 8 hour period.	**POD: mg/m^3 (Not stated) -** n= 6 Dose= 25,000, n= 6 Dose= 48,000, n= 6 Dose= 52,000, mg/m^3	In an acute inhalation toxicity study, male Wistar rats (6/group) were exposed, whole body, to atomized octamethylcyclotetrasiloxane (D4; purity not reported), also referred to as volatile silicone 7207, at 25,000 or 48,000 mg/m3 for 4 hours, or to 52,000 mg/m3 for 8 hrs (equivalent to 2,060, 3,956 to 4,286 ppm). Aerosol droplets had a mean diameter of 2 microns. Animals were observed for 14 days for mortality and clinical signs of toxicity. Body weights were measured and gross pathology was conducted on both dead and surviving rats. Death occurred in 0/6, 1/6, and 5/6 animals at 25,000, 48,000, and 52,000 mg/m3, respectively, all within one day of exposure. Clinical signs associated with death included sluggishness, wet fur, poor coordination, difficulty breathing, prostrate, closed eyes, and being unresponsive to noise. No clinical signs were observed in animals exposed to 25,000 mg/m3. Surviving animals gained weight. Gross pathology in two animals that died showed hemorrhaged lung lobes. No gross lesions were noted in survivors. No LC50 value was reported by the study authors. It was specified that a concentration of 25,000 mg/m3 was well tolerated.	Respiratory rates were not measured and the test substance as an aerosol is a known respiratory irritant. Animals exhibited difficulty breathing introducing uncertainty of the actual inhaled concentrations. The particle GSD was not reported. There test substance purity and source were not specified. Limited test model and animal husbandry details were provided.	Mortality-Mortality, and signs of toxicity related to death-Lung/Respiratory-Gross pathology-Neurological/Behavioral-clinical observations (tremors); Low	Union Carbide, 1993 5895928

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Octamethylcyclotetrasiloxane (D4)- Parent compound - Acute (less than or equal to 24 hr)

Guideline and Animal Species, Strain, Sex	Exposure Route and Exposure Duration	Study-wide POD and Dose/ Concentration(s)	Summary	Major Limitations	Principal Target Organs/Systems and OQD*	HERO ID
No guideline or adherence to GLP conditions was reported. Rat-Wistar - [rat]-Male	Inhalation-Vapor-Duration: Acute (less than or equal to 24 hr)-8 Single exposure. Single 8-hour exposure.	**POD: mg/m^3 (Other) -** n= 6 Dose= 41600, mg/m^3	In an acute inhalation toxicity study, male Wistar rats (n = 6) were exposed, whole body, to octamethylcyclotetrasiloxane (D4; purity not reported) as a "substantially saturated vapor" (41.6 mg/L) prepared by spreading 50 grams of the test chemical was spread over a 200 cm2 area on a shallow tray that was placed in a sealed chamber for a minimum of 16 hrs. The air was then introduced to rats in a cage designed to minimize vapor loss. Rats were exposed for 8 hours. The exposure atmosphere was not analytically examined. It is expected that at the concentration tested (equivalent to 3,429 ppm), animals would also be exposed to the aerosolized test substance, and that condensation on fur would occur resulting in substantial uncertainty regarding the accuracy of the actual exposure concentration. No deaths occurred, some loss of coordination and slow irregular breathing occurred after 7 hours of exposure, but rats returned to normal within 1 day. Animals gained weight. An LC50 was not reported.	Respiratory rates were not measured and the test substance at high concentrations and as an aerosol is a known respiratory irritant. Animals exhibited difficulty breathing introducing uncertainty about the actual inhaled concentrations. The test substance purity and source were not specified. Limited test model and animal husbandry details were provided.	Mortality-Mortality, and signs of toxicity related to death-Lung/Respiratory-Gross pathology-Neurological/Behavioral-clinical observations (tremors); Uninformative	Union Carbide, 1993 5895928
No guideline specified. The study was conducted under GLP conditions. Rat-Sprague-Dawley - [rat]-Female	Inhalation-Vapor-Duration: Acute (less than or equal to 24 hr)-6 Single exposure.	**POD: 706 ppm (in air, water, or food) (LOAEC) - Reproductive/Developmental (decreased LH, prolactin, and estradiol levels)** n= 55 Dose= 0, n= 50 Dose= 706, n= 55 Dose= 914, ppm (in air, water, or food)	See footnotes for full summary [4]	Limited parameters were evaluated in this study. The study was conducted with one exposure and was designed to evaluate levels of LH, prolactin, and estradiol up to 8 hours following termination of exposure. All animals were ovariectomized and received implants containing 17-β-estradiol; however, the content of silastic tubing containing 17-β-estradiol (4 mg/mL) was not reported.	Reproductive/Developmental-Luteinizing hormone (LH), prolactin, estradiol, and estrone levels; Medium	WIL Research, 2001 5884071

* Overall Quality Determination

[1] 5895941: In an acute inhalation lethality study, rats (6/group, strain and sex not specified) were exposed for 1 or 8 hours to substantially saturated vapor of Octamethylcyclotetrasiloxane (D4, also referred to as Silicone Y-7202) (actual concentration not reported). This substantially saturated vapor was prepared by spreading 50 grams of chemical over 200 cm^2 area on a shallow tray placed near the top of a 120-liter glass chamber. The chamber was then sealed for at least 16 hours while a fan agitated the chamber atmosphere before rats were introduced to the chamber. Rats were checked for mortality, weight changes, and clinical signs following exposure. The animals were then sacrificed and assessed for gross pathological changes. Two rats in the 8-hour exposure group died during the exposure period. None of the rats in the 1-hour exposure group perished during the study. The study authors note that the weight change for the 1-hour exposure group was 22 to 34, and for the 8-hour exposure group was 55 to 74 (units not specified). There were no clinical signs observed for the 1-hour exposure group. However, for the 8-hour exposure group it was noted that one rat exhibited salivation, pus from the nose, heavy breathing, and jumping by 2 hours; one rat exhibited poor coordination by 3 hours; two rats were prostrate by 6.3 hours; and one rat exhibited tonic spasms by 6.3 hours. From gross pathology observations, rats in the 1-hour exposure group had lungs appearing dull maroon in color, however, incidence was not reported. The rats that perished in the 8-hour exposure group displayed hemorrhaged lungs and capillary injection in intestines. Of the survivors in the 8-hour exposure group, there was some scattered focal consolidation of the lung. Gross pathology results for the animals exposed for 1 hour were not reported.No LC50 value was reported.

[2] 5895928: This PDF reports results from a collection of acute oral toxicity studies conducted using octamethylcyclotetrasiloxane (D4; purity not reported), also referred to as volatile silicone 7207, in male Wistar rats. In each experiment, rats (n = 2-5/group) were dosed with the test substance via gavage in corn oil. Mortality and clinical signs of toxicity were recorded. Animals were observed for 14 days. Those who died were grossly examined. In all studies the dose volumes were not held constant across groups, several studies used excessive dose volumes (>20 mL/kg bw), and only saw mortalities at these excessively high volumes. Excluding studies were all of the volumes were excessive, LD50 values ranged from 2.50 mg/kg to >2,000 mg/kg. Five studies reported doses in uL/kg and reported LD50 values ranging from 8.4 to 56.6 uL/kg. Using a density of 0.956 for D4, these are ~ 8.03 to 54.1 mg/kg. It appears that each experiment was conducted on a different sample of the "volatile silicone 7207" test substance. No details of the test material were provided (purity, composition), so the variation may be due to differences in the samples or batches used. In the most sensitive oral study, animals were administered either 2.5 or 10 mg/kg test substance in corn oil, where 1mL = 10 mg (equivalent to dose volumes of 250 uL and 1 mL, respectively), or 1.25, 2.5, or 5 mg/kg where 1 mL = 1 mg (equivalent to dose volumes of 1.25, 2.5, and 5 mL, respectively). In these tests, 100% of the animals dosed with 2.5 or 10 mg/kg died, and 0/4, 2/4, and 4/4 animals in the 1.25, 2.5, and 5.0 groups, respectively, died. Tremors were observed at all doses, and gross pathology in animals that died included slight petechial hemorrhages in the lings, mottled livers, gas-filled transparent stomachs, yellow, injected, gas-filled intestines, and congested kidneys and adrenals. The methods of LD50 calculations were not specified, but the LD50 was reported to be 2.50 (1.53 to 4.08) mg/kg. A few other studies that used appropriate dose volumes also identified low LD50 values (LD50 = 7.71, 12.3, 20, and 24.9). On the other hand, similarly designed studies, administering 10, 40, 160, or 640 mg/kg (at 1mL = 10 mg), or 1,000 or 2,000 mg/kg (at 1 mL = 100 mg), reported no mortalities, and animals exhibited no significant clinical signs and gross pathology revealed nothing remarkable.

[3] 5895928: In a series of 9 acute dermal toxicity studies, octamethylcyclotetrasiloxane (D4; purity and composition not reported), also referred to as volatile silicone 7207, was applied dry (2-tests), "as received" (4 tests), or moistened with saline (2 tests) to the clipped intact skin on the trunk of male rats (2-4/group) under occluded conditions for 4-hours. The tests were conducted using different lots or batches of the test substance. The doses tested were 5,000 and 10,000 mg/kg (dry), 6,400 mg/kg (moistened), and 400, 1,250, 1,600, 2,500, and 5,000 mg/kg "as received." For the two experiments where the test substance was moistened, the test area was wetted with 0.0086 mL/cm2 saline. Equivalent volumes of saline were added every 30 minutes through pinhole openings in the tape. If any liquids were used, the volume(s) applied were not reported; for some experiments, it was noted that 1mL = 0.05g or 50 mg. Animals were immobilized during the exposures. Animals were observed for 14 days. For all experiments, incidences of mortality and days to death were reported along with weight changes, and clinical signs and gross pathology (no incidences provided). In the two experiments that identified the lowest LD50 value of 1,770 mg/kg, deaths occurred in 0/4, 4/4, and 3/4 animals (study 1) and 1/4, 3/4, and 4/4 animals (study 2) at 1,250, 2,500, and 5,000 mg/kg. Most deaths occurred in less than 24 hours. No skin irritation was observed. Tremors were noted at all doses tested (including at 400 mg/kg). For all studies, gross pathological changes included lung petechial hemorrhages, mottled livers and spleens, distended gas-filled stomachs and intestines that were sometimes discolored, and speckled and congested kidneys. The reported 4-hr dermal LD50 values were: >10,000 mg/kg (dry); >6,400 mg/kg (moistened), and 1,770 (lowest value) – 3,540 ("as received").

[4] 5884071: In an inhalation study, ovariectomized female Sprague-Dawley rats with subcutaneous 17-β-estradiol implants were exposed to the test substance, D4, at target concentrations of 0, 700, and 900 ppm (n = 50/group, groups 1, 2, and 3, respectively) or 0 and 900 ppm (n = 5/group, groups 4 and 5, respectively), on one day, for 6 hours. Three days prior to the initiation of exposure, each animal had received surgically implanted silastic tubing containing 17-β-estradiol (4 mg/mL). During the study, all animals were observed twice daily for appearance, behavior, moribundity, and mortality beginning on the day of surgical implantation. Detailed physical examinations were recorded daily throughout the study. Animals were also observed for clinical signs at the completion of exposure (all animals) and within approximately 1 hour following the completion of exposure (animals not selected for 0-hour blood collection). The incision site on each animal was examined for signs of erythema, edema, and discharge. Body weights were recorded daily on the day of implantation and until euthanasia. At the completion of the 6-hour exposure, animals in groups 1 to 3 (10/group) were immediately sacrificed by decapitation (0-hour blood collection, 10/group), or at two, four, six, and eight hours following exposure (i.e., 2:00 p.m., 4:00 p.m., 6:00 p.m., 8:00 p.m., and 10:00 p.m., respectively, 10/group/time point). All animals in groups 4 and 5 (5/group) were anesthetized and sacrificed by exsanguination within 1 hour following exposure. Blood samples were collected by decapitation for groups 1, 2 and, 3 for analysis of luteinizing hormone (LH), prolactin, and estradiol levels. Blood samples were collected from the vena cava from groups 4 and 5 for analysis of estradiol and estrone.Mean measured D4 concentrations for the target exposures of 700 and 900 ppm were 706 and 914 ppm, respectively. One animal from each of the control groups (Groups 1 and 4), and one animal from the 700 and 900 ppm groups (Groups 2 and 5, respectively) was euthanized prior to scheduled sacrifice due to loss of the estradiol implant and subsequent removal from the study. No exposure-related clinical signs were observed at the completion of exposure or at one hour following termination of exposure. Other clinical findings, including hair loss on forelimbs and soft stool, were observed prior to exposure initiation. Mean body weights and body weight changes (measured beginning on the day of implant surgery until the day of exposure) in the D4-exposed groups were similar to controls. Mean body weight losses were observed in all groups (including control groups) following surgery and the study authors noted that these were not of sufficient magnitude to impact the study outcome. For blood samples collected from animals sacrificed by decapitation (groups 1-3), no statistically significant changes in LH levels (measured by radioimmunoassay, RIA) were observed. However, 4/10 animals at 700 ppm and 7/10 animals at 900 ppm sacrificed at 4 hours (LH peak) following termination of exposure had LH levels that were lower than the minimum LH level (6.9 ng/m) observed at the same time point in the corresponding controls. Statistically significant decreases in mean prolactin levels (measured by RIA) were observed at 700 and 900 ppm in animals sacrificed immediately following termination of exposure compared to controls. Mean estradiol levels (measured by chemilumescent method, 10 animals/group) were slightly decreased (not statistically significant) at 700 and 900 ppm immediately following exposure and were statistically significantly decreased at 700 and 900 ppm at 2 hours following exposure; estradiol levels were similar to control values in animals sacrificed at $\geq$4 hours following exposure. For blood samples collected from the vena cava within 1 hour following termination of exposure (groups 4 and 5), mean estradiol levels (measured by chemiluminescent method and RIA, 4 animals/group) were significantly decreased in the 900 ppm group animals compared to control levels. Mean estrone levels (measured by RIA) in blood collected by the vena cava were similar in D4-exposed and control animals; the estradiol:estrone ratio was slightly decreased at 900 ppm (not statistically significant) compared to controls. Based on the lower LH levels in animals at 700 and 900 ppm, and the requirement for LH surge for ovulation to occur, the study authors hypothesized that the reduced fertility rate observed in rats exposed to D4 by inhalation at 700 ppm on the day of proestrus in a previous study (WIL-51054, DC Study No. 8864, WIL Research Laboratories, 1999) may have been the result of a reduction in peak serum LH levels. A POD was not reported by the study authors. The LOAEC (determined by the reviewer) is 700 ppm based on decreased luteinizing hormone and prolactin levels at 700 ppm.

Octamethylcyclotetrasiloxane (D4)- Parent compound - Short-term (>1-30 days)

Guideline and Animal Species, Strain, Sex	Exposure Route and Exposure Duration	Study-wide POD and Dose/ Concentration(s)	Summary	Major Limitations	Principal Target Organs/Systems and OQD*	HERO ID
No guideline or adherence to GLP conditions was specified. Rat-Other (Hilltop Wistar)-Female	Oral-Diet-Duration: Short-term (>1-30 days)-7-7-day(s) 7 days/week 7 day(s) 7-days in diet	**POD: mg/kg (Other) -** mg/kg	In a short-term dietary inclusion study, Hilltop-Wistar female rats (number not specified) were administered octamethylcyclotetrasiloxane (D4, purity not reported), also referred to as volatile silicone 7207, at unspecified doses, via the diet for 7 consecutive days. At the end of the exposure period, body weights were measured. Liver and kidney weights were recorded and gross necropsy was performed. No additional methodological details were provided. The reported "minimum effect dosage level" (MiE) was >0.8 g/kg (>8,000 mg/kg). A Maximum no ill-effect dosage level (NIEL) was not identified. No further results were reported.	This study was limited by reporting deficiencies, including a lack of details on the test substance, test model, and exposure administration. No results were reported.	Mortality-Mortality; Low	Carnegie Mellon University, 1978 7310549
No guideline or adherence to GLP conditions was specified. Rat-Other (Hilltop Wistar)-Female	Dermal-Duration: Acute (less than or equal to 24 hr) 7 days/week 7 day(s) 7-days in diet	**POD: mL/kg (LD50) -LD50 >16.0 mL/kg** mL/kg	In an acute dermal lethality study, octamethylcyclotetrasiloxane (D4, purity not reported), also referred to as volatile silicone 7207, was applied to the clipped skin of Hilltop-Wistar female rats (number not specified), at unspecified doses, for 4 hours under occlusive conditions. Rats were immobilized during the exposure period. The study indicated that dosage levels differed by a factor of 2 in a geometric series and that liquid samples were "dosed undiluted unless toxicity was too great to determine without dilution." Animals were observed for 14 days. No additional methodological details were provided. The reported 4-hr dermal LD50 was >16.0 mL/kg.	This study was limited by reporting deficiencies, including a lack of details on the test substance, test model, and exposure administration.	Mortality-Mortality; Uninformative	Carnegie Mellon University, 1978 7310549
No guideline was specified; GLP compliant. Rat-Other (Cpb;Wu Wistar)-Both	Inhalation-Aerosol-Duration: Short-term (>1-30 days)-7-6-4-week(s) 6 hours/day 7 days/week 4 week(s) Animals were exposed daily, 6 hrs/day for 4 weeks	**POD: 1004 mg/m^3 (NOAEC) - Increased absolute and relative liver weights** n= 30 Dose= 0, n= 20 Dose= 201, n= 20 Dose= 1004, n= 30 Dose= 5074, mg/m^3	See footnotes for full summary [1]	The intended exposure was to the aerosolized test substance, but no particles were generated.	Hepatic/Liver-Clinical chemistry (total protein, albumin, ALP, GPT, ALT, AST, glucose, bilirubin), organ weight, gross pathology, histopathology; Medium	Civo Institute Tno, nan 7310568

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Octamethylcyclotetrasiloxane (D4)- Parent compound - Short-term (>1-30 days)

Guideline and Animal Species, Strain, Sex	Exposure Route and Exposure Duration	Study-wide POD and Dose/ Concentration(s)	Summary	Major Limitations	Principal Target Organs/Systems and OQD*	HERO ID
The authors cite: 58 FR 28511 (May 14, 1993) [OPPTS-82040; FRL-4182-1] Health and Safety Data Reporting; 40 CFR Part 716 ITC 30-Listed Siloxanes and Silicones Mouse-Not specified-Male	Oral-Diet-Duration: Short-term (>1-30 days)-48-hour(s) 48 hour(s) Results table title suggest animals were treated for 48 hours. No other details are provided. (in vivo carbon clearance assay)	**POD: Not provided (Other) -** Not provided	To study effects of oral administration of octamethylcyclotetrasiloxane (D4) on the reticuloendothelial system (RES) authors performed an interferon assay and in vivo carbon clearance assay.Carbon Clearance: Mice (sex, strain, or number/group were not reported) were either left untreated or pretreated via oral route (gavage or diet) with D4 (dose or vehicle not reported) 48 hours prior to inoculation. Mice were inoculated via the tail vein with a carbon ink suspension. Blood was collected via orbital bleed at 5-minute intervals until clearance was complete. Optical density of water-lysed blood was determined by spectrophotometry (590 nm). Clearance was expressed as time to reach 50% of initial OD590nm.Time for 50% clearance was increased in the D4 pretreated mice (6.1 ± 0.9 minutes in untreated group, 13.1 ± 2.0 minutes in oral gavage group, and 12.0 ± 2.5 minutes in feed group). As no statistical analysis was conducted and author provided data is not sufficient to conduct an independent statistical analysis, this study is marked uninformative, and no toxicity values could be determined.	The study does not report the dose used or number of animals tested.	Immune/Hematological-Reticuloendothelial system (RES): Endotoxin-induced serum interferon titer and in vivo carbon clearance assay; Uninformative	Dow Corning, 1975 5883902
The authors cite: 58 FR 28511 (May 14, 1993) [OPPTS-82040; FRL-4182-1] Health and Safety Data Reporting; 40 CFR Part 716 ITC 30-Listed Siloxanes and Silicones Mouse-Not specified-Male	Oral-Gavage-Duration: Short-term (>1-30 days)-48-hour(s) 48 hour(s) Results table title suggest animals were treated for 48 hours. No other details are provided. (in vivo carbon clearance assay)	**POD: Not provided (Other) -** Not provided	To study effects of oral administration of octamethylcyclotetrasiloxane (D4) on the reticuloendothelial system (RES) authors performed an interferon assay and in vivo carbon clearance assay.Carbon Clearance: Mice (sex, strain, or number/group were not reported) were either left untreated or pretreated via oral route (gavage or diet) with D4 (dose or vehicle not reported) 48 hours prior to inoculation. Mice were inoculated via the tail vein with a carbon ink suspension. Blood was collected via orbital bleed at 5-minute intervals until clearance was complete. Optical density of water-lysed blood was determined by spectrophotometry (590 nm). Clearance was expressed as time to reach 50% of initial OD590nm.Time for 50% clearance was increased in the D4 pretreated mice (6.1 ± 0.9 minutes in untreated group, 13.1 ± 2.0 minutes in oral gavage group, and 12.0 ± 2.5 minutes in feed group). As no statistical analysis was conducted and author provided data is not sufficient to conduct an independent statistical analysis, this study is marked uninformative, and no toxicity values could be determined.	The study does not report the dose used or number of animals tested.	Immune/Hematological-Reticuloendothelial system (RES): Endotoxin-induced serum interferon titer and in vivo carbon clearance assay; Uninformative	Dow Corning, 1975 5883902

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Octamethylcyclotetrasiloxane (D4)- Parent compound - Short-term (>1-30 days)

Guideline and Animal Species, Strain, Sex	Exposure Route and Exposure Duration	Study-wide POD and Dose/ Concentration(s)	Summary	Major Limitations	Principal Target Organs/Systems and OQD*	HERO ID
No guidelines or statements of adherence to GLP were provided. GLP compliance statement indicates it was not conducted in compliance. Rat-Sprague-Dawley - [rat]-Both	Oral-Gavage-Duration: Short-term (>1-30 days)-7-2-week(s) 7 days/week 2 week(s) Limited details, it is unclear if animals were gavaged daily, or 5 days/week	**POD: 1600 mg/kg (LOAEL) -Liver effects: increased liver weights and induced liver enzymes.** n= 10 Dose= 0, n= 10 Dose= 1600, mg/kg	Groups of Sprague Dawley rats (5/sex/dose) were administered D4 via gavage at doses of 0 (tap water) and 1600 mg/kg-day, for 14 days. Animals were observed for mortality, clinical signs, and food and water intake. Body weights were measured. At sacrifice, organs (unspecified) were weighed, and animals were grossly examined. Histopathology of the liver, lungs, and lymph nodes, and electron microscopy of unspecified tissues were performed (limited methodological details were provided). Enzymes (7-ethoxycoumarin deethylase [EOD]; 7-ethoxyresorufin deethylase [EOR]; aldrin epoxidase [ALD]; epoxide hydrolase [EH]; Glutathione-s-transferase [GST]; and UDP-Glucuronyl transferase GLU-T) from hepatic microsomal and cytosolic fractions were measured. Mortality, clinical signs, and body weight results were not reported. Both absolute and relative liver weights were purportedly increased in both sexes, up to 22% in males and 47% in females. Associated hypertrophy of liver cells and loss of glycogen content in treated animals were observed. Histopathological results for other tissues were not reported. In general, all liver enzymes in males except ALD were elevated in treated animals, increases in EOD, EH, and GST were presumably statistically significant; however, no statistical methods were reported. No author-provided toxicity values were provided. A LOAEL of 1600 (presumed) mg/kg-day was determined based on evidence of liver effects; however, there is uncertainty in the reported dose.	The study did not clearly report the frequency of the gavages. Data for several endpoints were not reported.	Hepatic/Liver-Absolute and relative liver weights (inhalation study); liver histopathology and liver enzymes (7-ethoxycoumarin deethylase [EOD]; 7-ethoxyresorufin deethylase [EOR]; aldrin epoxidase [ALD]; epoxide hydrolase [EH]; Glutathione-s-transferase [GST]; and UDP-Glucuronyl transferase [GLU-T]); oral study; Low	Dow Corning, 2001 5884201
The study was conducted under GLP conditions. Rat-Fischer 344 - [rat]-Female	Inhalation-Vapor-Duration: Short-term (>1-30 days)-6-5-day(s) 6 hours/day 5 day(s) Animals were exposed for 5 consecutive days.	**POD: 68 ppm (in air, water, or food) (NOAEL) - Increased relative liver weight** n= 10 Dose= 0, n= 10 Dose= 1, n= 10 Dose= 7, n= 10 Dose= 27.5, n= 10 Dose= 68, n= 10 Dose= 142.8, n= 10 Dose= 298.3, n= 10 Dose= 488.4, ppm (in air, water, or food)	See footnotes for full summary [2]	There were no major limitations with this study.	Other (please specify below) (Clinical signs)-Clinical signs of toxicity-Nutritional/Metabolic-Body weight and food intake-Hepatic/Liver-Liver weight and microsomal enzyme induction (CYP2B1/2 activity and protein content); High	Dow Corning, 1999 5884340

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Octamethylcyclotetrasiloxane (D4)- Parent compound - Short-term (>1-30 days)

Guideline and Animal Species, Strain, Sex	Exposure Route and Exposure Duration	Study-wide POD and Dose/ Concentration(s)	Summary	Major Limitations	Principal Target Organs/Systems and OQD*	HERO ID
Conducted as a pilot study; the study report indicated that the exposure regimen (5 days/week) is based on a typical occupational exposure scenario for workers and that the study protocol fulfilled the requirements of OECD TG 412. The study was conducted under GLP conditions with the following exceptions: 1) test article characterization and method development experiments were conducted using the best available technology; 2) the dosing solution concentrations of the intra-assay positive control (phenobarbital) were prepared by dissolving a mass of material in a known volume of saline and were not analytically determined; 3) software used for statistical analysis was not validated although some analyses (i.e., PROD enzyme measurements) were verified using SAS; 4) acquisition software used for body weights, randomization, and clinical signs was not validated;	Inhalation-Vapor-Duration: Short-term (>1-30 days)-5-6-28-day(s) 6 hours/day 5 days/week 28 day(s)	**POD: 70 ppm (in air, water, or food) (Other) -Liver (increases in liver weight; changes in liver enzyme activity and protein levels)** n= 24 Dose= 0, n= 24 Dose= 70, n= 24 Dose= 700, ppm (in air, water, or food)	See footnotes for full summary [3]	ThGroup sizes were small (3/sex/group) for some exposure durations/interim sacrifice time points.	Hepatic/Liver-Liver weight (absolute, relative-to-body weight and relative-to-brain weight); concentrations of total P450 and CYP4A, activities of selected P450 enzymes (7-ethoxycoumarin-O-deethylase [ECOD], 7-ethoxyresorufin O-deethylase [EROD], 7-pentoxyresorufin O-depentylase [PROD]), and NADPH-cytochrome c reductase activity in hepatic microsomal preparations; concentrations of cytosolic alpha-glutathione-S-transferase (alpha-GST).-Nutritional/Metabolic-Body weight; High	Dow Corning, 1996 5884497

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Octamethylcyclotetrasiloxane (D4)- Parent compound - Short-term (>1-30 days)

Guideline and Animal Species, Strain, Sex	Exposure Route and Exposure Duration	Study-wide POD and Dose/ Concentration(s)	Summary	Major Limitations	Principal Target Organs/Systems and OQD*	HERO ID
The authors report adherence to 58 FR 28511 (May 14, 1993) [OPPTS-82040; FRL-4182-1], Health and Safety Data Reporting; 40 CFR Part 716 ITC 30-Listed Siloxanes and Silicones Rat-Sprague-Dawley - [rat]- Both	Oral-Diet-Duration: Short-term (>1-30 days)-3-day(s) 3 day(s) Study B: Palatability study with emulsified D4	**POD: 2.5 % (in water or food) (LOAEL) - Decreased water consumption** n= 3 Dose= 0, n= 3 Dose= 1.25, n= 3 Dose= 2.5, % (in water or food)	See footnotes for full summary [4]	The test substance was found to be unpalatable in all vehicles. Many important aspects of the experimental design (test substance purity, storage conditions, animal housing conditions) are omitted.	Nutritional/Metabolic-Body weights, body weight gain, food consumption, Gross necropsy (body fat reserves); Low	Dow Corning, 1988 5885339
The authors report adherence to 58 FR 28511 (May 14, 1993) [OPPTS-82040; FRL-4182-1], Health and Safety Data Reporting; 40 CFR Part 716 ITC 30-Listed Siloxanes and Silicones Rat-Sprague-Dawley - [rat]- Both	Oral-Diet-Duration: Short-term (>1-30 days)-72-hour(s) 72 hour(s) Study C: Palatability study with D4 (and D5) mixed in liquid diet	**POD: % (in water or food) (Other) -** n= 4 Dose= 0, n= 4 Dose= 2.5, % (in water or food)	In a palatability study, rats (2/sex/group, strain not specified) were exposed to 0 or 2.5% octamethylcylcotetrasiloxane (D4) dissolved in a liquid diet (consisting of proteins, fats and carbohydrates, with the exact formulation not reported) and fed the diet ad libitum for 3 days. Food consumption and body weight gains over 3 days were evaluated. This study additionally included a group exposed to 2.5% D5, and the data for those groups of animals are not extracted in this summary.Weight loss was observed in both control animals (fed only liquid diet) and exposed animals. Control females lost and average of 11 grams, and males and average of 20 grams over 3 days. Animals in the D4 groups lost substantially more weight (females 38 grams and males 58 grams). Starting body weights were not provided. This decrease in body weight is likely due to the substantial decrease in liquid diet consumed. Females in the D4 group consumed 60% less liquid and males 48% less liquid over 3 days. No author reported toxicity values are available, and no toxicity values could be determined due to this study being uninformative due to severe palatability issues.	The test substance was found to have severely low palatability, causing the study to be uninformative . Many important aspects of the experimental design (test substance purity, storage conditions, animal housing conditions) are omitted.	Nutritional/Metabolic-Body weights, body weight gain, food consumption, Gross necropsy (body fat reserves); Uninformative	Dow Corning, 1988 5885339

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Octamethylcyclotetrasiloxane (D4)- Parent compound - Short-term (>1-30 days)

Guideline and Animal Species, Strain, Sex	Exposure Route and Exposure Duration	Study-wide POD and Dose/ Concentration(s)	Summary	Major Limitations	Principal Target Organs/Systems and OQD*	HERO ID
The authors report adherence to 58 FR 28511 (May 14, 1993) [OPPTS-82040; FRL-4182-1], Health and Safety Data Reporting; 40 CFR Part 716 ITC 30-Listed Siloxanes and Silicones Rat-Sprague-Dawley - [rat]-Both	Oral-Diet-Duration: Short-term (>1-30 days)-12-day(s) 12 day(s) Study E: Palatability study with microencapsulated D4	**POD: % (in water or food) (Other) -** n= 2 Dose= 0, n= 6 Dose= 3.2, % (in water or food)	In a palatability study, Sprague-Dawley rats (3/sex for exposed animals, 1/sex for controls) were exposed to 0 or 3.1-3.2% octamethylcylcotetrasiloxane (D4) through microcapsules (consisting of different formulations of modified cornstarch and gelatin) mixed in feed for 12 consecutive days. A placebo group containing 6.5% empty microcapsules was also included. Animals were monitored daily for mortality and clinical signs of toxicity, and food consumption and body weights were measured every 4 days.No mortality was observed over the course of the study and no clinical signs of toxicity were reported. Body weight loss and decreased food consumption were observed in animals exposed to D4, but no author reported statistics could be determined due to only having 1 animal/sex in control groups. Male and female body weight gains in the control groups were 79 and 35 grams, respectively. In the exposed groups, males lost an average of 22 grams and females lost an average of 18 grams. Average food intake reflected these decreases with males consuming 48% less food and females consuming 43% less. No author reported toxicity values are provided, and the study is uninformative due to severe palatability issues, so no toxicity values were derived.	The test substance was found to have significant issues with palatability, causing the study to be rated as uninformative. Many important aspects of the experimental design (test substance purity, storage conditions, animal housing conditions) are omitted and only 1 animal/sex was included in controls.	Nutritional/Metabolic-Body weights, body weight gain, food consumption, Gross necropsy (body fat reserves); Uninformative	Dow Corning, 1988 5885339

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Octamethylcyclotetrasiloxane (D4)- Parent compound - Short-term (>1-30 days)

Guideline and Animal Species, Strain, Sex	Exposure Route and Exposure Duration	Study-wide POD and Dose/ Concentration(s)	Summary	Major Limitations	Principal Target Organs/Systems and OQD*	HERO ID
The authors report adherence to 58 FR 28511 (May 14, 1993) [OPPTS-82040; FRL-4182-1], Health and Safety Data Reporting; 40 CFR Part 716 ITC 30-Listed Siloxanes and Silicones Rat-Sprague-Dawley - [rat]-Both	Oral-Diet-Duration: Short-term (>1-30 days)-28-day(s) 28 day(s) 28 day feeding study with microencapsulated D4	**POD: % (in water or food) (Other) -** n= 10 Dose= 0, n= 10 Dose= 2.1, % (in water or food)	In a 28-day feeding study, young and adult Sprague-Dawley rats (5/sex/group) were treated with 0% or 2.1% octamethylcylcotetrasiloxane (D4) via microencapsulated fluid dissolved in feed (ad libitum) for 28 days. Exact age of the animals was not reported. Animals were monitored daily for mortality and clinical signs of toxicity and body weights and food consumption were measured at the beginning of the study and every 4 days. Food that was not consumed or spilled out of the cage was also measured. At the end of the 28-day exposure period, animals were euthanized, and a gross necropsy was performed. No mortality was observed over the course of the study. Observed clinical signs of toxicity included signs of stress, rough fur and emaciated appearance in both young and adult males and females at 2.1% (incidence data not reported). Significantly decreased body weights and body weight gains were observed in animals exposed to 2.1% D4. Significantly decreased body weight was seen at day 4 and continued to be decreased throughout the study. Mean terminal body weights were significantly decreased by 25%, 26%, 23%, 32% in young male, adult male, young female and adult females respectively compared with control. Animals exposed to 2.1% D4 demonstrated significantly decreased average food consumption (by 24%, 29%, 25% and 32% in young male, adult male, young female and adult females respectively). Gross necropsy indicated that exposed to 2.1% D4 in both age and sex groups depleted body fat reserves and water cecal contents. Some males additionally displayed gross testicular pathology.No author reported toxicity values are available. Due to the substantial decrease in food intake in exposed animals, a NOAEL/LOAEL were not determined.	The test substance was found to have significant issues with palatability, as well as potential loss of the test substance through volatility. This study is rated as uninformative due to severe issues with palatability.	Nutritional/Metabolic-Body weights, body weight gain, food consumption, Gross necropsy (body fat reserves); Uninformative	Dow Corning, 1988 5885339

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Octamethylcyclotetrasiloxane (D4)- Parent compound - Short-term (>1-30 days)

Guideline and Animal Species, Strain, Sex	Exposure Route and Exposure Duration	Study-wide POD and Dose/ Concentration(s)	Summary	Major Limitations	Principal Target Organs/Systems and OQD*	HERO ID
Adherence to a guideline or GLP was not specified. Rat-Sprague-Dawley - [rat]-Both	Inhalation-Vapor-Duration: Short-term (>1-30 days)-7-6-14-day(s) 6 hours/day 7 days/week 14 day(s)	**POD: 854 ppm (in air, water, or food) (LOAEL) -Specific effect = Reductions in body weight and food consumption** n= 10 Dose= 0, n= 10 Dose= 854, ppm (in air, water, or food)	In a limited 14-day feasibility inhalation toxicity study, Sprague-Dawley rats (5 young rats/sex/group), were exposed whole body to octamethylcyclotetrasiloxane (D4) (purity not reported) at mean analytical concentrations of 0, or 854 ppm for 6 hours/day for 14 continuous days. Animals were observed daily during the exposure period and post-exposure period (1 week) for clinical signs of toxicity. Body weights and food consumption were measured every four days during the exposure period and post-exposure period. No treatment-related clinical signs of toxicity were observed in any of the animals, treated or untreated. Young males exhibited statistically significant reductions in body weight during both the exposure period and post-exposure period; however, the magnitudes of change were generally <10%. On treatment day 12, the reduction, compared with controls was 9.7%. Female body weights remained comparable to controls. Food consumption was significantly reduced by 13-21% in males and 12-20% in females during the exposure period. No author-reported toxicity values were provided. Based on the available data, a LOAEC of 854 ppm, the only concentration used in this study, was identified based on significantly reduced body weight and food consumption among exposed rats.	Missing information on the test substance purity results in some uncertainties. This was a focused study aimed at assessing the impacts of D4 exposure on food consumption and body weight. Therefore, it was limited and had no information on other relevant systemic endpoints.	Nutritional/Metabolic-Food consumption, body weight, body weight gain; Medium	Dow Corning, 1988 5885365

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Octamethylcyclotetrasiloxane (D4)- Parent compound - Short-term (>1-30 days)

Guideline and Animal Species, Strain, Sex	Exposure Route and Exposure Duration	Study-wide POD and Dose/ Concentration(s)	Summary	Major Limitations	Principal Target Organs/Systems and OQD*	HERO ID
Adherence to a guideline or GLP was not specified. Rat-Sprague-Dawley - [rat]-Both	Inhalation-Vapor-Duration: Short-term (>1-30 days)-7-6-14-day(s) 6 hours/day 7 days/week 14 day(s)	**POD: 854 ppm (in air, water, or food) (LOAEL) -Specific effect = Reductions in body weight and food consumption** n= 10 Dose= 0, n= 10 Dose= 854, ppm (in air, water, or food)	In a limited 14-day feasibility inhalation toxicity study, Sprague-Dawley rats (5 adult rats/sex/group), were exposed whole body to octamethylcyclotetrasiloxane (D4) (purity not reported) at mean analytical concentrations of 0, or 854 ppm for 6 hours/day for 14 continuous days. Animals were observed daily during the exposure period and post-exposure period (1 week) for clinical signs of toxicity. Body weights and food consumption were measured every four days during the exposure period and post-exposure period. No treatment-related clinical signs of toxicity were observed in any of the animals, treated or untreated. Female rats exhibited statistically significant reductions in body weight during both the exposure period and post-exposure periods; however, the magnitudes of change reached 10%, relative to controls on exposure day 12, but was <10% at all other timepoints. During treatment there was an overall loss in weight gain. Food consumption was significantly reduced by 16% in males during exposure days 8-12 and was reduced by 29-37% in females throughout the exposure period. No author-reported toxicity values were provided. Based on the available data, a LOAEC of 854 ppm, the only concentration used in this study, was identified based on significantly reduced body weight and food consumption among exposed rats.	Missing information on the test substance purity results in some uncertainties. This was a focused study aimed at assessing the impacts of D4 exposure on food consumption and body weight. Therefore, it was limited and had no information on other relevant systemic endpoints.	Nutritional/Metabolic-Food consumption, body weight, body weight gain; Medium	Dow Corning, 1988 5885365
The study was GLP compliant. Although not explicitly stated, study design agreed with OECD guideline 412. Rat-Fischer 344 - [rat]-Both	Inhalation-Vapor-Duration: Short-term (>1-30 days)-5-6-28-day(s) 6 hours/day 5 days/week 28 day(s) Animals exposed 6 hours/day, 5 days/week for 28 days	**POD: 56.7 ppm (in air, water, or food) (NOAEC) - Increased relative liver weights in female rats** n= 15 Dose= 0, n= 15 Dose= 7, n= 15 Dose= 20.2, n= 15 Dose= 56.7, n= 15 Dose= 178.1, n= 15 Dose= 529.5, ppm (in air, water, or food)	See footnotes for full summary [5]	No major limitations.	Hepatic/Liver-Liver weight, histopathology and serum chemistry parameters (alkaline phosphatase (AP), blood urea nitrogen (BUN), aspartate aminotransferase (AST), alanine aminotransferase (ALT), total bilirubin, total cholesterol, creatinine, total protein, albumin (A), globulin (G), gamma glutamyl transpeptidase, triglycerides and chloride); High	Dow Corning, 1997 5887598

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Octamethylcyclotetrasiloxane (D4)- Parent compound - Short-term (>1-30 days)

Guideline and Animal Species, Strain, Sex	Exposure Route and Exposure Duration	Study-wide POD and Dose/ Concentration(s)	Summary	Major Limitations	Principal Target Organs/Systems and OQD*	HERO ID
The study was GLP compliant; authors did not report which, if any guidelines were adhered to. Rat-Fischer 344 - [rat]-Both	Inhalation-Vapor-Duration: Short-term (>1-30 days)-5-6-28-day(s) 6 hours/day 5 days/week 28 day(s) Animals exposed 6 hours/day, 5 days/week for 28 days	**POD: 529.5 ppm (in air, water, or food) (NOAEC) -No effects observed** n= 10 Dose= 0, n= 10 Dose= 7, n= 10 Dose= 20.2, n= 10 Dose= 56.7, n= 10 Dose= 178.1, n= 10 Dose= 529.5, ppm (in air, water, or food)	As part of a larger study, independent groups of Fisher 344 rats (10/sex/group) designated for immunological tests were exposed to 0, 7, 20, 60, 180 and 540 ppm of octamethylcyclotetrasiloxane (D4) via whole-body inhalation 6 hours/day, 5 days/week for 28 days plus an additional two consecutive days prior to sacrifice. The average analytical concentrations were 0, 7.0, 20.2, 56.7, 178.1, and 529.5 ppm, respectively. Animals were observed for clinical signs (respiratory, dermal, behavioral, nasal, or ocular changes). Animals were immunized via an i.v. injection of 2 x 10e8 sheep red blood cells (sRBCs) in 1 ml 4 hours prior to sacrifice. Blood was collected for the determination of anti-sRBC IgM antibodies (ELISA) and spleens were removed for an AFC assay. Positive control groups (n=4/sex) were included that received CYP injections.No significant differences in clinical observation were seen compared with controls. No significant changes in immune system function (anti-sRBC IgM antibodies and AFC/spleen or AFC/10e6 splenocytes) related to exposure were observed. Positive controls gave the expected immunosuppressive responses. A NOAEC of 529.5 ppm was determined based on a lack of immunological effects.	No major limitations.	Immune/Hematological-Thymus weight; gross observations;Hematology (RBC count, packed cell volume, hemoglobin, hematocrit, mean corpuscular volume (MCV), mean corpuscular content (MCHC), mean corpuscular hemoglobin (MCH), platelet count, reticulocyte count, total and differential white blood cell count (WBC), spleen weight and histology on spleen, lymph nodes, spleen, thymus; Humoral reponse (IgM formation response to sRBC and AFC assay); High	Dow Corning, 1997 5887598

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Octamethylcyclotetrasiloxane (D4)- Parent compound - Short-term (>1-30 days)

Guideline and Animal Species, Strain, Sex	Exposure Route and Exposure Duration	Study-wide POD and Dose/ Concentration(s)	Summary	Major Limitations	Principal Target Organs/Systems and OQD*	HERO ID
Conducted as a pilot study; the study report indicated that the exposure regimen (5 days/week) is based on OECD TG 412. The study was conducted under GLP conditions with exceptions (p. 8 of the study report). Rat-Fischer 344 - [rat]-Both	Inhalation-Vapor-Duration: Short-term (>1-30 days)-5-6-28-day(s) 6 hours/day 5 days/week 28 day(s)	**POD: 70 ppm (in air, water, or food) (Other) -Liver (changes in liver enzyme activity and protein levels)** n= 48 Dose= 0, n= 48 Dose= 70, n= 48 Dose= 700, ppm (in air, water, or food)	See footnotes for full summary [6]	There was incomplete reporting of some animal husbandry conditions (e.g., age/life stage of animals used in the study; parity of animals used in the study) and group sizes were small (3/sex/group) for some exposure durations/interim sacrifice time points. Respiratory rates were not measured and there is potential for respiratory irritation for this test substance.	Hepatic/Liver-Liver weight (absolute and relative-to-body weight); total P450 concentrations, activities of selected enzymes (NADPH-cytochrome c reductase, 7-ethoxycoumarin-O-deethylase [ECOD]; 7-ethoxyresorufin O-deethylase [EROD]; 7-pentoxyresorufin O-depentylase [PROD]; 6-beta-hydroxylation of testosterone; 11- and 12-hydroxylation of lauric acid; epoxide hydrolase activity toward cis-stilbene oxide; UDP-glucuronosyltransferase [UDPGT] activity toward chloramphenicol or para-nitrophenol), and cytochrome P450 protein levels (cytochrome P450's CYP2B1/2, CYP3A1/2, CYP4A) were determined in hepatic microsomal preparations. alpha-Glutathione-S-transferase [alpha-GST]) protein levels in hepatic cytosol were also measured. Hepatic epoxide hydrolase mRNA and protein levels were determined. The enzyme assays performed were considered relatively specific for CYP1A1/2, CYP2B1/2, CYP3A1/2, CYP4A, and CYP2E1.; Medium	Dow Corning, 1996 5887837

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Octamethylcyclotetrasiloxane (D4)- Parent compound - Short-term (>1-30 days)

Guideline and Animal Species, Strain, Sex	Exposure Route and Exposure Duration	Study-wide POD and Dose/ Concentration(s)	Summary	Major Limitations	Principal Target Organs/Systems and OQD*	HERO ID
Study authors note that the methods for this study adhered to the EPA Toxic Substances Control Act Test Guidelines, part 798.2650 Health Effects Testing Guidelines "Oral Toxicity", published on September 27, 1985. However, the authors note that Section (e), Test Procedure, of the above guidelines was modified for this study by the Dow Corning Corporation. The study authors also note that this study was conducted in accordance with the EPA Toxic Substances Control Act; Good Laboratory Practices Regulations; 40 CFR, Part 792, Published August 17, 1989. Rabbit-New Zealand White - [rabbit]-Female	Oral-Gavage-Duration: Short-term (>1-30 days)-7-14-day(s) 7 days/week 14 day(s)	**POD: mg/kg-bw/day (Other) -** n= 6 Dose= 0, n= 6 Dose= 500, n= 6 Dose= 1000, mg/kg-bw/day	See footnotes for full summary [7]	Significant palatability issues resulting in decreased food consumption and body weights were confounding factors in this study. Minor limitations include insufficient details on animal age, missing statistical tests, uncertainties in the dose (e.g. animals were dosed based on weight and were only weighed once per week), uncertainties in the chemical concentrations of the dosing solutions (concentrations were not analytically confirmed), insufficient details on clinical signs, and insufficient details on food consumption prior to the initiation of the study.	Hepatic/Liver-liver weight, liver necropsy findings-Nutritional/Metabolic-body weight, food consumption-Other (please specify below) (General gross necropsy)-gross necropsy findings; Uninformative	Dow Corning, 1992 5897286

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Octamethylcyclotetrasiloxane (D4)- Parent compound - Short-term (>1-30 days)

Guideline and Animal Species, Strain, Sex	Exposure Route and Exposure Duration	Study-wide POD and Dose/ Concentration(s)	Summary	Major Limitations	Principal Target Organs/Systems and OQD*	HERO ID
This study was conducted in accordance with the EPA Good Laboratory Practice (GLP) Standards (Federal Register, Vol. 40, Part 792, August 17, 1989). No guideline was reported, but the study is similar to a 28-day repeated dose study. Rat-Crj: CD(SD) - [rat]-Male	Oral-Gavage-Duration: Short-term (>1-30 days)-7-14-day(s) 7 days/week 14 day(s)	**POD: 1600 mg/kg-bw/day (LOAEL) -Increased absolute and relative liver weights, hepatocyte inflammation and vacuolation, and increased total number of cells per liver.** n= 10 Dose= 0, n= 10 Dose= 1600, mg/kg-bw/day	See footnotes for full summary [8]	This was a focused study aimed at unveiling the mechanism of hepatomegaly previously observed in rats exposed to D4.	Hepatic/Liver-Liver weight (absolute and relative); liver histopathological changes; liver morphometrics (total cells in liver, number of cells/mm^3, hepatocyte profile diameter (centrilobular, midzonal, and peripherolobular))-Mortality-Survival; High	Dow Corning, 1992 5897618
This study was conducted in accordance with the Food and Drug Administration and Good Laboratory Practice Regulations 21 CFR Part 58. Rat-Sprague-Dawley - [rat]-Male	Oral-Gavage-Duration: Short-term (>1-30 days)-7-14-day(s) 7 days/week 14 day(s)	**POD: 1600 mg/kg-bw/day (NOAEL) -Absence of treatment-related effects on body weight and clinical signs.** n= 20 Dose= 0, n= 20 Dose= 1600, mg/kg-bw/day	In a subchronic, repeated dose oral toxicity study, male Sprague-Dawley rats (10/group) were exposed via gavage in 0.5% methylcellulose in water to Octamethylcyclotetrasiloxane (D4; purity = 96.5%) at doses of 0 or 1600 mg/kg/day for 2 weeks. After the exposure period one set of 10 animals were sacrificed and a second set of 10 animals were sacrificed daily in groups of 1-2 for ~5 days. The rats were weighed one day prior to the study, the first day of dosing, weekly throughout the exposure period, and immediately prior to sacrifice. Animals were observed daily during the exposure period for clinical signs of toxicity. Mean body weights were similar between the control and treated groups. Neither control nor treated animals exhibited any notable clinical signs during the exposure period. No author-reported toxicity values were provided. Based on the data presented in the study, a NOAEL of 1600 mg/kg/day was identified for male Sprague-Dawley rats based on an absence of treatment-related effects on body weight and clinical signs.	Major limitations included missing important information (age of animals, some animal husbandry conditions) and poor labeling of the body weight data tables (unclear which animals belong to Groups I, II, III, and IV).	Nutritional/Metabolic-Body weight; Medium	Dow Corning, 1991 5897627

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Octamethylcyclotetrasiloxane (D4)- Parent compound - Short-term (>1-30 days)

Guideline and Animal Species, Strain, Sex	Exposure Route and Exposure Duration	Study-wide POD and Dose/ Concentration(s)	Summary	Major Limitations	Principal Target Organs/Systems and OQD*	HERO ID
Food and Drug Administration; Good Laboratory Practice Regulations 21 CFR Part 58 Friday September 4, 1987 Rat-Other (Charles River CD (Sprague-Dawley))-Both	Oral-Gavage-Duration: Short-term (>1-30 days)-5-2-week(s) 5 days/week 2 week(s)	**POD: 25 mg/kg-bw/day (LOAEL) -Increased relative liver weights in females.** n= 16 Dose= 0, n= 16 Dose= 25, n= 16 Dose= 100, n= 16 Dose= 400, n= 16 Dose= 1,600, mg/kg-bw/day	See footnotes for full summary [9]	Many of the effects seen in body weights and liver weights may have been sensitive to gavage accidents. Mistakes in dosing were also identified, and some factors required to characterize confounding bias were not measured.	Mortality-Death-Nutritional/Metabolic-Body Weights-Hepatic/Liver-Absolute and relative liver weights; Medium	Dow Corning, 1984 5900289
No guidelines were reported and no GLP compliance was indicated. Study is in accordance with TSCA 15 U.S.C. 2607 (d), section 8 (d) Rat-Other (CD (Sprague-Dawley))-Both	Inhalation-Vapor-Duration: Short-term (>1-30 days)-7-6-14-day(s) 6 hours/day 7 days/week 14 day(s)	**POD: 400 ppm (in air, water, or food) (NOAEL) -No observed adverse effects** n= 10 Dose= 0, n= 10 Dose= 100, n= 10 Dose= 200, n= 10 Dose= 400, ppm (in air, water, or food)	Male and female Sprague-Dawley CD rats (5/sex/group) were exposed to 0, 100, 200 or 400 ppm (corresponding to analytical concentrations of 0, 103.0, 200.0, and 406.0 ppm, respectively) of octamethylcyclotetrasiloxane (D4) in the form of Dow Corning 244 Fluid via whole body inhalation for 6 hours/day, 7 days/week for 14 days. Animals were monitored for clinical signs of toxicity for respiratory, dermal, behavioral, and oculo-nasal effects. Body weights and food consumption were measured at initiation of the study and on days 4, 8, 12 and 14. All animals survived throughout the study. No clinical signs were observed over the course of the study. There were no statistically significant changes in body weights over the course the study. Food consumption was comparable in males throughout the study. Females at 400 ppm exhibited a transient significantly decreased food consumption (by 10%) on day 4 of the study, however no other change in food consumption was observed in females. This effect was not considered to be adverse because decreased food consumption was transient and recovered by the next timepoint for the remainder of the study. A NOAEL of 400 ppm was determined for nutritional/metabolic effects based on no observed adverse effects for body weights nor food consumption.	There are numerous ambiguities with how the exposure was conducted and a lack of any detail on statistical methods.	Nutritional/Metabolic-Body weights and food consumption; Medium	Dow Corning, 1988 5903742

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Octamethylcyclotetrasiloxane (D4)- Parent compound - Short-term (>1-30 days)

Guideline and Animal Species, Strain, Sex	Exposure Route and Exposure Duration	Study-wide POD and Dose/ Concentration(s)	Summary	Major Limitations	Principal Target Organs/Systems and OQD*	HERO ID
The study did not report any guidelines but was GLP compliant. Rabbit-New Zealand White - [rabbit]-Male	Dermal-Duration: Short-term (>1-30 days)-8-day(s) 8 day(s) Test substance was applied to the skin (non-occluded) each day for 8 days	**POD: 20 uL (Dichotomous (P/N)) -Non-irritating to skin** n= 30 Dose= 20, uL	Octamethylcyclotetrasiloxane (D4) was used as the vehicle for ten different chemicals examined in this study. These data are from the vehicle control site tested in conjunction with the different chemicals in the same animals. Male New Zealand white rabbits (n=30) had their entire back shaved with a straight razor 24-hours prior to dermal application. Just before application of D4, the skin on the left side of the rabbit was left intake whereas the right side was abraded in a crosshatch pattern with sharp hypodermic needle (only the stratum corneum penetrated). D4 (20 uL) was applied to a 5 cm2 circular site on both the intact and abraded side (4 uL/cm2) each day for 8 days. Test sites were left non-occluded. A neck collar was used in order to prevent animals from licking or rubbing at the test site. Body weight and clinical signs were assessed following each application. Dermal reactions were scored each day for 8 days. Irritation was scored on a 1-5 scale based on severity. An adjacent area of untreated skin served as a control. Body weight and clinical signs were not reported. No signs of erythema, edema, necrosis, or exfoliation were observed at either the intact or abraded test sites (score of 1). No data was reported regarding the untreated skin that served as a control. Since no reaction was seen at the treated sites, this is unlikely to substantially impact the results. D4 was considered non-irritating to the skin of rabbits.	Animals were treated with other chemicals at the same time as D4 (D4 was the vehicle control).	Irritation-Skin irritation; Medium	Dow Corning, 1984 5910402
No guidelines were followed. This study was not conducted to meet all the requirement to be considered GLP-compliant. Rat-Fischer 344 - [rat]-Female	Inhalation-Vapor-Duration: Short-term (>1-30 days)-5-6-26-day(s) 6 hours/day 5 days/week 26 day(s) Animals were exposed 6 hours/day, 5 days/week for 5, 12 or 26 days	**POD: 700 ppm (in air, water, or food) (LOAEC) - Increased liver and thyroid weights and hepatic and thyroid cell proliferation.** n= 10 Dose= 0, n= 10 Dose= 700, ppm (in air, water, or food)	See footnotes for full summary [10]	No major limitations were identified for this non-guideline study.	Nutritional/Metabolic-Body weight, food and water intake.-Hepatic/Liver-Liver weight, and cell proliferation (BrdU and PCNA staining). Liver tissue was fixed for histologic evaluation, but ultimately, these samples were not evaluated.-Thyroid-Thyroid weight and cell proliferation.; High	Dow Corning, 2002 7310071

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Octamethylcyclotetrasiloxane (D4)- Parent compound - Short-term (>1-30 days)

Guideline and Animal Species, Strain, Sex	Exposure Route and Exposure Duration	Study-wide POD and Dose/ Concentration(s)	Summary	Major Limitations	Principal Target Organs/Systems and OQD*	HERO ID
No guidelines were followed. This study was not conducted to meet all the requirement to be considered GLP-compliant. Rat-Fischer 344 - [rat]-Female	Inhalation-Vapor-Duration: Short-term (>1-30 days)-5-6-5-day(s) 6 hours/day 5 days/week 26 day(s) Animals were exposed 6 hours/day, 5 days/week for 5, 12 or 26 days	**POD: 29 ppm (in air, water, or food) (NOAEC) -Increased liver weight and hepatic cellular proliferation.** n= 10 Dose= 0, n= 10 Dose= 7, n= 10 Dose= 29, n= 10 Dose= 70, n= 10 Dose= 150, Dose= 300, Dose= 701, ppm (in air, water, or food)	See footnotes for full summary [11]	No major limitations were identified.	Nutritional/Metabolic-Body weight, food and water intake.-Hepatic/Liver-Liver weight, and cell proliferation (BrdU and PCNA staining). Liver tissue was fixed for histologic evaluation, but ultimately, these samples were not evaluated.-Thyroid-Thyroid weight and cell proliferation.; High	Dow Corning, 2002 7310071

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Octamethylcyclotetrasiloxane (D4)- Parent compound - Short-term (>1-30 days)

Guideline and Animal Species, Strain, Sex	Exposure Route and Exposure Duration	Study-wide POD and Dose/ Concentration(s)	Summary	Major Limitations	Principal Target Organs/Systems and OQD*	HERO ID
This was a non-guideline study. There is a GLP compliance statement in pdf p 53, stating it was in accordance with GLP under the EPA toxic substances control act (TSCA) Federal Regulations 40 CFR Part 792) with noted exceptions. The study authors indicate that the "in-life and experimental phase of this study was monitored by Dow Corning's Quality Assurance Unit according to HES SOPs to assure compliance with periodic auditing by Dow Corning Quality Assurance Unit." They also indicate that the final report and raw data were not audited by the HES Quality Assurance Unit. Rat-Fischer 344 - [rat]-Female	Oral-Gavage-Duration: Short-term (>1-30 days)-7-14-day(s) 7 days/week 14 day(s)	**POD: 301 mg/kg-bw/day (LOAEL) -Significant increase in liver weight (absolute and relative), and changes in hepatic microsomal enzymatic activity** n= 8 Dose= 0, n= 8 Dose= 301, mg/kg-bw/day	See footnotes for full summary [12]	This was a species comparison, short-term oral toxicity study focused on understanding how octamethylcyclotetrasiloxane exposure impacts hepatic responses in rats compared with guinea pigs. Major limitations include single dose and shorter duration (14d)	Hepatic/Liver-liver weight (absolute and relative), liver D4 content, histopathological analysis of liver-Nutritional/Metabolic-body weight, body weight gain, food consumption; High	Dow Corning, 2002 7310077

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Octamethylcyclotetrasiloxane (D4)- Parent compound - Short-term (>1-30 days)

Guideline and Animal Species, Strain, Sex	Exposure Route and Exposure Duration	Study-wide POD and Dose/ Concentration(s)	Summary	Major Limitations	Principal Target Organs/Systems and OQD*	HERO ID
This was a non-guideline study. There is a GLP compliance statement in pdf p 53, stating it was in accordance with GLP under the EPA toxic substances control act (TSCA) Federal Regulations 40 CFR Part 792) with noted exceptions. The study authors indicate that the "in-life and experimental phase of this study was monitored by Dow Corning's Quality Assurance Unit according to HES SOPs to assure compliance with periodic auditing by Dow Corning Quality Assurance Unit." They also indicate that the final report and raw data were not audited by the HES Quality Assurance Unit. Guinea pig-Hartley - [guinea pig]-Female	Oral-Gavage-Duration: Short-term (>1-30 days)-7-14-day(s) 7 days/week 14 day(s)	**POD: 301 mg/kg-bw/day (NOAEL) -** n= 8 Dose= 0, n= 8 Dose= 301, mg/kg-bw/day	See footnotes for full summary [13]	Major limitations include variability in body weights and liver D4 content among the treated group, and missing data for CYP3A and CYP4A levels in the liver. This was a species comparison, short-term oral toxicity study focused on understanding how octamethylcyclotetrasiloxane exposure impacts hepatic responses in rats and guinea pigs.	Gastrointestinal-stomach weight (absolute and relative), histopathological analysis of stomach-Hepatic/Liver-liver weight (absolute and relative), liver D4 content, histopathological analysis of liver-Mortality-survival-Nutritional/Metabolic-body weight, body weight gain, food consumption-Other (please specify below) (Clinical signs)-Staining of the eyes, stupor, urine staining of fur, loss of balance, lethargic, oil on fur, body soiling, damage to toenail, lethargy-Other (please specify below) (General gross necropsy)-Gross necropsy; High	Dow Corning, 2002 7310077

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Octamethylcyclotetrasiloxane (D4)- Parent compound - Short-term (>1-30 days)

Guideline and Animal Species, Strain, Sex	Exposure Route and Exposure Duration	Study-wide POD and Dose/ Concentration(s)	Summary	Major Limitations	Principal Target Organs/Systems and OQD*	HERO ID
Adherence to a guideline was not specified. Rat-Sprague-Dawley - [rat]-Both	Oral-Gavage-Duration: Short-term (>1-30 days)-7-4-week(s) 7 days/week 4 week(s) There were limited details provided on dosing. Authors state that rats were administered the test chemical for 4 weeks. It is assumed animals were gavaged, it is also assumed that animals were dosed daily based on wording.	**POD: Not provided (Other) -** n= 10 , n= 10 , Not provided	In a short-term, repeated dose oral toxicity study, Sprague-Dawley rats (5 animals/sex/group) were exposed via gavage to octamethylcyclotetrasiloxane (D4) at concentrations of 0 or an unknown concentration daily for 4 weeks. After 4 weeks of dosing, the animals were fasted for 16 hours prior to measuring individual oxygen consumption rates. Rats were then returned to their cages, fed, and sacrificed the following day. Final body weights were recorded. Nine organs (heart, liver, thyroid, spleen, seminal vesicles, ventral prostate, testes, ovary, and uterus) were removed and weighed. Silicon concentrations were measured in urine, thyroid, serum, liver, heart, and epididymal/ovarian fat. In addition, serum total cholesterol levels were measured at some point during the study, although the exact time is not clear.Whole body oxygen consumption rates were not statistically significantly different between the control and treated groups. There were no treatment-related changes in final body weight. Relative liver weights were significantly increased by 13% in treated females. There were no other treatment-related changes in relative organ weights. Thyroid silicon levels were not detectable in treated females, whereas control levels were 6.2 ppm. Fat silicon levels were significantly increased in treated males (1563% increase) and females (2280% increase). Serum cholesterol levels were not statistically significantly different between the control and treated groups, for both sexes. No author-reported toxicity values were provided. This study is uninformative due to lack of reporting on the dose of D4 used in this study. Therefore, this study is not suitable for POD determination.	This study is uninformative due to no reporting of test substance dose levels used in the study. Other major limitations include uncertainties in the exact method and frequency of administration, missing important information (e.g. animal age, temperature and humidity conditions, test substance purity), missing data (e.g. body weight data, control group values for urine silicon levels) and statistical comparisons (e.g. whole body oxygen consumption, thyroid silicon levels), sample pooling across sexes and dosing routes, and an overall lack of reporting.	Hepatic/Liver-Relative liver weight, serum total cholesterol-Other (please specify below) (ADME)-Silicon concentrations in serum, liver, heart, and epididymal/ovarian fat; Uninformative	Dow Corning, 1972 7310453

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Octamethylcyclotetrasiloxane (D4)- Parent compound - Short-term (>1-30 days)

Guideline and Animal Species, Strain, Sex	Exposure Route and Exposure Duration	Study-wide POD and Dose/ Concentration(s)	Summary	Major Limitations	Principal Target Organs/Systems and OQD*	HERO ID
Adherence to a guideline was not specified. Rat-Sprague-Dawley - [rat]-Both	Dermal-Duration: Short-term (>1-30 days)-7-4-week(s) 7 days/week 4 week(s) There were limited details provided on dosing. Authors state that rats were administered the test chemical for 4 weeks. It is assumed that the chemical was applied daily to skin based on wording.	**POD: Not provided (Other) -** n= 10 , n= 10 , Not provided	In a short-term, repeated dose dermal toxicity study, Sprague-Dawley rats (5 animals/sex/group) were exposed via dermal application to octamethylcyclotetrasiloxane (D4) at concentrations of 0 or an unknown concentration daily for 4 weeks. After 4 weeks of dosing, the animals were fasted for 16 hours prior to measuring individual oxygen consumption rates. Rats were then returned to their cages, fed, and sacrificed the following day. Final body weights were recorded. Nine organs (heart, liver, thyroid, spleen, seminal vesicles, ventral prostate, testes, ovary, and uterus) were removed and weighed. Silicon concentrations were measured in urine, thyroid, serum, liver, heart, and epididymal/ovarian fat. In addition, serum total cholesterol levels were measured at some point during the study, although the exact time is not clear.Whole body oxygen consumption rates were not statistically significantly different between the control and treated groups. There were no treatment-related changes in final body weight. Relative heart weights were significantly increased by 14% in treated females. There were no other treatment-related changes in relative organ weights. Serum silicon levels were significantly increased by 500% in treated males. Thyroid silicon levels were not detectable in treated males, whereas control levels were 6.2 ppm. Fat silicon levels were significantly increased by 240% in treated females. Serum cholesterol levels were significantly increased by 27% for treated females. No author-reported toxicity values were provided. This study is uninformative due to lack of reporting on the dose of D4 used in this study. Therefore, this study is not suitable for POD determination.	This study is uninformative due to no reporting of test substance dose levels used in the study. Other major limitations include uncertainties in the exact method and frequency of administration, missing important information (e.g. animal age, temperature and humidity conditions, test substance purity), missing data (e.g. body weight data, control group values for urine silicon levels) and statistical comparisons (e.g. whole body oxygen consumption, thyroid silicon levels), sample pooling across sexes and dosing routes, and an overall lack of reporting.	Cardiovascular-Relative heart weight-Hepatic/Liver-Relative liver weight, serum total cholesterol-Other (please specify below) (ADME)-Silicon concentrations in serum, liver, heart, and epididymal/ovarian fat; Uninformative	Dow Corning, 1972 7310453

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Octamethylcyclotetrasiloxane (D4)- Parent compound - Short-term (>1-30 days)

Guideline and Animal Species, Strain, Sex	Exposure Route and Exposure Duration	Study-wide POD and Dose/ Concentration(s)	Summary	Major Limitations	Principal Target Organs/Systems and OQD*	HERO ID
This study was conducted in accordance with EPA Toxic Substances Control; Good Laboratory Practices Regulations; 40 CFR, Part 792, Volume 48, Number 230. Hamster, Syrian-Other (LVG Golden Syrian)-Both	Inhalation-Vapor-Duration: Short-term (>1-30 days)-7-6-28-day(s) 6 hours/day 7 days/week 28 day(s)	**POD: 697 ppm (in air, water, or food) (LOAEL) -Increased relative liver weight (females) and relative testes weights (males)** n= 20 Dose= 0, n= 20 Dose= 697, ppm (in air, water, or food)	See footnotes for full summary [14]	Major limitations include lack of reporting on age of the animals and respiratory rate monitoring.	Reproductive/Developmental- Absolute and relative testes weight and histopathology; gross necropsy- Hepatic/Liver- Absolute and relative liver weight and histopathology; Gross necropsy; Medium	Dow Corning, 1989 7310562

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Octamethylcyclotetrasiloxane (D4)- Parent compound - Short-term (>1-30 days)

Guideline and Animal Species, Strain, Sex	Exposure Route and Exposure Duration	Study-wide POD and Dose/ Concentration(s)	Summary	Major Limitations	Principal Target Organs/Systems and OQD*	HERO ID
This study was conducted in accordance with EPA Toxic Substances Control; Good Laboratory Practices Regulations; 40 CFR, Part 792, Volume 48, Number 230. Guinea pig-Hartley - [guinea pig]-Both	Inhalation-Vapor-Duration: Short-term (>1-30 days)-7-6-28-day(s) 6 hours/day 7 days/week 28 day(s)	**POD: 697 ppm (in air, water, or food) (NOAEL) -** n= 20 Dose= 0, n= 20 Dose= 697, ppm (in air, water, or food)	In a short-term, repeated dose inhalation toxicity study, male and female Hartley guinea pigs (10/sex/group) were exposed via whole body inhalation in a dynamic chamber to octamethylcyclotetrasiloxane (D4; purity ≥97%) at concentrations of 0 or 697 ppm 6 hours/day, 7 days/week for 28 days. Animals were observed frequently during exposures (exact timing not reported) and daily during the postexposure period for mortality and clinical signs of toxicity (respiratory, dermal, behavioral, nasal or ocular changes). Other endpoints evaluated included body weights (initial, every fourth day, and terminal), food consumption (every fourth day), gross necropsy, and organ weight and histopathology on liver, lungs, trachea (histopathology only), kidneys, spleen, and testes. No animals died during the exposure period. The study authors mention one female in the control group was sacrificed during the study due to nontreatment-related reasons (physical trauma). No treatment-related changes in clinical signs were observed; study reports "all test animals appeared normal and their behavior was fully compatible with their respective control (details not provided). No significant differences in body weights, body weight gain or terminal body weights were seen compared to control. Mean food consumption was significantly decreased in males on day 19 (16%) and day 23 (11%) compared to control, however average daily was not different from control. No gross macroscopic changes were observed. No significant differences in absolute or relative organ weights were seen compared to control. No treatment-related histological changes were observed. No author-reported toxicity values were provided. A NOAEL of 697 ppm was identified.	Major limitations include lack of reporting on age of the animals and respiratory rate monitoring.	nan; High	Dow Corning, 1989 7310562

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Octamethylcyclotetrasiloxane (D4)- Parent compound - Short-term (>1-30 days)

Guideline and Animal Species, Strain, Sex	Exposure Route and Exposure Duration	Study-wide POD and Dose/ Concentration(s)	Summary	Major Limitations	Principal Target Organs/Systems and OQD*	HERO ID
This study was conducted in accordance with EPA Toxic Substances Control; Good Laboratory Practices Regulations; 40 CFR, Part 792, Volume 48, Number 230. Rabbit-New Zealand White - [rabbit]-Both	Inhalation-Vapor-Duration: Short-term (>1-30 days)-7-6-28-day(s) 6 hours/day 7 days/week 28 day(s)	**POD: 697 ppm (in air, water, or food) (NOAEC) -** n= 10 Dose= 0, n= 10 Dose= 697, ppm (in air, water, or food)	In a short-term, repeated dose inhalation toxicity study, male and female New Zealand White rabbits (5/sex/group) were exposed via whole body inhalation in a dynamic chamber to octamethylcyclotetrasiloxane (D4; purity ≥97%) at concentrations of 0 or 697 ppm 6 hours/day, 7 days/week for 28 days. Animals were observed frequently during exposures (exact timing not reported) and daily during the postexposure period for mortality and clinical signs of toxicity (respiratory, dermal, behavioral, nasal or ocular changes). Other endpoints evaluated included body weights (initial, every fourth day, and terminal), food consumption (every fourth day), gross necropsy, and organ weights and histopathology on liver, lungs, trachea (histopathology only), kidneys, spleen, and testes. No animals died during the exposure period. No treatment-related changes in clinical signs were observed; study reports "all test animals appeared normal and their behavior was fully compatible with their respective control (details not provided). No significant differences in body weights or terminal body weights were seen in either sex compared to control. Body weight gain in females was decreased (31%; statistical and biological significance is unclear) and similar in males compared to control. No significant difference in mean food consumption or average daily food intake were seen compared to control. No gross macroscopic changes were observed. No significant differences in absolute or relative organ weights were seen compared to control. No treatment-related histological changes were observed. No author-reported toxicity values were provided. A NOAEL of 697 ppm was identified (highest concentration tested).	Major limitations include lack of reporting on age of the animals and respiratory rate monitoring.	nan; High	Dow Corning, 1989 7310562
This study was conducted in accordance with EPA Toxic Substances Control; Good Laboratory Practices Regulations; 40 CFR, Part 792, Volume 48, Number 230. Mouse-CD-1 - [mouse]-Both	Inhalation-Vapor-Duration: Short-term (>1-30 days)-7-6-28-day(s) 6 hours/day 7 days/week 28 day(s)	**POD: 697 ppm (in air, water, or food) (LOAEL) -Increased absolute and relative liver weights** n= 20 Dose= 0, n= 20 Dose= 697, ppm (in air, water, or food)	See footnotes for full summary [15]	Major limitations include lack of reporting on age of the animals and respiratory rate monitoring.	Hepatic/Liver-Absolute and relative liver weight and histopathology; Gross necropsy-Nutritional/Metabolic-Body weight, Body weight gain, Food consumption; High	Dow Corning, 1989 7310562

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Octamethylcyclotetrasiloxane (D4)- Parent compound - Short-term (>1-30 days)

Guideline and Animal Species, Strain, Sex	Exposure Route and Exposure Duration	Study-wide POD and Dose/ Concentration(s)	Summary	Major Limitations	Principal Target Organs/Systems and OQD*	HERO ID
No guideline. GLP compliance statement provided . Rat-Sprague-Dawley - [rat]-Both	Oral-Gavage-Duration: Short-term (>1-30 days)-14-day(s) 14 day(s)	**POD: 300 mg/kg-bw/day (LOAEL) -Increased absolute and relative liver weights.** n= 10 Dose= 0, n= 10 Dose= 300, n= 10 Dose= 600, n= 10 Dose= 1200, mg/kg-bw/day	See footnotes for full summary [16]	No major limitations were identified	Mortality-Mortality, clinical signs-Nutritional/Metabolic-Body weights, body weight gain, food consumption, and gross necropsy of adipose-Hepatic/Liver-Liver weight and gross necropsy.-Immune/Hematological-Thymus weight, spleen weight, and gross necropsy-Other (please specify below) (Clinical signs)-clinical signs of skin and fur condition, overall condition, eyes and mucous membranes, respiratory signs, circulation, and nervous system.-Neurological/Behavioral-Clinical signs and brain weight.-Cardiovascular-Heart weight, clinical signs of circulation (not specified), and gross necropsy-Other (please specify below) (endocrine)-Weight of adrenal glands-Lung/Respiratory-Clinical signs of respiration and gross necropsy; High	Dow Corning, 2007 9653974

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Octamethylcyclotetrasiloxane (D4)- Parent compound - Short-term (>1-30 days)

Guideline and Animal Species, Strain, Sex	Exposure Route and Exposure Duration	Study-wide POD and Dose/ Concentration(s)	Summary	Major Limitations	Principal Target Organs/Systems and OQD*	HERO ID
No compliance to any guidance documents is stated. Rat-Sprague-Dawley - [rat]-Female	Oral-Gavage-Duration: Short-term (>1-30 days)-8-day(s) 8 day(s) Comparable experiment with non-pregnant animals	**POD: 5 mg/kg-bw/day (LOAEL) -Mechanistic: increased PROD activity and CYP2B1/2 and CYP3A1/2 protein expression.** n= 4 Dose= 0, n= 4 Dose= 5, n= 4 Dose= 20, n= 4 Dose= 100, mg/kg-bw/day	See footnotes for full summary [17]	There are some errors and discrepancies in the text as well as data omissions. The methods state a 1 mg/kg-day group was included, but this dose is not specified in the study abstract, and no data for a 1 mg/kg-day group was reported. The text refers to Table 1 for PROD activity; however, these data are in Table 2. The study reports relative liver weights without providing absolute weights or body weight data. There are some concerns regarding sample size.	Hepatic/Liver-Relative liver weight, Mechanistic endpoints in liver tissue: microsomal EROD and PROD activity, CYP1A1/2, CYP2B1/2, CYP3A1/2 protein expression, CYP2B1/2 mRNA expression.; Medium	Falany et. al 2005 99288
No guidelines were described. For animal husbandry practices, the authors cite, "Guide for the Care and Use of Laboratory Animals" DHEW' Publication No. (NIH) 78-23, and those currently acceptable to Good Laboratory Practices. (Federal Register, 1978. 43 (247): 60013-60020; 21 CFR Part 58)". Rabbit-New Zealand White - [rabbit]-Both	Dermal-Duration: Short-term (>1-30 days)-7-6-3-week(s) 6 hours/day 7 days/week 3 week(s)	**POD: 1 g/kg (LOAEL) -Increased incidence of skin lesions: red, dry skin, with sores and with histological lesions including thickening, hyperkeratosis, and inflammation.** n= 12 Dose= 0, n= 12 Dose= 1, g/kg	See footnotes for full summary [18]	Limitations include a lack of blinding and a lack of scoring for skin irritation. The authors also had issues with animal attrition (possibly due to stress) and a single dose used though multiple doses would characterize a dose-response of the outcome.	Irritation-Skin irritation; Medium	FDRL, 1979 5888541

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Octamethylcyclotetrasiloxane (D4)- Parent compound - Short-term (>1-30 days)

Guideline and Animal Species, Strain, Sex	Exposure Route and Exposure Duration	Study-wide POD and Dose/ Concentration(s)	Summary	Major Limitations	Principal Target Organs/Systems and OQD*	HERO ID
Adherence to a guideline was not specified. Rat-Not specified-Both	Inhalation-Vapor-Duration: Short-term (>1-30 days)-5-2-2-week(s) 2 hours/day 5 days/week 2 week(s) Animals were exposed twice per day, for 1-hour intervals (10:00 am and 2:00 pm), 5 days per week, for two weeks.	**POD: mg chemical / L air (Other) -** n= 12 Dose= 0, n= 12 Dose= 39.7, mg chemical / L air	See footnotes for full summary [19]	This study is uninformative and has many limitations. Major limitations include poor reporting quality (missing important information), confounding factors (missing respiratory rate measurements, hypoactivity and closed eyes in controls during exposure period), differences in initial body weight between control and treated rats, poor animal health (interstitial pneumonitis and lymphocytic infiltrates), uncertainty surrounding test substance characterization (missing source and purity, uncertainty on composition, lack of detail on exposure method), small sample size for most endpoints, lack of microscopic examination of fixed organ tissues, and unusual pooling of male and female data for statistical analysis. This was a short-term inhalation toxicity study focused on understanding how octamethylcyclotetrasiloxane inhalation affects rats, guinea pigs, and mice.	Nutritional/Metabolic-Body weight-Other (please specify below) (Clinical signs)-Manifestations of toxicity; Uninformative	Hazleton Laboratories, 1971 5885411

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Octamethylcyclotetrasiloxane (D4)- Parent compound - Short-term (>1-30 days)

Guideline and Animal Species, Strain, Sex	Exposure Route and Exposure Duration	Study-wide POD and Dose/ Concentration(s)	Summary	Major Limitations	Principal Target Organs/Systems and OQD*	HERO ID
Adherence to a guideline was not specified. Guinea pig-Not specified-Both	Inhalation-Vapor-Duration: Short-term (>1-30 days)-5-2-2-week(s) 2 hours/day 5 days/week 2 week(s) Animals were exposed twice per day, for 1-hour intervals (10:00 am and 2:00 pm), 5 days per week, for two weeks.	**POD: mg chemical / L air (Other) -** n= 12 Dose= 0, n= 12 Dose= 39.7, mg chemical / L air	See footnotes for full summary [20]	This study is uninformative and has many limitations. Major limitations include poor reporting quality (missing important information), confounding factors (missing respiratory rate measurements, hypoactivity and closed eyes during exposure period), differences in initial body weight between control and treated guinea pigs, poor animal health (interstitial pneumonitis and lymphocytic infiltrates), uncertainty surrounding test substance characterization (missing source and purity, uncertainty on composition, lack of detail on exposure method), small sample size for most endpoints, lack of microscopic examination of fixed organ tissues, and unusual pooling of male and female data for statistical analysis. This was a short-term inhalation toxicity study focused on understanding how octamethylcyclotetrasiloxane inhalation affects rats, guinea pigs, and mice.	nan; Uninformative	Hazleton Laboratories, 1971 5885411
Adherence to a guideline was not specified. Mouse-Not specified-Both	Inhalation-Vapor-Duration: Short-term (>1-30 days)-5-2-2-week(s) 2 hours/day 5 days/week 2 week(s) Animals were exposed twice per day, for 1-hour intervals (10:00 am and 2:00 pm), 5 days per week, for two weeks.	**POD: mg chemical / L air (Other) -** n= 12 Dose= 0, n= 12 Dose= 39.7, mg chemical / L air	See footnotes for full summary [21]	This study is uninformative and has many limitations. Major limitations include poor reporting quality (missing important information), confounding factors (missing respiratory rate measurements, hypoactivity and closed eyes during exposure period), uncertainty surrounding test substance characterization (missing source and purity, uncertainty on composition, lack of detail on exposure method), small sample size for most endpoints, lack of microscopic examination of fixed organ tissues, and unusual pooling of male and female data for statistical analysis. This was a short-term inhalation toxicity study focused on understanding how octamethylcyclotetrasiloxane inhalation affects rats, guinea pigs, and mice.	Immune/Hematological-Absolute and relative spleen weight.-Renal/Kidney-Absolute and relative kidney weight. Histopathology of kidney.-Other (please specify below) (Clinical signs)-Manifestations of toxicity; Uninformative	Hazleton Laboratories, 1971 5885411

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Octamethylcyclotetrasiloxane (D4)- Parent compound - Short-term (>1-30 days)

Guideline and Animal Species, Strain, Sex	Exposure Route and Exposure Duration	Study-wide POD and Dose/ Concentration(s)	Summary	Major Limitations	Principal Target Organs/Systems and OQD*	HERO ID
The study was " in compliance with the Standard Operating Procedures of International Research and Development Corporation (IRDC)." and was done in accordance with GLP. Rat-Sprague-Dawley - [rat]-Female	Inhalation-Vapor-Duration: Short-term (>1-30 days)-1-F0 - gestation (GD 6-15) Presumed pregnant dams were exposed from GD 6-15	**POD: 300 ppm (in air, water, or food) (NOAEC) -Maternal toxicity (decreased body weight and food consumption)** n= 30 Dose= 0, n= 30 Dose= 100, n= 30 Dose= 300, n= 30 Dose= 700, ppm (in air, water, or food)Total # of generations: 1 Female Exposure: F0 - gestation, GD 6-15	See footnotes for full summary [22]	No major limitations.	Mortality-Mortality-Other (please specify below) (Clinical signs)-Overt changes in appearance and behavior-Nutritional/Metabolic-Body weight and food intake-Reproductive/Developmental-Pregnancy rates, location of viable and nonviable fetuses, early and late resorptions, number of total implantations and corpora lutea, and fetal weight and sex. Visceral and skeletal malformations in the fetus.-Gastrointestinal-Gross pathology on intestines-Renal/Kidney-Gross pathology of kidney-Hepatic/Liver-Liver weight and gross necropsy; High	IRDC, 1993 5889471
Adherence to a guideline was not specified. Rat-Wistar - [rat]-Female	Oral-Gavage-Duration: Short-term (>1-30 days)-7-2-week(s) 7 days/week 2 week(s) For Wistar rats, there was a 4 week reversibility period (after 2 weeks of dosing) during which the rats were not dosed with D4. The study with Sprague-Dawley rats did not have a 4 week reversibility period.	**POD: 1600 mg/kg-bw/day (LOAEL) - Hepatic changes (increased liver enzyme activities, increased absolute and relative liver weights, histopathological an ultrastructural changes)** n= 20 Dose= 0, n= 20 Dose= 1600, mg/kg-bw/day	See footnotes for full summary [23]	Major limitations included missing important information (test animal characteristics, purity of test substance, and animal husbandry conditions), methods are sparsely reported, missing quantitative/qualitative data for multiple endpoints, conflicting information on the sample size, missing statistical comparisons, and a lack of incidence data for qualitative findings.	Immune/Hematological-Histopathology of mesenteric lymph nodes-Hepatic/Liver-Liver enzyme activity; absolute and relative liver weight; histopathology of the liver; electron microscopy of the liver-Lung/Respiratory-Histopathology of the lung; Low	Mobay Corp, 1991 5899001

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Octamethylcyclotetrasiloxane (D4)- Parent compound - Short-term (>1-30 days)

Guideline and Animal Species, Strain, Sex	Exposure Route and Exposure Duration	Study-wide POD and Dose/ Concentration(s)	Summary	Major Limitations	Principal Target Organs/Systems and OQD*	HERO ID
Adherence to a guideline was not specified. Rat-Sprague-Dawley - [rat]-Both	Oral-Gavage-Duration: Short-term (>1-30 days)-7-2-week(s) 7 days/week 2 week(s) For Wistar rats, there was a 4 week reversibility period (after 2 weeks of dosing) during which the rats were not dosed with D4. The study with Sprague-Dawley rats did not have a 4 week reversibility period.	**POD: 1600 mg/kg-bw/day (LOAEL) -Hepatic changes (increased liver enzyme activities, increased absolute and relative liver weights, and histopathological changes)** n= 5 Dose= 0, n= 5 Dose= 1600, mg/kg-bw/day	See footnotes for full summary [24]	Major limitations included missing information (test animal characteristics, purity of test substance, and animal husbandry conditions), methods sparsely reported, missing quantitative/qualitative data for multiple endpoints, missing statistical comparisons, and a lack of incidence data for qualitative findings.	Hepatic/Liver-Liver enzyme activity; absolute and relative liver weight; histopathology of the liver; electron microscopy of the liver; Uninformative	Mobay Corp, 1991 5899001
A guideline was not specified, but the study was conducted in a manner that was similar to OECD TG 440. The study was GLP compliant. Rat-Sprague-Dawley - [rat]-Female	Oral-Gavage-Duration: Short-term (>1-30 days)-4-4-day(s) 4 days/week 4 day(s) Animals were dosed daily for 4 consecutive days	**POD: 100 mg/kg-bw/day (NOAEL) -Increased liver weight and uterine weight, increased uterine epithelial heights** n= 12 Dose= 0, n= 12 Dose= 10, n= 12 Dose= 50, n= 12 Dose= 100, n= 12 Dose= 250, n= 12 Dose= 500, n= 12 Dose= 1,000, mg/kg-bw/day	See footnotes for full summary [25]	No major limitations were identified. The study was generally consistent with guideline specifications.	Hepatic/Liver-Liver weights (absolute and relative)-Reproductive/Development-Uterine weights (absolute and relative), gross necropsy (ovary, uterus), epithelial field measurements (uterus), uterotrophic assay; High	MPI Research, 1999 5887187
A guideline was not specified, but the study was conducted in a manner that was similar to OECD TG 440. The study was GLP compliant. Rat-Fischer 344 - [rat]-Female	Oral-Gavage-Duration: Short-term (>1-30 days)-4-4-day(s) 4 days/week 4 day(s) Animals were dosed daily for 4 consecutive days	**POD: 100 mg/kg-bw/day (NOAEL) -Increased liver weights.** n= 12 Dose= 0, n= 12 Dose= 10, n= 12 Dose= 50, n= 12 Dose= 100, n= 12 Dose= 250, n= 12 Dose= 500, n= 12 Dose= 1,000, mg/kg-bw/day	See footnotes for full summary [26]	No major limitations were identified. The study was generally consistent with guideline specifications.	Hepatic/Liver-Liver weights (absolute and relative)-Reproductive/Development-Uterine weights (absolute and relative), gross necropsy (ovary, uterus), epithelial field measurements (uterus), uterotrophic assay; High	MPI Research, 1999 5887187

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Octamethylcyclotetrasiloxane (D4)- Parent compound - Short-term (>1-30 days)

Guideline and Animal Species, Strain, Sex	Exposure Route and Exposure Duration	Study-wide POD and Dose/ Concentration(s)	Summary	Major Limitations	Principal Target Organs/Systems and OQD*	HERO ID
The authors did not report any adherence to any guidance, nor compliance documents. Rat-Other (Sprague-Dawley Crl:CD (SD) IGS BR)-Female	Inhalation-Vapor-Duration: Short-term (>1-30 days)-3-14.5-hour(s) 3 days/week 14.5 hour(s) Phase I study: Animals were exposed for 6 hours/day on diestrus days 1 and 2; and for 2.5 hours on the day of proestrus	**POD: 702 ppm (in air, water, or food) (LOAEC) - Increased plasma E1** n= 24 Dose= 0, n= 22 Dose= 702, n= 27 Dose= 905, ppm (in air, water, or food)	Non-cannulated female Sprague-Dawley Crl:CD (SD) IGS BR rats (22-27/group) were exposed to target concentrations of 0, 700 or 900 ppm (with analytical concentrations of 0, 702 and 905 ppm) of octamethylcyclotetrasiloxane (D4) vapor (99.6% purity) via whole body inhalation 6 hours/day for 2 days on diestrus days 1 and 2 and for 2.5 hours during proestrus (3 days total). Vaginal lavages were performed 10-12 days prior to exposure to determine estrous stage; rats were entered into the study after their third normal cycle. Animals were euthanized following the last exposure at 10 am and trunk blood was harvested. Endpoints assessed included terminal body weights, plasma concentrations of follicle stimulating hormone (FSH), estradiol (E2), estrone (E1), progesterone (P4), and organ weights (uterus, ovary, and brain). The number of ova in the right and left oviducts was determined and uteri were assessed for fluid distension. Terminal body weights were significantly decreased at 702 ppm (4%) and 905 ppm (3%) compared to control. No significant differences in absolute or relative brain, uterine or ovarian weights were observed (data not shown). Significant increases in plasma E1 (~16% at ≥702 ppm), and plasma P4 (~60% at 905 ppm) were observed on the morning of proestrus. No significant differences in E2, E1/E2 ratio or FSH were observed compared to control. Study does not report number ova in oviducts or information on uteri fluid distension. No author reported PODs were reported. Based on the available data, a study-wide LOAEC of 702 ppm was observed for reproductive/developmental effects based on increased plasma E1. A NOAEC could not be determined.	This study may have issues with unmeasured respiratory irritant effects of D4 at concentrations >700 ppm. There is also inconsistent reporting of sample sizes for some endpoints, which may imply that not every endpoint was measured in every animal.	Reproductive/Developmental Serum follicle stimulating hormone (FSH), estradiol (E2), estrone (E1), progesterone (P4), luteinizing hormone (LH) and prolactin (PRL), E1/E2 ratio, ovulatory status. Organ weights uterus and ovary, histopathology: ovary. Number of ova in oviduct, fluid distension of uteri; Medium	Quinn et. al-2007 1297415

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Octamethylcyclotetrasiloxane (D4)- Parent compound - Short-term (>1-30 days)

Guideline and Animal Species, Strain, Sex	Exposure Route and Exposure Duration	Study-wide POD and Dose/ Concentration(s)	Summary	Major Limitations	Principal Target Organs/Systems and OQD*	HERO ID
The authors did not report any adherence to any guidance, nor compliance documents. Rat-Other (Sprague-Dawley Crl:CD (SD) IGS BR)-Female	Inhalation-Vapor-Duration: Short-term (>1-30 days)-3-6-3-day(s) 3 days/week 14.5 hour(s) Phase I study: Animals were exposed for 6 hours/day on diestrus days 1 and 2; and for 2.5 hours on the day of proestrus	**POD: 711 ppm (in air, water, or food) (LOAEC) - Decreased plasma LH, PRL and E1/E2 ratio, increased plasma E1 and E2, decreased percentage of ovulatory animals and ova in the oviduct/rat** n= 24 Dose= 0, n= 22 Dose= 711, n= 27 Dose= 895, ppm (in air, water, or food)	See footnotes for full summary [27]	This study may have issues with unmeasured respiratory irritant effects of D4 at concentrations >700 ppm. There is also inconsistent reporting of sample sizes for some endpoints, which may imply that not every endpoint was measured in every animal.	Reproductive/Developmental- Serum follicle stimulating hormone (FSH), estradiol (E2), estrone (E1), progesterone (P4), luteinizing hormone (LH) and prolactin (PRL), E1/E2 ratio, ovulatory status. Organ weights uterus and ovary, histopathology: ovary. Number of ova in oviduct, fluid distension of uteri; Medium	Quinn et. al- 2007 1297415
A guideline or adherence to GLP conditions was not specified; however, the assays fulfill the Tier 1 Endocrine Screening Procedure set forth by the Endocrine Disruptors Testing and Assessment Commission and the Organization for Economic Co-operation and Development validation process. Rat-Sprague-Dawley - [rat]-Female	Inhalation-Vapor-Duration: Short-term (>1-30 days)-16-3-day(s) 16 hours/day 3 day(s) Exposure for 16hrs/day for 3 (uterotrophic assay) days.	**POD: 700 ppm (in air, water, or food) (LOAEC) -Positive for weak estrogenic activity.** n= 10 Dose= 0, n= 10 Dose= 700, ppm (in air, water, or food)	See footnotes for full summary [28]	Limitations included missing information (animal source, age, initial body weights, parity, and all animal husbandry details), and lack of analytical measurements of D4 in the test atmosphere. The test substance may form aerosols at concentrations >700 ppm. The study did not test food for the presence of phytoestrogens (as specified by OEDD guidelines), or indicate whether measures were taken to reduce exposure to plasticizers.	Reproductive/Developmental- Uterotrophic assay: Absolute and relative wet uterus weight, relative dry uterus weight, histopathology on uteri (glandular and luminal epithelial cell height);Hershberger assay: ventral prostate weight (fresh and fixed), ani/bulbocavernosus muscle weight, seminal vesicle weight, glans penis weight, Cowper's gland weight.; Medium	Quinn et. al- 2007 1297690

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Octamethylcyclotetrasiloxane (D4)- Parent compound - Short-term (>1-30 days)

Guideline and Animal Species, Strain, Sex	Exposure Route and Exposure Duration	Study-wide POD and Dose/ Concentration(s)	Summary	Major Limitations	Principal Target Organs/Systems and OQD*	HERO ID
A guideline or adherence to GLP conditions was not specified; however, the assays fulfill the Tier 1 Endocrine Screening Procedure set forth by the Endocrine Disruptors Testing and Assessment Commission and the Organization for Economic Co-operation and Development validation process. Rat-Fischer 344 - [rat]-Female	Inhalation-Vapor-Duration: Short-term (>1-30 days)-16-3-day(s) 16 hours/day 3 day(s) Exposure for 16hrs/day for 3 (uterotrophic assay) days.	**POD: 700 ppm (in air, water, or food) (LOAEC) -Positive for weak estrogenic activity.** n= 10 Dose= 0, n= 10 Dose= 700, ppm (in air, water, or food)	See footnotes for full summary [29]	Limitations included missing information (animal source, age, initial body weights, parity, and all animal husbandry details), and lack of analytical measurements of D4 in the test atmosphere. The test substance may form aerosols at concentrations >700 ppm. The study did not test food for the presence of phytoestrogens (as specified by OEDD guidelines) or indicate whether measures were taken to reduce exposure to plasticizers.	Reproductive/Developmental-Uterotrophic assay: Absolute and relative wet uterus weight, relative dry uterus weight, histopathology on uteri (glandular and luminal epithelial cell height);Hershberger assay: ventral prostate weight (fresh and fixed), ani/bulbocavernosus muscle weight, seminal vesicle weight, glans penis weight, Cowper's gland weight.; Low	Quinn et. al-2007 1297690
A guideline or adherence to GLP conditions was not specified; however, the assays fulfill the Tier 1 Endocrine Screening Procedure set forth by the Endocrine Disruptors Testing and Assessment Commission and the Organization for Economic Co-operation and Development validation process. Rat-Fischer 344 - [rat]-Male	Inhalation-Vapor-Duration: Short-term (>1-30 days)-16-3-day(s) 16 hours/day 3 day(s) Exposure for 16hrs/day for 3 (uterotrophic assay) days.	**POD: 700 ppm (in air, water, or food) (NOAEC) -Negative for androgenic or antiandrogenic activity** n= 10 Dose= 0, n= 10 Dose= 700, ppm (in air, water, or food)	In a Hershberger assay, castrated male Fisher 344 rats (10/group) were exposed whole-body, to Octamethylcyclotetrasiloxane (D4; purity >99%) vapors, at 0 (filtered air) or 700 ppm, for 16 hours/day for 10 consecutive days. Positive control animals (6/group) were treated subcutaneously with 0.1 to 1.6 mg/kg-day testosterone propionate (frequency and duration not clearly reported). Control animals were sacrificed 24 hours after the last dose; animals exposed to D4 were sacrificed immediately following the last 16-hour exposure period. Negative (corn-oil) control groups were used for the control and the test article exposure to control for the time differences in necropsy. Additional groups of animals were administered testosterone propionate in combination with the antiandrogenic compound flutamide, or with D4. Ventral prostate (fresh and fixed), seminal vesicle, glans penis, ani/bulbocavernosus muscle, Cowper's gland, liver, and brain weights were recorded. No significant increases in organ weights were observed in animals exposed to D4 suggesting the lack of androgenic activity. Testosterone propionate treatment resulted in the expected dose-dependent increases. D4 also did not express any antiandrogenic activity when administered in combination with testosterone propionate. D4 was negative in the Hershberger assay.	Limitations included missing information (animal source, age, initial body weights, parity, and all animal husbandry details), and lack of analytical measurements of D4 in the test atmosphere. The test substance may form aerosols at concentrations >700 ppm. The study did not test food for the presence of phytoestrogens (as specified by OEDD guidelines) or indicate whether measures were taken to reduce exposure to plasticizers.	Reproductive/Developmental-Uterotrophic assay: Absolute and relative wet uterus weight, relative dry uterus weight, histopathology on uteri (glandular and luminal epithelial cell height);Hershberger assay: ventral prostate weight (fresh and fixed), ani/bulbocavernosus muscle weight, seminal vesicle weight, glans penis weight, Cowper's gland weight.; Uninformative	Quinn et. al-2007 1297690

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Octamethylcyclotetrasiloxane (D4)- Parent compound - Short-term (>1-30 days)

Guideline and Animal Species, Strain, Sex	Exposure Route and Exposure Duration	Study-wide POD and Dose/ Concentration(s)	Summary	Major Limitations	Principal Target Organs/Systems and OQD*	HERO ID
The study adhered to OECD TG 412 and was GLP compliant. US EPA TG 40 CFR 1, 798.2450 was also cited (with deviations) Rat-Fischer 344 - [rat]-Both	Inhalation-Vapor-Duration: Short-term (>1-30 days)-5-6-1-month(s) 6 hours/day 5 days/week 1 month(s) Animals were exposed for 6hrs/day, 5 days/week for one month (a total of 20-21 days)	**POD: 2.78 mg chemical / L air (LOAEC) -Increased absolute and relative liver weights** n= 20 Dose= 0, n= 20 Dose= 2.78, n= 20 Dose= 5.13, n= 20 Dose= 8.62, mg chemical / L air	See footnotes for full summary [30]	The high exposure concentration was too high resulting in mortality. This concentration was also above the level of saturation resulting in aerosolization and was evaluated separately.	Other (please specify below) (Endocrine)-Adrenal gland organ weights, histopathology (adrenals, pancreas, pituitary)-Lung/Respiratory-Lung weights, histopathology (nasoparyngeal tissues, lungs, larynx, trachea)-Reproductive/Developmental-Organ weights (ovaries, testes), histopathology (mammary gland, ovaries, uterus, vagina, testes, epididymis, prostate, seminal vesicles)-Hepatic/Liver-Clinical chemistry (glucose, bilirubin, total cholesterol, triglycerides, phospholipids, AST, ALT, LDH, ALP, total protein, globulin, albumin/globulin ratio); Liver weights, histopathology, electron microscopy; High	RCC, 1995 5888822

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Octamethylcyclotetrasiloxane (D4)- Parent compound - Short-term (>1-30 days)

Guideline and Animal Species, Strain, Sex	Exposure Route and Exposure Duration	Study-wide POD and Dose/ Concentration(s)	Summary	Major Limitations	Principal Target Organs/Systems and OQD*	HERO ID
The study adhered to OECD TG 412 and was GLP compliant. US EPA TG 40 CFR 1, 798.2450 was also cited (with deviations) Rat-Fischer 344 - [rat]-Both	Inhalation-Aerosol-Duration: Short-term (>1-30 days)-5-6-1-month(s) 6 hours/day 5 days/week 1 month(s) Animals were exposed for 6hrs/day, 5 days/week for one month (a total of 20-21 days)	**POD: mg chemical / L air (Other) -** n= 20 Dose= 0, n= 20 Dose= 13.25, mg chemical / L air	See footnotes for full summary [31]	The high exposure concentration was too high resulting in mortality. This concentration was also above the level of saturation resulting in aerosolization.	Mortality-Mortality-Other (please specify below) (Endocrine)-Adrenal gland organ weights, histopathology (adrenals, pancreas, pituitary)-Lung/Respiratory-Lung weights, histopathology (nasoparyngeal tissues, lungs, larynx, trachea)-Reproductive/Developmental-Organ weights (ovaries, testes), histopathology (mammary gland, ovaries, uterus, vagina, testes, epididymis, prostate, seminal vesicles)-Immune/Hematological-Hematology; organ weights (spleen and thymus); histopathology (spleen, thymus, lymph nodes)-Hepatic/Liver-Clinical chemistry (glucose, bilirubin, total cholesterol, triglycerides, phospholipids, AST, ALT, LDH, ALP, total protein, globulin, albumin/globulin ratio); Liver weights, histopathology, electron microscopy; Uninformative	RCC, 1995 5888822

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Octamethylcyclotetrasiloxane (D4)- Parent compound - Short-term (>1-30 days)

Guideline and Animal Species, Strain, Sex	Exposure Route and Exposure Duration	Study-wide POD and Dose/ Concentration(s)	Summary	Major Limitations	Principal Target Organs/Systems and OQD*	HERO ID
Non-guideline study; GLP was not specified. Mouse-CD-1 - [mouse]-Both	Oral-Gavage-Duration: Short-term (>1-30 days)-5-5-day(s) 5 days/week 5 day(s) Animals were dosed via gavage on 5 consecutive days	**POD: 1,700 mg/kg-bw/day (LD50) -Lethality** n= 10 Dose= 0, n= 10 Dose= 1000, n= 10 Dose= 2000, n= 10 Dose= 4000, n= 10 Dose= 8000, mg/kg-bw/day	In a short-term study, CD1 (COBS) mice (5/sex) were administered D4 at doses of 0 (vehicle) 1,000, 2,000, 4,000, and 8,000 mg/kg-day, via gavage in peanut oil, for 5 consecutive days. The gavage volume was 25 mL/kg, which is considered to be excessive. Animals were observed for mortality and clinical signs for 10 days after treatment. Body weights were recorded at study initiation, on the last day of treatment, and on the 5th and 10th days of observation. Deaths occurred in 0/10, 7/10, 10/10, and 10/10 animals in the 1,000, 2,000, 4,000, and 8,000 mg/kg-day groups, respectively. Animals that died were purportedly emaciated. No variations in mortality occurred after 3 days of observation. It was not specified whether any control animals died. Observed clinical signs included diarrhea, and spontaneous hyperactivity (incidences and dose groups not specified). Body weight results were reported in Table 2, which was missing from the study report. The authors used the method of Gragstedt and Lang to determine a 5-day LD50. The LD50 = 1,700 mg/kg-day.	Atypical study design without author justification. Excessive gavage volumes and dosing was used and the study had several reporting deficiencies.	Nutritional/Metabolic-Body weights-Mortality-Mortality-Other (please specify below) (General clinical signs)-Clinical observations (diarrhea, spontaneous hyperactivity, emaciation); Low	Rhone-Poulenc Inc, 1971 5888536
The study was conducted under GLP conditions. Rat-Fischer 344 - [rat]-Both	Oral-Gavage-Duration: Short-term (>1-30 days)-7-28-day(s) 7 days/week 28 day(s) Doses administered daily for 28 days.	**POD: 10 mg/kg-bw/day (NOAEL) -increased relative liver weights in male rats when D4 was delivered in corn oil** n= 10 Dose= 0, n= 10 Dose= 1, n= 10 Dose= 3, n= 10 Dose= 10, n= 10 Dose= 30, n= 10 Dose= 100, n= 10 Dose= 300, mg/kg-bw/day	See footnotes for full summary [32]	Since studies were conducted independently over time, comparisons across studies may be inappropriate.	Nutritional/Metabolic-Body weight, body weight gain and food consumption-Hepatic/Liver-Liver weight; High	Virginia Commonwealth University, 1997 5887620

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Octamethylcyclotetrasiloxane (D4)- Parent compound - Short-term (>1-30 days)

Guideline and Animal Species, Strain, Sex	Exposure Route and Exposure Duration	Study-wide POD and Dose/ Concentration(s)	Summary	Major Limitations	Principal Target Organs/Systems and OQD*	HERO ID
The study was conducted under GLP conditions. Rat-Fischer 344 - [rat]-Both	Oral-Gavage-Duration: Short-term (>1-30 days)-7-28-day(s) 7 days/week 28 day(s) Doses administered daily for 28 days.	**POD: 10 mg/kg-bw/day (NOAEL) -Increased absolute and relative liver weights in female rats** n= 10 Dose= 0, n= 10 Dose= 10, n= 10 Dose= 30, n= 10 Dose= 100, n= 10 Dose= 300, mg/kg-bw/day	See footnotes for full summary [33]	All studies were not conducted simultaneously. The studies were conducted independently over two years in three separate laboratories.	Nutritional/Metabolic-Body weight, body weight gain and food consumption-Hepatic/Liver-Liver weight-Immune/Hematological-Hematology, spleen and thymus weight. Splenic phenotyping, peripheral blood phenotyping; Humoral immunity (IgM response to sheep RBC and antibody plaque assay, and serum antibody titers); cell-mediated immunity (one-way mixed lymphocyte response (MLR) of splenocytes, and peripheral blood leukocytes, natural killer cell activity, macrophage function).; High	Virginia Commonwealth University, 1997 5887620

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Octamethylcyclotetrasiloxane (D4)- Parent compound - Short-term (>1-30 days)

Guideline and Animal Species, Strain, Sex	Exposure Route and Exposure Duration	Study-wide POD and Dose/ Concentration(s)	Summary	Major Limitations	Principal Target Organs/Systems and OQD*	HERO ID
The study was conducted under GLP conditions. Rat-Fischer 344 - [rat]-Both	Oral-Gavage-Duration: Short-term (>1-30 days)-7-28-day(s) 7 days/week 28 day(s) Doses administered daily for 28 days.	**POD: 10 mg/kg-bw/day (LOAEL) -Increased absolute and relative liver weights in both sexes and RBC-related hematological changes** n= 10 Dose= 0, n= 10 Dose= 10, n= 10 Dose= 30, n= 10 Dose= 100, n= 10 Dose= 300, mg/kg-bw/day	See footnotes for full summary [34]	All studies were not conducted simultaneously. The studies were conducted independently over two years in three separate laboratories.	Hepatic/Liver-Liver weight-Immune/Hematological-Hematology, spleen and thymus weight. Splenic phenotyping, peripheral blood phenotyping; Humoral immunity (IgM response to sheep RBC and antibody plaque assay, and serum antibody titers); cell-mediated immunity (one-way mixed lymphocyte response (MLR) of splenocytes, and peripheral blood leukocytes, natural killer cell activity, macrophage function).; High	Virginia Commonwealth University, 1997 5887620

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Octamethylcyclotetrasiloxane (D4)- Parent compound - Short-term (>1-30 days)

Guideline and Animal Species, Strain, Sex	Exposure Route and Exposure Duration	Study-wide POD and Dose/ Concentration(s)	Summary	Major Limitations	Principal Target Organs/Systems and OQD*	HERO ID
The study was conducted under GLP conditions. Rat-Fischer 344 - [rat]-Both	Oral-Gavage-Duration: Short-term (>1-30 days)-7-28-day(s) 7 days/week 28 day(s) Doses administered daily for 28 days.	**POD: 10 mg/kg-bw/day (NOAEL) -increased absolute liver weights in male and female rats** n= 10 Dose= 0, n= 10 Dose= 10, n= 10 Dose= 30, n= 10 Dose= 100, n= 10 Dose= 300, mg/kg-bw/day	See footnotes for full summary [35]	All studies were not conducted simultaneously. The studies were conducted independently over two years in three separate laboratories.	Nutritional/Metabolic-Body weight, body weight gain and food consumption-Hepatic/Liver-Liver weight-Immune/Hematological-Hematology, spleen and thymus weight. Splenic phenotyping, peripheral blood phenotyping; Humoral immunity (IgM response to sheep RBC and antibody plaque assay, and serum antibody titers); cell-mediated immunity (one-way mixed lymphocyte response (MLR) of splenocytes, and peripheral blood leukocytes, natural killer cell activity, macrophage function).; High	Virginia Commonwealth University, 1997 5887620
Non-guideline study; adherence to GLP not specified. Rat-Sprague-Dawley - [rat]-Both	Oral-Gavage-Duration: Short-term (>1-30 days)-4-4-day(s) 4 days/week 4 day(s) Animals were dosed for 4 consecutive days.	**POD: 5 mg/kg-bw/day (NOAEL) -Increased relative liver weights** n= 6 Dose= 0, n= 6 Dose= 1, n= 6 Dose= 5, n= 6 Dose= 20, n= 6 Dose= 100, mg/kg-bw/day	See footnotes for full summary [36]	Missing information on the test substance source and purity results in some uncertainties. This was a focused study that was primarily mechanistic in nature and therefore had a limited scope of relevant systemic endpoints.	Hepatic/Liver-Relative organ weight, Hepatic microsomal levels of CYP enzyme protein expression (CYP 1A1/2, 3A1/2, 2B1/2), NADPH cytochrome P-450 reductase, and PROD and EROD activity.; Medium	Zhang et. al 2000 6835125

* Overall Quality Determination

[1] 7310568: Groups of Cpb;Wu Wistar random rats (10/sex) were exposed, whole body, to aerosolized D4 (purity not reported) at analytical concentrations of 0, 201, 1,004, and 5,074 mg/m3 for 6 hrs/day, 7 days/week, for 4 weeks. An additional 5/sex were included in the control and high-exposure groups and these animals were held for a 14-day recovery period. Animals were monitored for mortality and clinical signs of toxicity. Other endpoints included weekly body weight and food consumption measurements, hematology, urinalysis, clinical chemistry, organ weights, gross necropsy, and limited histopathology (adrenals, heart, kidney, liver, lungs with trachea and larynx, nose, ovaries, spleen, testes, and all gross lesions) in control and high-exposure groups. Only the liver was examined from animals from all groups. It was noted that no particles were detected in the atmospheres and no MMAD or GSD values were reported. No further information was provided, but it is assumed that animals were instead exposed to test substance vapors. No animals died, and there were no exposure-related clinical signs of toxicity.The mean body weights of high-exposure females decreased significantly but slightly (<10%) throughout the exposure period. Food consumption changes were directionally inconsistent and not exposure-concentration related. Hematology measurements were comparable across groups with the exception of a significant decrease in lymphocytes in male rats at 5,074 mg/m3. Significant clinical chemistry changes were reported to be unrelated to exposure concentration or were within normal ranges and of no toxicological significance. No changes in urine parameters were observed. Organ weight changes were limited to a slight, but significant increase in relative (7%) but not absolute liver weights in males, and significant increases in absolute (10%) and relative (16%) liver weights in females at 5,074 mg/m3. Liver weights returned to normal by the end of the recovery period. No gross abnormalities or statistically significant histological changes were identified. However, a non-significant increase in the number of mitotic figures in hepatocytes of males from all exposure groups (0/10, 2/10, 3/10, 4/10) and in mid-and high-exposure females (0/10, 0/10, 3/10, 2/10) was described, and the effect was considered by the authors to be treatment-related. No author-derived toxicity values were provided. Based on the available data, a NOAEC of 1,004 mg/m3 and a LOAEC of 5,074 mg/m3 were identified for this review based on increased absolute and relative liver weights, with some supporting evidence of histological changes in the livers of both sexes.

[2] 5884340: Nine-to-eleven-week-old female Fisher 344 rats (10/group) were exposed to 0, 1, 7.0, 27.5, 68, 142.8, 298.3, 488.4, 701.7, or 888.8 ppm of octamethylcyclotetrasiloxane (D4) 6 hours/day for 5 days via whole-body inhalation. Clinical signs of toxicity were assessed daily. Body weights were measured on the first day of exposure and at termination. Food intake was recorded weekly. Immediately after last exposure (typically within 5 minutes), 4 rats/group were sacrificed and blood, fat and liver were collected to determine D4 content. The remaining 6 rats/group were sacrificed 12-24 hours after the last exposure and livers were weighed and collected to assess CYP2B1/2 activity (7-pentoxyresorufin o-dealkylation; PROD) and content (Western Blot and immunohistochemistry). A positive control group was included in which rats were treated with phenobarbital (0.05% w/v) in drinking water for 5 days. No clinical signs of toxicity were observed. Terminal body weights were not significantly different from control. Food intake in the 888.8 ppm group was significantly decreased 11% compared to control, although no significant decreases in body weight were seen compared to control. Relative liver weights were significantly increased (8.5%, 10.9%, 15.5%, 20.7%, and 24.0%) at 142.8, 298.3, 488.4, 701.7, and 888.8 ppm, respectively. Significant increases in CYP2B1/2 activity (1.6-fold, 6.8-, 12.4-, 18.1-, 25.0-, 28.7-, 26.0-, and 21.3-fold) and CYP2B1/2 protein expression (1.3-, 4.6-, 10.8-, 58.6-, 73.0-, 83.5-, 86.7-, 87.3-fold) were seen at 7.0, 27.5, 68, 142.8, 298.3, 488.4, 701.7, and 888.8 ppm. Immunohistochemistry CYP2B staining was dose-related and reported to be moderate at 70 ppm with centrilobular to midzonal expression. At 700 and 900 ppm, there was extensive CYP2B staining occurring in all regions of the liver expanding into the hepatic lobule. Total D4 in plasma, fat and liver increased with increasing exposure concentration with greatest concentration at 888.8 ppm found in fat, followed by liver and the lowest in plasma. Positive controls gave expected results.

[3] 5884497: In a repeated-dose inhalation toxicity pilot study, Fischer 344 rats (24/sex/group) were whole-body exposed to the test substance, D4 (purity: 99.8%), at target concentrations of 0 (control), 70, and 700 ppm, for 6 hours/day, 5 days/week, for up to 28 days. Interim sacrifices were performed on exposure day 3, 7, 14, or 21 (3/sex/group), on exposure day 28 (6/sex/group), or on post-exposure day 7 or 14 following 28 days of exposure (3/sex/group). Controls were exposed to filtered room air without test substance. Analytically determined concentrations for the 70 and 700 ppm exposure levels ranged from ~68-72 ppm and ~501-726 ppm (mean daily concentrations are reported in Table 11 of the study report; however, some values in the table are illegible). Intra-assay positive control animals were administered phenobarbital (80 mg/kg) via intraperitoneal injection for four consecutive days (except for 14-day recovery group animals, which received treatment for 2 days) prior to sacrifice. [Note: The study authors stated that enzyme activities for positive control-treated animals were not compared to those for animals exposed to D4 and thus were not included in the summary results tables; results are provided in appendices of the study report.] Animals were observed daily for clinical signs of toxicity (including but not limited to respiratory, nasal, behavioral, and ocular changes) and morbidity/mortality checks were performed once or twice daily. Body weights were determined on study day 1 and then every 7 days during the study. Absolute and relative liver weights were determined at necropsy. Concentrations of total protein, total P450, and CYP4A, activities of selected P450 enzymes (7-ethoxycoumarin-O-deethylase [ECOD], 7-ethoxyresorufin O-deethylase [EROD], 7-pentoxyresorufin O-depentylase [PROD]), and NADPH-cytochrome c reductase activity in hepatic microsomal preparations were determined. Concentrations of cytosolic alpha-glutathione-S-transferase (alpha-GST) were also measured. The CYP2B1inhibitor 9-ethynylphenanthrene (9EPH) was tested to further evaluate the mechanism of effects of D4 on PROD and EROD activity.No treatment-related clinical signs of toxicity or mortalities were observed during the study. Mean final body weights were slightly, but not significantly decreased in males at 700 ppm (-3 to 9%) and in females at both concentrations (-2 to 6%) compared to controls; the decreases attained statistical significance only for females exposed to 700 ppm and sacrificed on day 14 (-6%). Statistical and biologically relevant changes in relative liver weights were observed in both sexes. Relative liver weights in males were increased 16% (non-significant), 10%, and 14% on days 3, 21, and 28, respectively, at 700 ppm. Relative liver weights in high exposure females were maximally increased by 20% by day 14 and were increased 9.1% (non-significant) and 20.1% on days 21 and 28, respectively. The only significant relative liver weight changes in the 70 ppm group was a 13% increase in females on day 14. Absolute liver weights were not reported. Relative liver weights remained elevated in 7-day recovery males (non-significant increases of 11% and 20.4% at 70 and 700 ppm, respectively), and females (12%), compared with controls, but returned to normal by recovery day 14. Total cytochrome P450 levels in liver microsomes (measured on exposure day 14) were significantly increased in both sexes at 700 ppm and in males only at 70 ppm. NADPH-cytochrome c reductase activity (measured on exposure day 28) was significantly increased in males only at 700 ppm. In males, significant increases in enzyme activities of ECOD, EROD, and PROD were observed at 70 and 700 ppm at all interim sacrifice time points (exposure days 3, 7, 14, 21, and 28), compared to controls. Similarly, in females, enzyme activities of ECOD, EROD, and PROD were significantly increased for most exposure time points at both concentrations (except for ECOD at 70 ppm on days 3, 7, and 14). In recovery group animals, ECOD activities were similar to control values by post-exposure day 14 in both sexes. However, PROD activity remained significantly increased at 700 ppm in recovery animals of both sexes sacrificed on post-exposure day 14, and EROD activity remained significantly increased at 700 ppm in males only. No significant changes in CYP4A or alpha-GST protein (both measured on exposure day 28) were observed at either concentration in males or females, suggesting that D4 is not a peroxisome proliferator. PROD and EROD activity assays conducted with 9EPH indicated that the increase in PROD activity was primarily due to CYP2B1/2 and that the modest increase in EROD was not due to CYP2B1/2 metabolism of 7-ethoxyresorufin. A POD was not reported by the study authors. The LOEC (determined by the reviewer) is 70 ppm based on liver effects including a biologically significant increase in relative liver weights in females and increases in liver enzyme activities and protein levels. Statistically significant increases in liver weights were observed in the highest exposure group. A NOEC was not determined.

[4] 5885339: In a palatability study, study authors tested octamethylcylcotetrasiloxane (D4) in five different emulsifier/vehicle combination and in reconstituted powdered milk to determine if any solution would increase the palatability of D4. Adult Sprague-Dawley rats (3-4/group, sex not specified) were exposed to emulsified D4 at the following administered doses with respective combinations of water emulsifiers/vehicles: 0% with tween 80 + glycomal L, 1.25% with tween 80+ sorbitol laureate, 2.50% with tween 20 + glycomal L, 2.50% with tween 20 + span 80, and 2.50% with reconstituted powered milk administered through in their water ad libitum for 3 days. Controls groups received water, emulsions, or reconstituted powdered milk alone, without D4. Water consumption over the 3-day exposure period was assessed.Decreased water consumption was seen in some emulsion controls compared to water alone. Water consumption was similar in the reconstituted powdered milk, and the Tween 80 + sorbitol laureate control groups compared with water alone (within 8% of water control). More substantial decreases were seen in the tween 80 + glycomal L (62%), tween 20 + glycomal L (35%), tween 20 + span 80 (65%), and tween 80 + span 80 (30%) control groups, compared to water alone. These data suggest that some emulsion solutions alone decreased palatability of the water.The addition of D4, significantly reduced water consumption in all treatment groups compared to water alone and the respective control. The authors concluded that emulsified D4 was not palatable in any of the emulsion/vehicle combinations examined or in powdered milk. The 1.25% D4 in tween 80 + sorbitol laureate group had the highest palatability of all combinations examined, but the overall water consumption was still significantly less than the water control (by a 28% reduction), whereas the 2.50% in tween 20 + span 80 group had the lowest palatability (95% reduction in water consumption). In other groups, the following decreases in water consumption were seen: 2.5% in tween 20 + glycomal L (89%); 2.5% in tween 80 + span 80 (90%); and 2.5% in reconstituted powder milk (80%), compared to water alone.No author reported toxicity values are available. Based on the available data, a LOAEL of 1.25% was determined for nutritional/metabolic effects due to decreased water consumption. No NOAEL could be determined.

[5] 5887598: Fisher 344 rats (15/sex/group) were exposed to nominal concentrations of 0, 7, 20, 60, 180 and 540 ppm of octamethylcyclotetrasiloxane (D4) via whole body inhalation 6 hours/day, 5 days/week for 28 days. The average analytical concentrations were 0, 7.0, 20.2, 56.7, 178.1, and 529.5 ppm, respectively. One set of animals (10/sex/group) were sacrificed the day after the last exposure, while another group (5/sex/group) was allowed to recover for 14 days prior to sacrifice. Endpoints evaluated included mortality, clinical signs (respiratory, dermal, behavioral, nasal, or ocular changes), body weight, body weight gain, food consumption, hematology, serum chemistry, urinalysis, gross pathology, organ weights (liver, lung, spleen, thymus, adrenals, ovaries/testes, heart, kidneys, and brain), and histopathology on a complete panel of 45 tissues or organs.No deaths occurred. Females in the 529.5 ppm group had increased incidences of urine staining (12/15), drainage near the eyes (12/15) and opacity of eyes (7/15) compared to controls (4/15, 0/15, and 3/5, respectively). These clinical signs were not observed in males in a dose-related manner. No significant differences in body weights, or body weight gain were observed, compared with controls. Food consumption was transiently decreased in the 7 and 178 ppm groups during week; however, this was not considered to be toxicologically relevant. Changes in hematological parameters seen in terminal and 14-day recovery animals were marginal and within normal range. Observed changes in serum chemistry included decreased triglycerides in high-exposure males, and increased total cholesterol, ALT, and globulin in females at 529.5 ppm. Serum glucose was generally decreased in exposed females,

significant at 20.2, 178.1, and 529.5 ppm. Decreases in BUN and ALP were not considered to be toxicologically relevant. No significant differences in urinalysis endpoints were seen, compared to controls. There were no exposure related gross pathological changes. Significant increases in liver weights were observed in males at ≥178.1 ppm and in females at ≥20.2 ppm. In the 529.5 ppm group, significant increases in absolute and relative liver weights were 16% and 17% in males and females 30% and 27% in females, respectively, compared with controls. At 178.1 ppm, increases were 8% (absolute) and 11% (relative) in females, and 8% (relative) in males. At the lower concentrations, increases in absolute and relative liver weights in females were statistically significant, but low in magnitude (<10%). The increases in liver weights were reversible and no significant difference in liver weights were seen after the 14-day recovery period. No other organ weights were significantly different compared to controls. An increase in the severity of hyaline droplets in the proximal convoluted tubules of the kidneys was observed. The morphology was consistent with alpha-2u globulin nephropathy; however, no specific tests were performed to confirm this. No compound-related histological changes were seen in any group compared to controls. The study authors reported a NOEL of 7.0 ppm for females and 178.1 ppm for males, based on hepatomegaly. A NOAEC of 56.7 ppm and a LOAEC of 178.1 ppm was determined based on biologically relevant increased relative liver weight in female rats in the absence of supporting histopathology.

[6] 5887837: In a repeated-dose inhalation toxicity study, Fischer 344 rats (24/sex/group) were whole-body exposed to the test substance, D4 (purity: 99.8%), at target concentrations of 0 (control), 70, and 700 ppm, for 6 hours/day, 5 days/week, for up to 28 days. Interim sacrifices were performed on exposure day 3, 7, 21, and 28 (3/sex/group); on exposure day 14 (6/sex/group); and in recovery group animals (3/sex/group) on post-exposure day 7 or 14 following 28 days of exposure. Controls were exposed to filtered room air without test substance. Analytically determined concentrations for the 70 and 700 ppm exposure levels ranged from ~67-75 ppm and ~659-732 ppm (mean daily concentrations are reported in Table 20 of the study report; however, some values in the table are illegible). Intra-assay positive control animals were administered phenobarbital (80 mg/kg) via intraperitoneal injection for two to three days prior to sacrifice. Animals were observed daily for clinical signs of toxicity (including but not limited to respiratory, nasal, behavioral, and ocular changes) and morbidity/mortality checks were performed once or twice daily. Body weights were determined on study day 1 and then every 7 days during the study. Absolute and relative liver weights were determined at necropsy. Concentrations of total P450, activities of selected enzymes, and cytochrome P450 protein levels (cytochrome P450's CYP2B1/2, CYP3A1/2, CYP4A) were evaluated in hepatic microsomal preparations. alpha-Glutathione-S-transferase [alpha-GST]) protein levels in hepatic cytosol were also measured and hepatic epoxide hydrolase mRNA and protein levels were determined. No treatment-related clinical signs of toxicity or prescheduled mortalities occurred during the study. No significant changes in mean final body weight were observed in males or females. Relative (to body weight) liver weights in males and females were significantly increased compared to the corresponding controls in 700 ppm group males (9-15%) and females (13-17%) sacrificed on day 7 and 14, and in 700 ppm group males only sacrificed on day 28 (19%). No significant differences in relative liver weights were observed in recovery males or females sacrificed on post-exposure day 7 or 14 at 700 ppm, or on any exposure day at 70 ppm. Total cytochrome P450 levels and NADPH-cytochrome c reductase activity in hepatic microsome preparations (measured on exposure day 28) were significantly increased in both sexes at 70 ppm and in males only at 700 ppm. In both males and females, significant increases in enzyme activities of ECOD (measured on exposure days 3 and 28) were observed at 70 and 700 ppm in hepatic microsomes. There were also significant increases in EROD and PROD in both sexes at both 70 and 700 ppm on all exposure days measured (exposure days 3, 7, 14, 21, and 28; recovery days 7 and 14), except for recovery days 7 and 14 at 70 ppm. For analyses of protein levels, there were also significant increases in CYPA1/2 protein in hepatic microsomes (measured by ELISA on exposure day 28) in both sexes at 700 ppm, and in females only at 70 ppm. When samples taken on exposure days 3 and 28 were evaluated by Western blotting, CYPA1/2 protein in hepatic microsomes was significantly increased in males and females at 700 ppm, and in males only at 70 ppm. Testosterone 6-beta-hydroxylase activity in hepatic microsomes (measured on exposure days 3 and 28) was significantly increased in males at 70 and 700 ppm on both days, in females at 700 ppm on both days, and in females at 70 ppm only on day 28. No significant changes in 12-or 11-hydroxylation of lauric acid (indicator of CYP4A and CYP2E1 activity, respectively), CYP4A protein, or alpha-GST protein (all measured on exposure day 28) were observed at either concentration in males or females. Hydroxylation of para-nitrophenol (indicator of CYP2E1 activity, measured on exposure day 28) and epoxide hydrolase mRNA levels (measured on exposure day 28) were significantly increased in males and females at 700 ppm and in females only at 70 ppm. Hepatic epoxide hydrolase protein levels and hepatic epoxide hydrolase activity toward cis-stilbene oxide in microsomes (both measured on exposure day 28) were significantly increased in males and females at 70 and 700 ppm. UDPGT activity toward chloramphenicol in hepatic microsomes (measured on exposure day 28) was significantly increased in both sexes only at 70 ppm; no significant changes in UDPGT activity toward para-nitrophenol (also measured on exposure day 28) were observed in males or females. There were no significant effects in PROD activity in lung microsomes (exposure days 3, 14, 21, and 28; recovery day 14) or 9EPH inhibition of lung PROD activity. A POD was not reported by the study authors. The LOEL (determined by the reviewer) is 70 ppm based on mechanistic liver effects (changes in liver enzyme activity and protein levels). The LOEL based on apical and mechanistic effects is 700 ppm based on increases in relative liver weights and changes in liver enzyme activities and protein levels. [Reviewer note: Some results tables in HERO ID 5887837 include combined test data from HERO ID 5887837 and HERO ID 5884497. HERO ID 5884497 was evaluated independently.]

[7] 5897286: In a short-term study, conducted as a follow-up of a previous study, female New Zealand White Rabbits (6 rabbits/group), were exposed via gavage to octamethylcyclotetrasiloxane (purity 99.8%) at doses of 0, 500, or 1,000 mg/kg/day, 7 days/week for 14 days. Animals were observed for clinical signs of toxicity, behavioral abnormalities, and mortality. Body weights were recorded weekly and food consumption was measured every two days. All animals were subjected to gross necropsy, and organ weights (liver and brain) were recorded.One animal in the 500 mg/kg/day treatment group died, due to a "gavage-related error." Clinical signs of toxicity were observed among treated animals and included decreased feces and concentrated urine; however, the incidence of these clinical signs among the 500 and 1,000 mg/kg/day groups was not provided. Body weights and food consumption were significantly decreased in both treatment groups relative to controls, but the changes were not consistently dose-related. Body weights were reduced at week 1 and at termination by 20-22% at 500 mg/kg/day group and 16-20% at 1000 mg/kg/day, compared with controls. Throughout the study period, low-dose animals showed greater reductions in food consumption (59-93%) than high-dose animals (34-77%), from controls. Food consumption reductions suggest palatability issues, which is consistent with the previous study noted above, and the subsequent weight loss is expected to confound the results for other endpoints measured. Significant increases in relative, but not absolute liver weights (19% and 29% at 500 and 1000 mg/kg/day, respectively) were considered to be secondary to body weight changes. No changes in absolute or relative brain weights were observed. Gross changes were also reflective of body weight loss and stress and included a marked decrease in thymus gland size in all animals at 500 mg/kg/day and in 4 out of 6 animals at 1000 mg/kg/day. Spleens and lymph nodes appeared smaller in size in some animals, but the decreases were not significant. Marked reductions in body fat were observed in 1 animal of the 500 mg/kg/day group and 2 animals of the 1000 mg/kg/day group. 1000 mg/kg/day animals exhibited structural changes in the liver at an increased incidence compared to the controls, including accentuated lobular pattern (3/6 animals), pale areas (3/6 animals), friable liver (2/6 animals), and decreased liver size (2/6 animals). Brown urine was also observed at necropsy in 2 animals of the 500 mg/kg/day group and 1 animal of the 1000 mg/kg/day group. No author-reported toxicity values were provided. A POD for this study was not determined due to confounding palatability issues that rendered this study unacceptable.

[8] 5897618: In a subchronic, repeated dose oral toxicity study, male CD (Sprague-Dawley derived) rats (10 males/group) were administered Octamethylcyclotetrasiloxane (D4; purity ~98%) via gavage in 0.5% methylcellulose in distilled water at doses of 0 or 1600 mg/kg/day for 2 weeks. Rats were observed once a day during the exposure period for mortality. After the exposure period, rats were euthanized by perfusion fixation and livers were dissected, weighed, and sectioned for histopathology and morphometrics (the total number of cells in each liver, the number of cells per mm^3 of liver, and the hepatocyte profile diameter (centrilobular, midzonal, and perilobular) examination. One rat in the control group died during anesthesia prior to perfusion fixation and was exempt from examination. Absolute and relative liver weights of treated rats were significantly increased by 41% and 45%, respectively, compared to controls. Hepatic histopathological lesions were observed including: inflammation was noted in 6/10 treated animals compared to 1/9 in controls and vacuolation in 5/10 treated , compared with 1/9 in controls. The study authors stated that histopathological changes observed in the livers of the treated group were not treatment-related and were normal findings for rats of this age and strain. The number of cells per mm^3 of liver and hepatocyte profile diameter (centrilobular, midzonal, and perilobular) were not significantly different between the control and treated groups. The total number of cells per liver was significantly

increased (by 31%) in treated rats compared to control rats. This suggests that the increase in liver weight is due to hyperplasia, rather than hypertrophy No author-reported toxicity values were provided. Based on the data presented in the study, a LOAEL of 1600 mg/kg/day was identified for male CD rats based on significantly increased absolute liver weights, relative liver weights, and total number of cells per liver among the treated group.

[9] 5900289: Male and female Charles River CD (Sprague-Dawley) rats (8/sex/group) were treated with 0, 25, 100, 400, or 1,600 mg/kg/day of octamethylcyclotetrasiloxane (D4) via gavage in methocel vehicle for 5 days/week for 2 weeks. Animals were monitored for mortality and clinical signs of toxicity (weekdays only). Body weights were measured one day prior to the start of the study, on day 7 and just before termination. At the end of the experiment, animals were sacrificed; livers were harvested and weighed, and all animals were necropsied. The authors used multiple statistical tests to analyze liver weight data, including ANOVA and TGXSTAT system statistical packages (including linear contrasts, Welch trend test with and without logarithmic transformation, and Jonckheere's test for trend). 2/8 females died at 1600 mg/kg/day, but the deaths were attributed to a dosing error. There were no behavioral changes or overt signs of toxicity. Five additional animals (group or sex not specified) showed lesions consistent with gavage accidents (no additional details provided). These same animals also had slight to severe reductions in terminal body weights. Based on individual animal data provided in the report, these appear to be 1 male each in the 100 and 1,600 mg/kg/day groups, and 1 female each in the 25, 400, and 1,600 mg/kg/day groups. Significantly decreased terminal group mean body weights (which include data from the gavage accident animals noted above) were observed at 1600 mg/kg/day (by 17% in males and 12% in females). When gavage accident animals are excluded from the datasets (conducted for this review), the magnitudes of change are 14% in males and 9% in females. Day 7 body weights were not reported. Relative liver weights were increased in males by 9, 7, 27, and 39% at 25, 100, 400, or 1,600 mg/kg/day, respectively, reaching statistical significance at all doses except 100 mg/kg/day. Compared to controls, absolute liver weights in males showed no dose response but were significantly increased by 22% and non-significantly increased 14% at 400 and 1,000 mg/kg/day, respectively. In females, clear dose-related increases in relative liver weights were (9.7-39%) at $\geq$25 mg/kg/day. Absolute female liver weights were increased 8, 17, 24, and 24% at 25, 100, 400, and 1,000 mg/kg/day, respectively. Statistical significance for these changes depended on the test used; however, the statistical tests were not specified in some data tables. One unspecified test, but not others reported significant changes ($P < 0.05$) in both absolute and relative liver weights at 25 mg/kg/day, and the authors noted that there was a positive "appearance of a response trend through the lowest dose group in both male and female rats." Based on the sample sizes provided, the animals experiencing "gavage accidents" were included in the statistical analysis. The study authors considered the significance (biologic and toxicologic) of liver weight changes at 25 mg/kg/day to be unclear. The magnitude of change of relative liver weights in females at 25 mg/kg/day was 9.7% which is borderline for being considered biologically relevant. Beyond the identification of unspecified lesions suggestive of gavage accidents in 5 animals, two animals (dose/sex not reported) had liver lesions that the authors stated were spontaneous. Gross necropsy data were not shown.Based on the conclusions presented, the author reported LOAEL was 100 mg/kg/day based on increased relative liver weights in females, and a clear NOAEL was not determined.

[10] 7310071: Female Fisher 344 rats (10/group/time point) were exposed to 0 or 700 ppm octamethylcyclotetrasiloxane (D4) via whole-body inhalation 6 hours/day, 5 days/week for up to 4 weeks. Interim sacrifices were made on days 6 and 13. Six days prior to each sacrifice, rats were implanted with a BrdU mini osmotic pump that delivered BrdU continuous subcutaneously. Rats were monitored for mortality and clinical signs of toxicity daily. Body weight and food and water consumption were assessed weekly. Other endpoints evaluated included gross necropsy, organ weights (liver, and thyroid), proliferation of liver and thyroid (BrdU staining and PCNA) and lung (BrdU staining), and liver hypertrophy (as measured by a reduction in the number of nuclei within a fixed microscopic field size). A positive control group was included in which animals were provided drinking water containing 0.05% phenobarbital. No animals died during the exposure period. Increased incidences of urine staining on the perineal region (21/30 compared to 14/30 in controls) and clear fluid around the eyes (8/30 compared to 1/10 in controls) were seen in exposed rats compared to control. Body weights were slightly, but significantly decreased (-4%) at day 6 compared to control but returned to control levels for the remainder of the study. Food and water consumption were not different from control. Absolute and relative liver weight were significantly increased on day 6 (14 and 18%), day 13 (19 and 20%) and day 27 (20 and 22%), respectively, compared to controls. Absolute and relative thyroid weights were significantly increased on day 13 (18 and 19%) and day 27 (15 and 18%) respectively, and relative thyroid weight on day 6 (18%), compared to control. Hepatic cell proliferation was significantly increased on day 6 (3-fold, assessed by BrdU labeling; and 4-fold assessed by PCNA staining) and day 13 (2-fold assessed by PCNA staining) compared to control. No difference in proliferation was seen on day 13 via BrdU labeling or at day 27 by either method. In the liver, the number of nuclei per microscopic field (measure of hypertrophy) was significantly decreased (9, 15, and 11%) and days 6, 13, and 27, respectively compared to controls, indicating an increase in hypertrophy. Thyroid cell proliferation (BrdU incorporation) was increased on day 6 (7-fold) and day 13 (5-fold) and was similar to control levels at day 27. No BrdU staining was seen in the lungs. The positive control gave expected results.A LOAEC of 700 ppm was identified for increased liver and thyroid weights and hepatic and thyroid cell proliferation.

[11] 7310071: Female Fisher rats (10/group) were exposed to 0, 7, 30, 70, 150, 300, or 700 ppm octamethylcyclotetrasiloxane (D4) via whole-body inhalation 6 hours/day for 5 days. Actual concentrations were 7, 29, 70, 150, 300, and 701 ppm, respectively. Animals were implanted subcutaneously with a mini osmotic pump the day before exposure began, which continuously delivered BrdU. Rats were monitored for mortality and clinical signs of toxicity daily. Endpoint evaluated included body weight, food and water intake, gross necropsy, organ weight (liver and thyroid), cell proliferation of the liver (BrdU staining and PCNA) and thyroid (BrdU staining).No animals died during the exposure period. Increased incidences of urine staining on the perineal region was seen at 701 ppm (3/10) compared to control (0/10). Body weights were slightly, but significantly decreased (-4%) in the 701-ppm group compared to control. No significant differences in food or water intake were seen compared to control, except for a 13% decrease in water consumption at 701 ppm. Absolute liver weights were significantly increased 10, 13, and 13% at 150, 300 and 701 ppm, respectively. Relative liver weights were significantly increased 6, 8, 12, and 18% at 70, 150, 300, and 701 ppm, respectively. No differences in absolute or relative thyroid weights were seen compared to control. In the liver, BrdU labeling was significantly increased at 70 ppm (2-fold), 150 ppm (3-fold), 300 ppm (3-fold), and 701 ppm (4-fold) compared to control. Similarly, significant increases in PCNA labeling were seen at 7 ppm (2-fold), 70 ppm (2-fold), 150 ppm (3-fold), 300 ppm (4-fold) and 701 ppm (4-fold) compared to control; no increase was seen at 29 ppm. In the liver, the number of nuclei per microscopic field (measure of hypertrophy) was not significantly different from control. No significant difference in thyroid BrdU labeling was seen compared to control. A NOAEC of 29 ppm and a LOAEC of 70 ppm were identified for increased liver weight and hepatic cellular proliferation.

[12] 7310077: In a short-term oral toxicity study, female Fischer 344 rats (8 rats/group) were exposed via oral gavage to octamethylcyclotetrasiloxane (D4; purity $\geq$99%) at doses of 0 or 301 mg/kg/day, 7 days/week for 14 continuous days. Animals were observed for mortality, morbidity, and moribundity during the study period (twice daily on weekdays and once daily on weekends) as well as clinical signs (once daily). Body weights were recorded on days 1, 8, and 15. Food consumption was measured on days 1, 8, and 15. Stomach and liver weights were recorded following euthanasia. Macroscopic observations of the liver and stomach tissue were made following gross necropsy. Stomach tissue was formalin fixed for microscopic examination by histopathological analysis. The liver was split in half and used in determining liver D4 content and preparing microsomes. Microsomal protein, total microsomal cytochrome P450, microsomal NADPH cytochrome C reductase, microsomal enzymatic activity (PROD, BROD, EROD, and MROD), and CYP1A1/2, CYP2B1/2, CYP3A1/2, CYP4A1-3, and epoxide hydrolase protein content were measured in the liver microsomes. No animals died during the study period. Treated rats exhibited a low incidence (1/8 or 2/8 rats of the treated group) of porphyrin staining and clear fluid around the eyes. There were no statistically significant treatment-related effects observed on body weight or body weight gain. Food consumption was statistically significantly increased (10% increase relative to control group) in treated rats from day 8-15. Treated rats exhibited a statistically significant increase in absolute (59%) and relative (59%) liver weight. There were no statistically significant treatment-related effects observed on stomach weight in treated rats. Macroscopic observations of the liver included a hepatodiaphragmatic nodule among one treated rat. Total microsomal cytochrome P450 was unchanged in treated rats as compared to controls. Microsomal NADPH cytochrome C reductase activity was increased 142% in both treated rats relative to controls. Treated rats exhibited a statistically significant increase (61%) in microsomal EROD activity and a statistically significant decrease (37%) in microsomal MROD activity. There was also a reduction (69%) in CYP1A protein among treated rats, however, this change was not statistically significant. Treated rats exhibited a statistically significant increase in microsomal PROD and BROD activities, as well as an increase in CYP2B protein as compared to the undetectable level in controls. Treated rats exhibited

decreased CYP4A and increased microsomal epoxide hydrolase and CYP3A relative to controls. However, statistics were not performed to determine whether these changes were statistically significant. Liver D4 content of treated rats was increased relative to control rats in which liver D4 content was undetectable. No author-reported toxicity values were provided. Based on the data presented in the study, a LOAEL of 301 mg/kg/day was identified for rats based on a significant increase in food consumption and liver weight (absolute and relative) and changes in microsomal enzymatic activity. A NOAEL was not identified.

[13] 7310077: In a short-term oral toxicity study, female Hartley guinea pigs (8 /group) were administered octamethylcyclotetrasiloxane (D4; purity ≥99%) via gavage in corn oil at doses of 0 or 301 mg/kg/day for 14 continuous days. A positive control using phenobarbitol was also included. Animals were observed for mortality, morbidity, and moribundity twice daily on weekdays and once daily on weekends and clinical signs once daily. Body weights and food consumption were measured on days 1, 8, and 15. Animals were sacrificed on day 15 and gross necropsy was performed followed by macroscopic observations of the liver and stomach tissue. Organ (stomach and liver) weights were recorded and evaluated for histopathology. Additional evaluations include liver D4 content and microsome isolation for enzyme analysis (total microsomal protein, total cytochrome P450, NADPH cytochrome C reductase, enzymatic activity (PROD, BROD, EROD, and MROD), and enzyme levels of CYP1A1/2, CYP2B1/2, CYP3A1/2, CYP4A1-3, and epoxide hydrolase). No animals died during the study period. Clinical signs were comparable to the controls. Body weight was unchanged with treatment, however, the study authors note that there was large intragroup variability in body weights. Body weight gain was significantly reduced from days 8-15 when compared to controls. Treated guinea pigs displayed a statistically significant decrease (35%) in food consumption from day 11-15 and an overall significant decrease (25%) in food consumption throughout the duration of the study period. There were no statistically significant treatment-related effects observed on absolute or relative liver or stomach weights. There were no treatment-related effects on gross necropsy. Changes in liver microsomal enzymes include: increased NADPH cytochrome C reductase activity, CYP2B, and epoxide hydrolase; and decreased CYP1A. No effects were observed on total protein, PROD, BROD, EROD or MROD activity. CYP3A and CYP4A were not detected, speculated by the study authors to be due to experimental error.No author-reported toxicity values were provided. A NOAEL of 301 mg/kg/day was identified for guinea pigs based on no significant effects. A LOAEL was not identified.

[14] 7310562: In a short-term, repeated dose inhalation toxicity study, male and female LVG Golden Syrian hamsters (10/sex/group) were exposed via whole body inhalation in a dynamic chamber to octamethylcyclotetrasiloxane (D4; purity ≥97%) at concentrations of 0 or 697 ppm 6 hours/day, 7 days/week for 28 days. Animals were observed frequently during exposures (exact timing not reported) and daily during the postexposure period for mortality and clinical signs of toxicity (respiratory, dermal, behavioral, nasal or ocular changes). Other endpoints evaluated included body weights (initial, every fourth day, and terminal), food consumption (every fourth day), gross necropsy, and organ weight and histopathology on liver, lungs, trachea (histopathology only), kidneys, spleen, and testes. No animals died during the exposure period. No treatment-related changes in clinical signs were observed; study reports “all test animals appeared normal and their behavior was fully compatible with their respective control (details not provided). No significant differences in body weights, body weight gain or terminal body weights were seen compared to control (body weight gain in males tended to be lower). No significant difference in food consumption was seen compared to control in either sex. No treatment-related gross macroscopic changes were observed. Relative liver weights in females were significanlty increased (16%) compared to control; absolute liver weights were not different from control. Relative testes weights were significantly increased (22%) compared to control; absolute testes weight was not different from control. There were no other treatment-related changes in absolute or relative organ weights. No treatment related histological changes were observed compared to control. No author-reported toxicity values were provided. A LOAEL of 697 ppm was identified for hamsters based on significantly increased relative liver weights in females and significantly increased relative testes weights in males. A NOAEL was not identified.

[15] 7310562: In a short-term, repeated dose inhalation toxicity study, male and female CD-1 Swiss mice (10 /sex/group) were exposed via whole body inhalation in a dynamic chamber to octamethylcyclotetrasiloxane (D4; purity ≥97%) at concentrations of 0 or 697 ppm 6 hours/day, 7 days/week for 28 days. Animals were observed frequently during exposures (exact timing not reported) and daily during the postexposure period for mortality and clinical signs of toxicity (respiratory, dermal, behavioral, nasal or ocular changes). Other endpoints evaluated included body weights (initial, every fourth day, and terminal), food consumption (every fourth day), gross necropsy, and organ weights and histopathology on liver, lungs, trachea (histopathology only), kidneys, spleen, testes, and skin (histopathology only). No animals died during the exposure period. No treatment-related changes in clinical signs were observed; study reports “all test animals appeared normal and their behavior was fully compatible with their respective control (details not provided). No significant differences in body weights, body weight gain or terminal body weights were seen compared to control. Mean food consumption was statistically significantly increased on day 27 in males (11% increase) and day 11 (8% increase) in females; however no differences in the average daily food intake were seen compared to control. No gross macroscopic changes were observed. Significantly increases in absolute (12% and 34%) and relative (16% and 30%) liver weights were seen in males and females, respectively, compared to control. No other treatment-related changes in organ weights were observed. No treatment-related histological changes were observed. No author-reported toxicity values were provided. Based on the data presented in the study, a LOAEL of 697 ppm was identified for mice based increased absolute and relative liver weights. A NOAEL was not identified.

[16] 9653974: In a short-term range-finding study, groups of SD rats (5/sex/group) were administered dimethylsilanediol at doses of 0, 300, 600, 1,200 mg/kg/day via gavage for 14 days. Animals were evaluated for mortality and clinical signs of toxicity daily during exposure. Body weights and food consumption were measured weekly (on days 1, 8, and 15), and body weight gains were determined. After sacrifice, a gross necropsy was performed and organs were excised and weighed (liver, thymus, adrenal gland, brain, epididymides, heart, kidney, spleen, testes, and ovaries).One male in the 1,200 mg/kg/day group was found dead on study day 10, the death was attributed to an injury and not test substance-related. No other deaths occurred. Clinical signs were observed in males and females in the 1,200 mg/kg/day group and included noisy respiration, soiling, and hypoactivity. Body weights were significantly decreased in males (10%) at 1,200 mg/kg/day. High-dose males also showed significant reductions in body weight gains (~46%) throughout the entire study period. Female body weight changes did not reach statistical significance but were decreased by ~46% relative to controls. Male food consumption was decreased during week 1 at 1,200 mg/kg/d. Female Significant decreases in food consumption in females occurred at ≥600 mg/kg/day during week 2. Relative liver weights were significantly increased in all treated groups: 13, 32, 59% in males, and 24, 43, 79% in females at 300, 600, and 1200 mg/kg/day, respectively. Absolute liver weights at 300, 600, and 1,200 mg/kg/day, respectively, were increased (by 12, 29, and 42% in males and 19, 35, and 67% in females) reaching statistical significance at ≥ 600 mg/kg/day. Absolute heart weights were decreased by 11% and 18% in females at 600 and 1,200 mg/kg/day, respectively, reaching statistical significance at 1,200 mg/kg/d. Absolute and relative thymus weights were significantly reduced in males of the 1,200 mg/kg/day group by 53% and 48%, respectively.As this was a range-finding study, the authors did not derive a NOAEL. A LOAEL of 300 mg/kg/day was determined based on increased absolute and relative liver weights.

[17] 99288: Young and mature (retired non-pregnant breeders with 4-5 previous pregnancies) female Sprague-Dawley rats (4/group) were exposed to 0, 5, 20 or 100 mg/kg/day of octamethyltetracyclosiloxane (D4) via gavage in corn oil vehicle for 8 consecutive days. A 1 mg/kg/day group was mentioned once in the study text; however, no data were reported and it is presumed to be reported in error. Body weights were measured daily but were not reported in the results. At the end of the experiment, animals were sacrificed, and livers were extracted and weighed. Data for relative liver weights were presented. Several mechanistic endpoints, including microsomal pentoxyresorufin O-deethylation (PROD) and 7-ethoxyresorufin O-deethylation (EROD) activity and CYP1A1/2, CYP2B1/2, CYP3A1/2 protein expression.No significant difference in relative liver weights was observed in the young rats. Significantly increased relative liver weight (by ~21%) was observed at 100 mg/kg/day in the mature rats only. Increased EROD activity (typically an indicator of CYP1A1/2 activity) was observed at ≥20 mg/kg/day in mature rats, whereas no difference was observed for young rats. The increases did not correspond with increases in CYP1A1/2 protein expression suggesting EROD activity is likely not specific to CYP1A1/2. Increased PROD activity (an indicator of CYP2B1/2 activity) was observed at ≥20 mg/kg/day in young rats and at ≥5 mg/kg/day in mature rats but peaking at 20 mg/kg/day. Significantly increased CYP2B1/2 protein expression was observed at ≥5 mg/kg/day in both young and old rats. Significantly increased CYP3A1/2 protein expression was observed at ≥20 mg/kg/day in young rats and ≥5 mg/kg/day in mature rats.No author-reported

toxicity values were provided. Based on the available data, a NOAEL of 20 mg/kg/day and LOAEL of 100 mg/kg/day for apical hepatic/liver endpoints was determined based on relative liver weights in the mature rats. A LOAEL of 5 mg/kg/day for mechanistic endpoints was determined based on increased PROD activity and CYP2B1/2 and CYP3A1/2 protein expression. No NOAEL for mechanistic endpoints could be determined.

[18] 5888541: New Zealand white rabbits (6/sex/group) were exposed to 0 or 1.0 g/kg of octamethylcyclotetrasiloxane (D4) (identified as SF1173) in saline via dermal application under occlusion for 6 hours/day, at which time the skin was wiped, for 3 weeks. Half of the animals had the skin abraded while the other half had intact skin. Animals were monitored daily for mortality, clinical signs of toxicity and skin irritation. Body weights were measured weekly on days 0, 7, 14 and 21 (fasted terminal). At the end of the experiment animals were euthanized and gross necropsy was performed, and organ weights (lungs, heart, liver, urinary bladder, spleen, testes, ovaries, epididymis and uterus) were measured. Microscopic examination of the skin was also performed. Two exposed animals died on day 12 and one was sacrificed moribund on day 14, and 2 control animals died on days 14 and 15 and one was sacrificed moribund on day 18 during the study. The authors attributed the deaths to the stress of their experimental procedure and did not conclude any effect of D4 on mortality. Surviving females had significantly decreased body weights by 16% at terminal sacrifice. Body weights in males were comparable across groups. No significant difference in clinical signs were observed over the course of the study at any time point. In males, spleen weights were significantly increased by 39% (absolute) and by 37% (relative). In females, spleen weights were significantly reduced by 39% (absolute) and 28% (relative) and ovary weights were significantly decreased by 25% (absolute) compared to controls, while relative ovary weights were reduced by 15%, they were not statistically significant. Absolute and relative uterus weights were decreased by 21-33% but were not statistically significant. No other differences in organ were observed in D4 exposed animals. Gross necropsy results were limited to skin lesions. Gross abnormalities were observed in 6/6 males and 6/6 females had red scaly spot with sores (compared to 1/6 males and 0/6 females in control). These lesion occurred primarily in the intact animals.Microscopic examination showed epidermal thickening, hyperkeratosis, and acute inflammation of the skin of all exposed animals compared with few to none in controls. Crust formation was observed in 2/6 males and 4/6 females, with none in controls.Increased incidence of skin lesions were observed in animals exposed to 1.0 g/kg. Dry skin was observed with histological lesions including thickening, hyperkeratosis, and inflammation. A LOAEL of 1.0 g/kg was determined based on skin effects. No NOAEL was determined.

[19] 5885411: In a short-term inhalation toxicity study, male and female rats (6/sex/group) were exposed via whole-body inhalation in a dynamic chamber to CF-1173 (reported in hand-written text as a formulation containing ~10% octamethylcyclotetrasiloxane [D4], 0.1% SF-666, trace amounts of an illegible compound, and water to 100%) vapor at nominal concentrations of 0 or 39.7 mg/l. Animals were exposed twice daily (1 hour per exposure), 5 days/week for two consecutive weeks. Control animals were exposed to 35.1 mg/L water vapor. After two weeks of exposure, on day 12, one half of each treatment group (n=3/sex) was sacrificed and necropsied. The remaining animals were retained and observed over the course of a 14-day postexposure observation period.Rats were assessed for mortality and the day of death was noted. Animals were observed for clinical signs of toxicity during each exposure and during the periods between exposures. Body weights were recorded prior to the initial exposure and on a weekly basis during the exposure and postexposure periods. Fifteen tissues and organs were removed from rats upon gross necropsy and fixed in formalin. Select organs (lung, liver, kidney, spleen, adrenals, and heart) were weighed following necropsy. Histopathological examinations were conducted on the trachea, lungs, liver, and kidney only. Additionally, any tissues with gross abnormalities were excised, fixed, and assessed by histology. No animals died during the exposure or postexposure period. Exposed rats exhibited a white nasal exudate during the second week of exposure and nose shuffling throughout the exposure period. Both the control and treated groups exhibited hypoactivity, partially closed eyes, and wet fur during the exposure. No clinical signs were observed between exposures. The authors stated that growth patterns “in both the control and experimental groups can be considered normal.” Quantitative body weight measurements were reported; however, no statistical analysis was conducted. Body weights of males and females in the exposure groups were lower than controls (11% and 6%, respectively) at the start of the study; statistical analysis conducted for this review shows that for males, this difference was statistically significant. Therefore, it appears that animals were not normalized based on body weights during allocation into groups. Body weights separated by sex were not reported at the day 12 sacrifice. Organ weights of males and females were combined and means ± SE were reported for all 6 animals/group. The only significant changes observed in organ weights were statistically significant increases in relative heart (18% increase relative to controls), liver (9% increase), and adrenal gland (100% increase) weights at the day 26 sacrifice. No organ weight changes were observed immediately after the exposure period, and absolute organ weights were similar to controls. The clear differences in animal starting body weights may have confounded the organ weight results. The study authors dismissed the importance of these findings as “no pattern or trend of effect” was apparent. None of the animals, control or treated, displayed gross lesions. No significant treatment-related histopathological changes were observed. No author-reported toxicity values were provided. Due to confounding differences in initial body weights between animals in the exposure and control groups, and other deficiencies in the study, reliable toxicity values cannot be determined.

[20] 5885411: In a short-term inhalation toxicity study, male and female guinea pigs (6 animals/sex/group) were exposed via whole body inhalation in a dynamic chamber to CF-113 (reported in hand-written text as a formulation containing ~10% octamethylcyclotetrasiloxane [D4], 0.1% SF-666, trace amounts of an illegible compound, and water to 100%) vapor at nominal concentrations of 0 or 39.7 mg/l. Animals were exposed twice daily (1 hour per exposure), 5 days/week for two consecutive weeks. Control animals were exposed to 35.1 mg/L water vapor. After two weeks of exposure, on day 12, one half of each treatment group (3/sex/group) was sacrificed and necropsied. The remaining animals were retained and observed over the course of a 14-day postexposure observation period.Guinea pigs were assessed for mortality and the day of death was noted. Animals were observed for clinical signs of toxicity during each exposure and during the periods between exposures. Body weights were recorded prior to the initial exposure and on a weekly basis during the exposure and postexposure periods. Fifteen tissues and organs were removed from guinea pigs upon gross necropsy and fixed in formalin. Histopathological examinations were conducted on the trachea, lungs, liver, and kidney. Additionally, any tissues with gross abnormalities were excised, fixed, and assessed by histology. Select organs (lung, liver, kidney, spleen, adrenals, and heart) were weighed following necropsy. One male guinea pig in the control group displayed slow shallow respiration on day 5 and died later that day during the second inhalation exposure. There was no mortality among the treated group. Both the control and treated groups exhibited hypoactivity, partially closed eyes, and wet fur during the exposure and all animals were found to have interstitial pneumonitis. Animal body weights were reported but were not statistically analyzed. The starting body weights, measured immediately prior to the initial exposure, were significantly different across groups. Initial body weights of males in the exposure group were 17% higher than control males, and the initial body weights of the females in the exposed group were 27% higher than controls. Since body weights were not evenly distributed across groups at the start of the study, this confounds the ability to interpret the remaining body weight data, and data for other endpoints that may be influenced by body weights (e.g., organ weights). In order to increase statistical power, male and female organ weights were combined allowing an n=6 at the Day 12 and Day 26 time points. Generally, organ weights vary by sex and the appropriateness of combining these data is questionable. There were no statistically significant organ weight changes as presented. None of the animals, control or treated, displayed gross lesions. In addition, there were no significant treatment-related histopathological changes. No author-reported toxicity values were provided. No significant effects were observed; however, due to several deficiencies in the study, reliable toxicity values cannot be determined.

[21] 5885411: In a short-term inhalation toxicity study, male and female mice (6 animals/sex/group) were exposed via whole body inhalation in a dynamic chamber to CF-1173 (reported in hand-written text as a formulation containing ~10% octamethylcyclotetrasiloxane [D4], 0.1% SF-666, trace amounts of an illegible compound, and water to 100%) vapor at nominal concentrations of 0 or 39.7 mg/l. Animals were exposed twice daily (1 hour per exposure), 5 days/week for two consecutive weeks. Control animals were exposed to 35.1 mg/L water vapor. After two weeks of exposure, on day 12, one half of each treatment group (3/sex/group) was sacrificed and necropsied. The remaining animals were retained and observed over the course of a 14-day postexposure observation period.Mice were assessed for mortality and the day of death was noted. Animals were observed for clinical signs of toxicity during each exposure and during the periods between exposures. Body weights were recorded prior to the initial exposure and on a weekly basis during the exposure and postexposure periods. Fifteen tissues and organs were removed from mice upon gross necropsy and fixed in formalin. Histopathological examinations were conducted on the trachea, lungs, liver, and kidney. Additionally, any tissues with gross abnormalities were excised, fixed, and assessed by histology. Select organs (lung, liver, kidney, spleen, adrenals, and heart) were weighed following necropsy. One female mouse in the control group was accidentally killed

on day 10; however, they do not expand on the circumstances surrounding this "accidental death." Treated rats exhibited a white nasal exudate during the second week of exposure and nose shuffling throughout the exposure period. Both the control and treated groups exhibited hypoactivity, partially closed eyes, and wet fur during the exposure. Body weights were reported; the data were not statistically analyzed but remained within 10% of controls at each time point. In order to increase statistical power, male and female organ weights were combined allowing an n=6 at the Day 12 and Day 26 time points. Generally, organ weights vary by sex and the appropriateness of combining these data is questionable. The only significant organ weight changes were statistically significant reductions in relative spleen (45% decrease relative to controls) and kidney (24% decrease) weights at the day 12 sacrifice. No changes in absolute organ weights were observed, and organ weights were comparable to controls following the 14-day recovery period. None of the animals, control or treated, displayed gross lesions and no associated histopathological changes were observed. No author-reported toxicity values were provided. Due to deficiencies in exposure methods and characterization, a reliable toxicity value cannot be determined.

[22] 5889471: The concentration in ppm was converted to mg/m3 using the following equation: (ppm * mw)/24.45 = mg/m3. The mw of D4 is 296.62 g/mol. Therefore, a concentration of 300 ppm of D4, would be equivalent to (300 ppm * 296.62 g/mol) / 24.45 = 3,639.5 mg/m3 or 3,640 mg/m3. Fourteen-week-old virgin Sprague-Dawley rats were mated in a 1:1 ratio until presence of copulation plug was observed (gestation day; GD 0). Presumed pregnant females (30/group) were exposed to 0, 100, 300, or 700 ppm octamethylcyclotetrasiloxane (D4) via whole-body inhalation 6 hours/day from GDs 6-15. Dams were observed twice a day for mortality and clinical signs of toxicity. Maternal body weights and food consumption were assessed on GDs 0,6, 9, 12, 16, and 20. Dams were sacrificed on GD 20. Endpoints evaluated included maternal organ weights (liver and gravid uterine), gross pathology, and histopathology of gross lesions, location and number of viable and nonviable fetuses, early and late resorptions, and number of total implantations and corpora lutea. Fetuses were weighed and sexed. Approximately one-half of the fetuses were examined for visceral malformations and variations and the heart was dissected. The remaining fetuses were stained with Alizarin Red S to examine skeletal malformations or variations. No maternal deaths occurred. No overt clinical sings of toxicity related to the test substance were observed. There were no concentration-related effects on body weights, body weight gains, or food consumption. Maternal bodyweights were significantly decreased at 700 ppm on GD 12 (7%) and GD 16 (7%) and at 100 ppm at GD 12 (10%), GD 16 (8%), and GD 20 (9%) compared to control. There were no significant effects in the 300 ppm group. Body weight gains were significantly decreased from GD 9-12 (66%, 29%, 48%) at 100, 300, and 700 ppm, respectively; from GD 6-16 (36% and 42%) and GD 0-20 (18%, 28%) at 100 and 700 ppm, respectively. Decreases in food consumption mirrored body weight decreases. Food consumption was significantly decreased from GD 9-12 (22%, 10%, 20%) at 100, 300, and 700 ppm, respectively; GDs 12-16 (10% and 20%), GDs 6-16 (13% and 15%) and GDs 0-20 (10% and 8%) at 100 and 700 ppm, respectively. No significant test-substance related gross pathology was observed. No significant difference in liver or uterine weights were seen compared to control. Liver histology was not reported. No significant difference pregnancy rates were seen (86.7, 90, 93.3, and 83.3%) at 0, 100, 300, and 700 ppm, respectively, compared to control. No significant difference in the number of corpora lutea, implantation sites, post-implantation loss, preimplantation loss, resorptions, dead fetuses (0 for all groups), viable fetuses, live fetuses, sex ratio or fetal weights were seen. There were no test substance-related fetal malformations or developmental variations seen compared to control and historical controls. The study authors made a NOAEC call of 300 ppm for maternal toxicity and > 700 ppm for developmental toxicity.

[23] 5899001: In a short-term, repeated dose oral toxicity study, female Wistar rats (10 females /group/timepoint) were exposed via gavage to octamethylcyclotetrasiloxane (D4) at concentrations of 0 or 1600 mg/kg body weight (vehicle not reported; controls received tap water) for 2 weeks. Animals were then either sacrificed (n=10/group) or allowed to recovery for 4 weeks (n=10/group). Endpoints evaluated included mortality, clinical signs, food and water intake, gross pathology, liver weights, histopathology (liver, lung, and mesenteric lymph node), liver enzyme activities (in the liver), and electron microscopy of the liver. Liver enzymes measured included 7-ethoxycoumarin deethylase (EOD), 7-ethoxyresorufin deethylase (EOR), aldrin epoxidase (ALD), epoxide hydrolase (EH), glutathione-S-transferase (GSH-T), and UDP-Glucuronyl transferase (GLU-T). No information was reported on mortality, clinical signs, food and water intake or gross necropsy. After 2 weeks of exposure, absolute and relative liver weights were increased (by 28%) in treated rats (data is not shown and authors did not perform statistical analysis). Histologically, changes observed in the liver of exposed animals included increased hypertrophy and loss of glycogen content (data not shown), and mitoses in 5/10 exposed animals (control data not reported). In the lungs, "interstitial inflammation with an increased occurrence of alveolar macrophages" was seen in exposed animals (data not shown; control data not reported). In the mesenteric lymph nodes, increased eosinophilic was observed in exposed animals (data not shown; control data not reported). From electron microscopy of the liver, it was determined that there was a "decrease in rough endoplasmic reticulum and glycogen content and proliferation of smooth endoplasmic reticulum" in the exposed animals (data not shown; control data not reported). Following exposure, significant increases in the following liver enzymes were seen: EOD (88%), EH (283%), GSH-T (107%), and GLU-T (55%) compared to control. Other enzymes were not significantly different from control. Statistical analysis was performed by this Reviewer using GraphPad unpaired t-test with reported data. After recovery, relative liver weights were increased slightly (up to 5%) in exposed rats (data not shown, statistics performed). Histopathological changes in liver, lungs and mesenteric lymph nodes had all resolved and no relevant changes were observed (data not shown). Liver enzyme activity levels in the recovery animals returned to control levels. No author-reported toxicity values were provided. Based on the data presented in the study, a LOEL of 1600 mg/kg body weight was identified for female Wistar rats based on increased liver enzyme activities, increased absolute and relative liver weights, histopathological and ultrastructural changes in the liver.

[24] 5899001: In a short-term, repeated dose oral toxicity study, male and female Sprague-Dawley rats (5 animals/sex/group) were exposed via gavage to octamethylcyclotetrasiloxane (D4) at concentrations of 0 or 1600 mg/kg body weight (vehicle not reported; controls received tap water) for 2 weeks Endpoints evaluated included mortality, clinical sings, food and water intake, gross pathology, liver weight, histopathology (liver, lung, and mesenteric lymph node), liver enzyme activities (in the liver), and electron microscopy of the liver. Liver enzymes measured included 7-ethoxycoumarin deethylase (EOD), 7-ethoxyresorufin deethylase (EOR), aldrin epoxidase (ALD), epoxide hydrolase (EH), glutathione-S-transferase (GSH-T), and UDP-Glucuronyl transferase (GLU-T).No information on mortality, clinical signs, food and water intake or gross necropsy was reported. Absolute and relative liver weights were increased (by up to 22% in males and up to 47% in females) in exposed rats (no statistics performed). Histological observation included hypertrophy of liver cells and loss of glycogen content in exposed rats (data not shown, control data not reported). Histopathology on lungs and lymph nodes were not reported. Significant increases in some liver enzymes were seen in males: EOD (294%), EH (166%), GSH-T (89%); and females: EOD (103%), ALD (65%), and EH (144%). All other enzymes were not significantly different from control. Statistical analysis was performed by this Reviewer using GraphPad unpaired t-test with reported data. Data on electron microscopy was not reported. No author-reported toxicity values were provided. Based on the data presented in the study, a LOAEL of 1600 mg/kg body weight was identified for Sprague-Dawley rats based on increased liver enzyme activities, increased absolute and relative liver weights, histopathological changes in the liver.

[25] 5887187: Groups of 18-day-old Sprague-Dawley rats (12 females/group) were administered D4, via gavage, at doses of 0 (sesame oil vehicle control), 10, 50, 100, 250, 500, or 1,000 mg/kg-day over 4 consecutive days. Additional groups included positive controls: animals dosed with 1, 3, 10, or 30 µg/kg-day ethinyl estradiol (EE), animals dosed with 0.15, 1.5, 5, or 15 µg/kg-day diethylstilbestrol dipropionate (DES-DP), and animals dosed with 10, 35, 75, or 150 mg/kg-day coumestrol (CE), and mixed groups: animals dosed with 500 mg/kg-day D4 plus 3, 10, or 30 µg/kg-day EE, with ICI 82,780 (ICI, an antiestrogen) plus 3, 10, or 30 µg/kg-day EE. Animals were observed for mortality and clinical signs. Body weights were measured. Animals were sacrificed after dosing and were subjected to necropsy . Liver and uterine weights were measured. The left uterine horn was microscopically evaluated (6 rats/group) to determine the epithelial cell height of the endometrial surface lining. No treatment-related effects on mortality or clinical signs were observed. One animal in the 500 mg/kg/day group was found dead, all other animals survived until the scheduled sacrifice. No effects on body weight were observed; however, reductions in body weight gain were noted at ≥250 mg/kg-day. During the first 24 hours of dosing, animals in the 500 and 1,000 mg/kg-day groups lost weight. D4 alone resulted in significant increases in absolute and relative liver weights at ≥ 500 mg/kg-day and ≥250 mg/kg-day, respectively. Uterine absolute and relative weights were significantly increased at ≥250 mg/kg-day. The increases in uterine weight in D4-treated animals were lower in magnitude than those observed in animals treated with the positive controls, and D4

was 1.2 million times less potent than the positive controls. Significant increases in uterine epithelial height occurred with D4 doses ≥250 mg/kg-day. No treatment-related macroscopic effects were observed, although 1 animal in the 1,000 mg/kg-day group showed uterine distention. The positive controls were valid and gave the expected responses. The negative control (ICI) abrogated the uterotrophic response of EE when co-administered. Co-administration of D4 with EE resulted in a reduction in the utertrophic dose response of EE, suggestive of antiestrogenic properties. Overall, the authors concluded that, under the conditions of the study, D4 was weakly estrogenic. A NOAEL of 100 mg/kg-day (suggesting a LOAEL of 250 mg/kg-day) was reported, presumably based on uterine organ weights and an increase in uterine epithelial height in rats. An increase in liver weight was also observed at this dose.HERO number 1310507 (corresponding journal article) was also considered during this review.

[26] 5887187: Groups of 18-day-old Fisher 344 rats (12 females/group) were administered D4, via gavage, at doses of 0 (sesame oil vehicle control), 10, 50, 100, 250, 500, or 1,000 mg/kg-day over 4 consecutive days. Additional groups included positive controls: animals dosed with 1, 3, 10, or 30 µg/kg-day ethinyl estradiol (EE), animals dosed with 0.15, 1.5, 5, or 15 µg/kg-day diethylstilbestrol dipropionate (DES-DP), and animals dosed with 10, 35, 75, or 150 mg/kg-day coumestrol (CE), and mixed groups: animals dosed with 500 mg/kg-day D4 plus 3, 10, or 30 µg/kg-day EE, with ICI 82,780 (ICI, an antiestrogen) plus 3, 10, or 30 µg/kg-day EE. Animals were observed for mortality and clinical signs. Body weights were measured. Animals were sacrificed after dosing and were subjected to necropsy. Liver and uterine weights were measured. The left uterine horn was microscopically evaluated (6 rats/group) to determine the epithelial cell height of the endometrial surface lining. One animal in the 1,000 mg/kg-day group was sacrificed in extremis and showed signs of hair loss, high carriage, decreased activity and ataxia; all other animals survived until the scheduled sacrifice. An increased incidence of material around the nose was reported at 1,000 mg/kg-day. Mean body weights were significantly decreased at ~10% at 1,000 mg/kg-day. Reductions in body weight gain were observed during the first 1-2 days of dosing and overall, from day 1-5 at ≥250 mg/kg-day. D4 alone resulted in significant increases in absolute and relative liver weights at ≥ 100 mg/kg-day, and in absolute and relative uterine weights at ≥ 250 mg/kg-day. The increases in uterine weight in D4-treated animals were lower in magnitude than those observed in animals treated with the positive controls, and D4 was determined to be 25 million times less potent than the positive controls. No organ weight changes were observed in groups exposed to D4 plus EE. Uterine epithelial height was significantly increased in a dose-related manner. However, the increases were only statistically significant in the 250 and 500 mg/kg-day groups, likely due to higher variation at 1,000 mg/kg-day. No treatment-related macroscopic effects were observed in animals treated with D4. Animals treated with EE (11/12) or DES-DP (9/12) showed increased incidences of uterine distention, compared to controls. In animals treated with D4 + EE, only 2/12 females showed moderate uterine distention. The positive controls were valid and gave the expected responses. The negative control (ICI) abrogated the uterotrophic response of EE when co-administered. Co-administration of D4 with EE resulted in a reduction in the utertrophic dose response of EE, suggestive of antiestrogenic properties.Overall, the authors concluded that, under the conditions of the study, D4 was weakly estrogenic. A NOAEL of 100 mg/kg-day (suggesting a LOAEL of 250 mg/kg-day) was reported, presumably based on uterine organ weights and an increase in uterine epithelial height in rats. However, in F344 rats, a significant increase in liver weights occurred at 100 mg/kg-day. Other liver endpoints (e.g., serum chemistry and histopathology) were not assessed, it is unclear whether the observed changes in liver weights were indicative of liver-specific toxicity.HERO number 1310507 (corresponding journal article) was also considered during this review.

[27] 1297415: Cannulated female Sprague-Dawley Crl:CD (SD) IGS BR rats (44-51/group) were exposed to target concentrations of 0, 700 or 900 ppm (with analytical concentrations of 0, 711 and 895 ppm) of octamethylcyclotetrasiloxane (D4) vapor (99.6% purity) via whole body inhalation 6 hours/day for 3 days from diestrus days 1-2 and proestrus. Vaginal lavages were performed 10-12 days prior to exposure to determine estrous stage; rats were entered into the study after their third normal cycle. Blood samples were collected on the day of proestrus at 2, 4, 6, 8, and 10 pm to evaluate levels of luteinizing hormone (LH) and prolactin (PRL). Animals were euthanized the next morning at 8 am (day of estrus) and truck blood was collected for analysis of plasma levels of estradiol (E2), estrone (E1), progesterone (P4), and follicle stimulating hormone (FSH). Terminal body weights, ovulatory status, organ weights (uterus, ovary, and brain), the number of ova in the right and left oviducts, fluid distension of the uteri, and histopathology of the ovaries (for number of large follicles, corpora lutes, and atretic antral follicles) were assessed. Rats were considered ovulators or non-ovulators based on presence of absence of corpora lutea and ova presence in the oviducts (morning of day on estrous). Terminal body weights were significantly decreased (4%) at 895 ppm compared to control; no difference was seen at 711 ppm compared to control. The study reports there were "treatment related decrease in absolute ovarian weight" and relative uterine to body weight, ovarian to body weight and ovarian to brain weight at 895 ppm; however, significance is not reported, and data is not shown. When grouped by ovulatory status, significant decreases in absolute ovarian weight (15%) and relative ovarian to brain weight (14%) were observed at 895 ppm in ovulating animals. Plasma levels of LH were significantly decreased at 711 ppm at 6 pm (~46%) and at 895 ppm at 4, 6, and 8 pm (13%, 57%, and 42%, respectively) compared to control. The area under the curve for LH was significantly reduced at 895 ppm (but not at 711 ppm) compared to control. When time relative to peak LH value was plotted against plasma LH levels (peak-centered to account for temporal differences), LH concentrations were significantly decreased only at 895 ppm compared to control. When animals were grouped by ovulatory status (ovulating vs non-ovulating), no significant difference in plasma LH levels were seen compared to control. The percentage of animals that ovulated was significantly decreased in both D4 groups: 79% of controls ovulated compared to 42% at 711 ppm and 31% at 905 ppm. Significant decreases in plasma PRL levels were seen at 711 ppm (~ 50%) and 895 ppm (~60%) at 2 pm compared to control; area under the PRL curves were not statistically different from control. When grouped by ovulating status, plasma PRL levels were only significantly decreased at 895 ppm (40%) compared to control. Plasma E2 levels were significantly increased at 711 ppm (186%) and 895 ppm (173%) compared to control. When grouped by ovulation status, the significant increase remained in non-ovulating (185% and 146%) and ovulating (99% and 100%) at 711 and 895 ppm, respectively compared to control. Significant increases in plasma E1 were seen at 711 ppm (40%) and 895 ppm (54%) compared to control. Significant decreases in E1/E2 ratios were observed at ≥711 ppm; when grouped by ovulation status, E1/E2 ratios were only significant decreased in non-ovulating rats at 895 ppm (52%) compared to control. Plasma FSH levels were significantly decreased at 711 ppm (~20%) and 895 ppm (~40%) compared to control. No significant difference in plasma P4 levels were seen compared to control. Significant decreases in the number of ova in the oviducts/rat were seen at 711 ppm (45%) and 895 ppm (68%) compared to control (total number in left and right oviduct). Significant decreases were also seen when analyzed by the left or right oviduct independently. When analyzed by ovulatory status, the mean number of ova in ovulating D4 exposed rats was not significantly different from control. In ovulating rats, no difference in the number of corpora lutea were seen (data not shown). There was a weak trend for increased number of persistent mature follicles in D4 exposed rats (significant at 711 ppm, but not at 895 ppm; data not shown); which correlated with increased plasma E2 levels. No author reported PODs were reported. Based on the data, a study-wide LOAEC of 711 ppm was observed for reproductive/developmental effects based on decreased LH, PRL and E1/E2 ratio, increased E1 and E2, decreased percentage of ovulatory animals, and ova in the oviduct/rat. A NOAEC could not be determined.

[28] 1297690: In a rat uterotrophic assay, ovariectomized Sprague Dawley rats (10 females/group) were exposed, whole-body, to Octamethylcyclotetrasiloxane (D4; purity >99%) vapors, at 0 (filtered air) or 700 ppm for 16 hours/day for 3 consecutive days. For comparison, separate groups of positive control rats (6/group) were administered 17β-estradiol (EE) at 0.3, 1.0, or 3.0 ug/kg/day and genistein at 10, 25, or 50 mg/kg-day, subcutaneously, followed by control inhalation exposure. To evaluate antiestrogenic activity, final groups (6/group) were administered 3 ug/kg-day EE in combination with the ER antagonist, ICI 192,780, or D4. Positive control animals were sacrificed 6 hours after subcutaneous dosing and animals exposed to D4 were sacrificed immediately after the 3rd exposure day. The study noted that a corn oil control group was used for the 6-h positive controls and for the 16-hour exposure groups. Endpoints evaluated included uterine wet and blotted weights, necropsy, and histopathological analysis of uteri. Absolute wet and blotted uterine weights of animals exposed to D4 were significantly increased compared with filtered air controls, and the increases were slightly greater than the 0.3 ug/kg-day EE positive controls but less than the 1.0 ug/kg-day EE controls. Uterine fluid was present in 10/10 exposed animals as well as in positive control animals at necropsy vs. 0/10 in filtered air controls. The positive controls gave the expected responses. Histological examinations showed significant increases in luminal and glandular epithelial cell height in uterine horn tissue in animals exposed to D4. The increase in glandular cell height was slightly less than that observed following treatment with the lowest dose of EE but was statistically significant when compared to air-only controls. The ~2.5-fold increase in luminal cell height was similar to the increase induced by the highest EE level tested (3 ug/kg-day). D4 exhibited no antiestrogenic activity when co-administered EE, compared with animals treated with EE alone. Genistein data were not presented. Overall, D4 exhibited weak estrogenic activity.

[29] 1297690: In a rat uterotrophic assay, ovariectomized Fisher 344 rats (10 females/group) were exposed, whole-body, to Octamethylcyclotetrasiloxane (D4; purity >99%) vapors, at 0 (filtered air) or 700 ppm for 16 hours/day for 3 consecutive days. For comparison, separate groups of positive control rats (6/group) were administered 17β-estradiol EE at 0.3, 1.0, or 3.0 ug/kg/day and genistein at 10, 25, or 50 mg/kg-day, subcutaneously, followed by control inhalation exposure. To evaluate antiestrogenic activity, final groups (6/group) were administered 3 ug/kg-day EE in combination with the ER antagonist, ICI 192,780, or D4. Positive control animals were sacrificed 6 hours after subcutaneous dosing and animals exposed to D4 were sacrificed immediately after the 3rd exposure day. The study noted that a corn oil control group was used for the 6-h positive controls and for the 16-hour exposure groups. Endpoints evaluated included uterine wet and blotted weights, necropsy, and histopathological analysis of uteri. Absolute wet and blotted uterine weights of animals exposed to D4 were significantly but slightly increased compared with filtered air controls, and the increases were less than those induced by the lowest dose of EE (0.3 ug/kg-day). Uterine fluid was present in 10/10 exposed animals as well as in positive control animals at necropsy vs. 0/10 in filtered air controls. The positive controls gave the expected responses. Histological examinations showed significant increases in luminal and glandular epithelial cell height in uterine horn tissue in animals exposed to D4, compared with the filtered air controls. The increase in glandular cell height was slightly less than that observed following treatment with the lowest dose of EE. The ~2.5-fold increase in luminal cell height was greater than that observed following treatment with 0.3 ug/kg-day EE, but less than that observed in the 1.0 ug/kg-day EE group. When compared with animals exposed to EE alone, co-exposure with D4 resulted in mild suppression of the EE-induced increase in uterine weight which is suggestive of weak antiestrogenic activity in this strain. Genistein data were not presented. Overall, D4 exhibited weak estrogenic activity.

[30] 5888822: Groups of Fisher 344 rats (10/sex/group) were exposed, nose-only, to D4 analytical vapor concentrations of 0, 2.78, 5.13, and 8.62 mg/L for 6 hours per day, 5 days per week, for 4 weeks. An additional high concentration of 14.21/13.25 (days 1-5/6-termination) mg/L was used, however this concentration was initially greater than vapor saturation leading to an atmospheric mixture of vapor and aerosol, therefore, after the initial exposure days, the high exposure concentration was reduced to a concentration at the vapor saturation (reported in the study to be 13 mg/L, experimentally determined) for the remainder of the exposure. Due to this, the high concentration was examined separately.Animals were observed for mortality and clinical signs of toxicity. Other endpoints included ophthalmoscopic examinations, body weights, weight gain, food consumption and food efficacy, hematology, clinical chemistry, urinalysis, select organ weights, and histopathology on >25 organs/tissues. Liver samples were also examined via electron microscopy. No deaths occurred at 8.62 mg/L during exposure. One male in the 8.62 mg/L group and one female in the control group were found dead on the day of necropsy. The causes of death were unknown. Exposure-related clinical signs included abnormal (hunched) posture, stiff or abnormal gait, head tilt, and ruffled fur. These signs were noticed after exposure in most females in the 8.62 mg/L group, and in 2/10 females in the 5.13 mg/L group. Body weights, body weight gains and food consumption were comparable across groups. Exposed males and females (all groups) showed significant increases in MCV and corresponding decreases in MCHC however, no changes to other RBC parameters were observed. Similarly in females, MCV was increased and MCHC was decreased in a concentration-dependent manner. No other hematological changes in females were exposure concentration-related. The authors did not consider any hematological changes to be toxicologically relevant. Male rats showed generally non-concentration-dependent increases in serum glucose at 8.62 mg/L, increased total cholesterol, and total protein, and decreased ALP at ≥5.13 mg/L. Albumin was increased in all exposure groups (water intake was not reported.) In females increases in albumin and decreased urea at 8.62 mg/L and increases in globulin and total protein at ≥5.13 mg/L appear to be responsive to concentration. Other changes (e.g., increases in total cholesterol, decreased ALP, and changes in glucose were not exposure-concentration responsive and/or were not considered to be toxicologically relevant. In the 8.62 mg/L group males, animal number 37 (p 223) appears to be an extreme outlier, due to being found dead prior to necropsy, but this was not accounted for in the statistical analysis. The authors attributed some serum chemistry changes may be related to adrenocortical functional activity. Urinalysis showed no treatment related effects. Exposure-related organ weight changes were observed in the liver and thymus. Males showed concentration-related increases in absolute liver weights (16-22%) at ≥5.13 mg/L and in relative liver weights (10-23%) in all exposure groups. Similarly, in females, both absolute (11-33%) and relative (14-38%) liver weights were increased at ≥2.78 mg/L, absolute thymus weights were decreased at 8.62 mg/L, and absolute and relative adrenal gland weights were increased at 8.62 mg/L.No gross pathology attributed to exposure was observed. Exposure-related microscopic findings were observed in the lungs, liver, adrenal gland, ovaries, and vagina. Incidences of alveolar inflammation in the lungs were higher in animals from all exposure groups, compared with controls. The authors considered this to be adaptive responses to a mild irritant. Incidences of liver hypertrophy and minimal to slight vacuolation in the adrenal cortex were significantly increased at 8.62 mg/L. Incidences of vaginal mucification were noted only in exposed females but were not statistically significant. This was seen along with exposure-related decreases in the mean corpora lutea scores in all groups. Ultrastructural changes to hepatocytes (e.g., reductions in mitochondrial volume and in rough endoplasmic reticulum, and/or an increase of smooth endoplasmic reticulum) were noted in all exposure groups. No author-derived toxicity values were provided. Based on the data available a LOAEC of 2.78 mg/L (2,780 mg/m3) was determined based on increased liver weights in male and female rats. Ultrastructural changes were also noted and incidences of hepatocellular hypertrophy occurred at higher exposure concentrations.

[31] 5888822: Groups of Fisher 344 rats (10/sex/group) were exposed, nose-only, to D4 analytical vapor concentrations of 0, 2.78, 5.13, and 8.62 mg/L for 6 hours per day, 5 days per week, for 4 weeks. An additional high concentration of 14.21/13.25 (days 1-5/6-termination) mg/L was used, however this concentration was initially greater than vapor saturation leading to an atmospheric mixture of vapor and aerosol, therefore, after the initial exposure days, the high exposure concentration was reduced to a concentration at the vapor saturation (reported in the study to be 13 mg/L, experimentally determined) for the remainder of the exposure.Animals were observed for mortality and clinical signs of toxicity. Other endpoints included ophthalmoscopic examinations, body weights, weight gain, food consumption and food efficacy, hematology, clinical chemistry, urinalysis, select organ weights, and histopathology on >25 organs/tissues. Liver samples were also examined via electron microscopy. Three females in the high-exposure group died during the first 5 days of exposure; therefore, the exposure concentration was reduced starting on exposure day 6 through the end of the study. A 4th female in this group died on day 7. One female in the control group was found dead on the day of necropsy. The causes of death were unknown. Exposure-related clinical signs included abnormal (hunched) posture, stiff or abnormal gait, head tilt, and ruffled fur. These signs were noticed after exposure in all animals from the high-exposure group. Sedation, excitement, and tremors were also sporadically observed in high-exposure animals. Body weights of animals in the high-exposure group were transiently decreased early during the study period, but the changes were <10% in both sexes. Significant reductions in terminal body weights were similarly low in magnitude (<7%). Body weight gain was reduced (39%) in high-exposure males during week 1. High-exposure females lost weight during the first two weeks of the study. Weight gain changes corresponded with transient decreases in food intake early in the study (days 1-9) in both sexes. Exposed males (all groups) showed significant increases in MCV and corresponding decreases in MCHC however, no changes to other RBC parameters were observed. In the high-exposure males, reticulocytes (% and T/L) and monocyte counts were increased, and prothrombin time was decreased. No hematological changes in females were exposure concentration-related. The authors did not consider any hematological changes to be toxicologically relevant. Male rats of the high concentration group showed increases in serum glucose, increased total cholesterol, and total protein, and decreased ALP, and decreased bilirubin. Albumin was also increased however water intake was not reported. In females of the high concentration group, increases in albumin, globulin, and total protein, and decreased urea was observed. An electrolyte imbalance was noted in high-exposure females. Other changes were not considered to be toxicologically relevant. Urinalysis showed significant increases in specific gravity and osmolality and a decrease in pH in high-exposure males only; these changes were not considered by the authors to be toxicologically significant. Exposure-related organ weight changes were observed in the liver, thymus, spleen, and adrenal glands. Males in the high concentration group showed changes in organ weights including increases in absolute and relative liver weights (26-34%), significant decreases in absolute and relative thymus and spleen weights, and an increase in absolute and relative adrenal weights. Similarly, in high-exposure females, both absolute and relative liver weights (43-49%) were increased and absolute and relative thymus weights were decreased. No changes in spleen weights were observed in females. Relative, but not absolute, adrenal gland weights were increased at the highest exposure concentration.No gross pathology attributed to exposure was observed. Exposure-related microscopic findings in the highest exposure group were observed in the nasal cavity, lungs, liver, ovaries, vagina, adrenal cortex. An increase in the incidence and severity of goblet cell proliferation in the nasopharyngeal duct was observed. Incidences of alveolar inflammation in the lungs were higher in animals from all exposure groups, compared with controls. The authors considered respiratory histopathology effects to be adaptive responses to a mild irritant. Incidences of liver hypertrophy and minimal to slight vacuolation in the adrenal cortex were

significantly increased. Incidences of vaginal mucification were significantly increased in the high-exposure group. This was seen along with exposure-related decreases in the mean corpora lutea scores. Increased incidences of thymic atrophy were significant in high-exposure animals. The authors attributed this to a stress response. Ultrastructural changes to hepatocytes (e.g., reductions in mitochondrial volume and in rough endoplasmic reticulum, and/or an increase of smooth endoplasmic reticulum) were noted at the high concentration. No author-derived toxicity values were provided. Based on the data available a LOAEC of 13.25 mg/L (13,250 mg/m3) was determined based on increased absolute and relative liver weights, hepatic ultra-structural changes, histopathological effects of the respiratory system, liver, thymus, and female reproductive tract.

[32] 5887620: To study the effects of different vehicles on octamethylcyclotetrasiloxane (D4) toxicity, Fisher 344 rats (10/sex/group) were administered 0, 1, 3, 10, 30, 100, or 300 mg/kg/day of octamethylcyclotetrasiloxane (D4) dissolved in either corn oil, Maalox Therapeutic concentrate, Emulphor EL 620, or PDMS 35 Centristoke Fluid via gavage for 28 days. Studies in males and females were conducted separately. In the studies using PDMS, an additional group of naïve rats (10/sex) were included to evaluate the effects of the vehicle alone. Rats were observed for clinical signs of toxicity, weighed weekly, and food consumption was monitored. On day 29, rats were sacrificed, and liver weights were determined. One female in the Maalox vehicle group and two males in the PDMS vehicle group died due to a gavage error. Animals treated with PDMS showed some anal leakage that transferred to the fur (no further details provided). No significant differences in body weights or body weight changes were seen in females treated with D4 in corn oil or Maalox. There were no statistically significant changes in body weights of females exposed to the test substance in Emulphor, compared with controls; however, increases were dose-related and trend analysis showed a positive trend for body weight on days 15, 22, and 29. Body weight gains were significantly increased from day 0-15 at 300 mg/kg/day, with a positive trend throughout the treatment period. Results in females with the PDMS vehicle showed a decreasing trend in body weight with an increasing trend in body weight gains during the first 15 days of treatment; however, there appear to be issues with the negative control responses. In males, there was a decreasing trend in body weight gain on Day 0-8 when the corn vehicle was used, but no significant changes or trends with the other vehicles were observed. Significant increases (17- 23%) in male and female food intake were seen at 300 mg/kg/day group in the corn oil group and at ≥100 mg/kg/day (females) in the Emulphor EL620 group, compared to their respective controls. Significant trends were observed in both cases throughout most of the study period. No difference in food intake was seen in the Maalox Therapeutic concentrate group. Significant increases in food intake in females in the PDMS 35 Centristoke Fluid vehicle and male Emulphor groups were transient. In the corn oil group, significant increases in absolute (18 to 44%) and relative (18 to 58%) liver weights were seen in males at ≥100 and ≥30 mg/kg/day, respectively, although the relative weights did not show a clear relation to dose. In the corn oil vehicle female groups, absolute (27 to 72%) and relative (27 to 73%) liver weights were significantly increased at ≥100 mg/kg/day, compared with controls. In Maalox Therapeutic concentrate groups, liver weights were not significantly different in males; however, in females, significant increases in absolute (18%) and relative (21%) liver weights were seen at 300 mg/kg/day, compared to controls. In the Emulphor EL620 group, significant increases in absolute and relative liver weights were seen in males (14% and 7-14%, respectively) and females (15-40% and 15-39%, respectively) at ≥100 mg/kg/day, compared to controls. No significant changes in absolute or relative liver weights were seen in rats in the PDMS 35 Centristoke Fluid vehicle groups, compared to controls. Naïve rats had similar body weight and body weight gains as the PDMS 35 Centristoke Fluid control group. In both sexes, absolute liver weights in naïve and PDMS 35 Centristoke Fluid vehicle controls were also comparable. Naïve females showed a 10% increase in absolute liver weights, compared with the PDMS 35 Centristoke Fluid vehicle group.No author-reported toxicity values were provided. A NOAEL of 10 mg/kg/day and a LOAEL of 30 mg/kg/day were determined based on increased relative liver weights in male rats when D4 was delivered in corn oil.

[33] 5887620: A collection of similar studies focused on assessing the potential for octamethylcyclotetrasiloxane (D4) mediated immunotoxicity in rats, was conducted over a two-year period. Studies in male and female rats were done separately. Repeat studies were conducted at later time points to test reproducibility, to add additional time points, or to test for recovery. This form corresponds to studies related to humoral immune responses and includes study 1 (females), 3 (males), 9 (repeat of study 1 in females), 9rec (repeat of study 1 in females, but with an extended recovery period after dosing), 13, and 14 (females only), specified in the PDF. For all of the studies, Fisher 344 rats (10-20 females [studies, 1, 9, 9rec, 13, and 14] or males [study 3] were administered 0, 10, 30, 100 or 300 mg/kg/day of octamethylcyclotetrasiloxane (D4) in corn oil via gavage for 28 days. The recovery experiment was done with control and the high dose only, and rats were allowed a 14-day recovery period before sacrifice on day 43. Rats were evaluated for mortality, clinical signs of toxicity, body weights (days 1, 8, 15, 22, and 29 and also on days 36 and 43 in the recovery group), body weight gain, and food intake (studies 1 and 3 only) two times a week. For studies 1, 3, 9, and 9rec, half of the animals per group were sacrificed on day 29 to evaluate toxicological endpoints, liver, spleen, and/or thymus weights, and gross pathology examinations. To study the effects on humoral immunity, the other half of the animals were administered an i.v. of 2x10e8 sheep red blood cells (sRBC) on day 25 and sacrificed on day 29. Endpoints examined in the immunized mice included gross pathology, serum IgM titers, spleen weights, number of spleen cells, and number of IgM sRBC antibody forming colonies (AFC) in the antibody plaque assay. Recovery animals were immunized with sRBC on day 39 and sacrificed on day 43. Group 13 female rats were administered an i.v. of 2x10e8 sheep red blood cells (sRBC) on 25 and sacrificed on day 29. To determine if a longer immunization period would affect serum antibody levels and AFC, on day 23 (as opposed to day 25 in previous studies), 10 females/group (group 14) were immunized (iv) with 2x10e8 sRBC and sacrificed on day 29. Both studies evaluated gross pathology and immune endpoints described above in the immunized groups. A positive control group for immunosuppression was included in studies 1 and 9. These rats (6/group) received 25 mg/kg of cyclophosphamide on days 25-28 via intraperitoneal injection. One male in study 3 and one female in study 9 died due to gavage errors. No overt signs of toxicity were seen compared to controls. No biologically significant changes in body weight or body weight gains were seen throughout the study periods. Food consumption was slightly increased in both sexes in a variable manner, primarily in the higher dose groups. Gross pathological observations were not reported.Absolute and relative liver weights were significantly increased in both sexes in each study indicating this as a reproducible effect across similar study types. The increases were generally dose-related, but there was variation at which significance was achieved. For females, study 1 showed changes at the lowest doses with significantly increased absolute liver weights (7, 19, 42, 86%) at 10, 30, 100, and 300 mg/kg/day, respectively, and increased relative liver weights (18, 38, 84%) at 30, 100, 300 mg/kg/day, respectively, compared with controls. The low magnitude 7% increase in absolute liver weights at 10 mg/kg/day is not considered to be biologically relevant. The repeat experiment (study 9) showed a significant increase in both absolute and relative liver weights at ≥30 mg/kg/day. Significant increases were retained in the 300 mg/kg/day group after 14-day recovery (study 9rec) with significant increases in absolute (21%) and relative (24%) liver weights. In study 14 females, and study 3 males, liver weights were significantly increased at ≥100 mg/kg-day. In males (study 3), absolute thymus weights were increased (16%) in males at 300 mg/kg/day. No significant differences in spleen weights were seen in non-immunized female or male rats.In animals used for the humoral immune assays, no significant changes in spleen weights or numbers of spleen cells were seen in any group compared to controls. No significant differences in serum IgM or AFC responses were seen in male rats. In females, increases in IgM responses to sRBC (increased AFC) were seen at ≥100 mg/kg/day. These increases occurred in the absence of changes in serum IgM titers. Significant increases in AFC remained after a 14-day recovery period, and no significant change in serum antibody titers was seen compared to control. Similar to the 4-day response (study 13) significant increases in AFC responses were seen at 300 mg/kg/day after 6 days (study 14), however no significant increases in serum antibody titers were seen compared to control.The positive controls gave the expected results. No author-reported toxicity values were provided. A NOAEL of 10 mg/kg/day and a LOAEL of 30 mg/kg/day was determined based on increased absolute and relative liver weights in female rats. A significant increase in absolute (but not relative) liver weight was observed in one of the studies in females, the magnitude of change was small (<10%), and no effects were observed at this dose in repeated studies.

[34] 5887620: A collection of similar studies focused on assessing the potential for octamethylcyclotetrasiloxane (D4) mediated immunotoxicity in rats were conducted over a two-year period. Studies on male and female rats were done separately. Repeat studies were conducted at later time points to test the reproducibility of specific effects observed and to utilize newer techniques as they become available. Some repeated studies also added recovery groups. This form corresponds to studies 5, 6, 12, and 12 (recovery) specified in the PDF. For all of the studies, Fisher 344 rats (10 females [studies 5, 12, and 12rec] or males [study 6] group) were administered 0, 10, 30, 100 or 300 mg/kg/day of octamethylcyclotetrasiloxane (D4) in corn oil via gavage for 28 days. Recovery experiments were done with control and the high dose only. Rats were evaluated for mortality, clinical signs of toxicity, body weight (days 1, 8, 15, 22, and 29 and also on days 36 and 43 in the recovery group), and food intake (studies 5 and 6 only) two times a week. At sacrifice, blood was collected for hematology (RBC, WBC, hemoglobin, hematocrit, mean corpuscular volume, mean corpuscular hemoglobin, mean corpuscular hemoglobin concentration, and leukocyte differentials). Reticulocytes were not measured in study 5, so a repeat study

(study 12) was conducted. Peripheral blood and splenocyte leukocytes were used for phenotyping. Liver, spleen, and thymus organs were weighed. Splenocytes and peripheral blood leukocytes (PBLs) were also used in cell-mediated immunity assays (one-way mixed lymphocyte (MLR), and natural killer cell activity assay) in studies 5 and 6. For these assays, a positive control group was included and received 25 mg/kg of cyclophosphamide on days 25-28 via intraperitoneal injection. Positive controls for the natural killer (NK) cell assay received 1.0 ml of 1:10 v/v anti asialo GM1 (rabbit) antibody) on day 28 via intravenous injection.No compound-related deaths occurred. No overt signs of toxicity were seen compared to controls. No biologically significant changes in body weight or body weight gains were seen throughout the study period. Food consumption was slightly increased in both sexes in a variable manner, primarily in the higher dose groups. Gross pathological observations were not reported. In males, significant increases in absolute (13ns,16, 25, and 46%) and relative (8, 11, 20, and 47%) liver weights were observed at 10, 30, 100, and 300 mg/kg/day, respectively, compared with controls. In study 5 females, significant increases in absolute (10, 15, 44, and 88%) and relative (10, 14, 40, and 81%) liver weights were seen at 10, 30, 100, and 300 mg/kg/day, respectively, compared with controls. In the repeat studies, similar increases in absolute (10, 28, and 64%) and relative (11, 25, and 66%) liver weights at 30, 100, and 300 mg/kg/day, were observed. After recovery, relative liver weight remained increased 8% at 300 mg/kg/day, compared with controls. Absolute and relative thymus weights were generally decreased, but only relative thymus weights in males (27%) and absolute (17%) and relative 19%) thymus weights in females were statistically significant at 300 mg/kg/day. Thymus weights were not recorded in the main repeat study. No significant differences in absolute or relative spleen weights were seen in either sex. Dose-dependent changes in hematological parameters in males included decreases in erythrocyte counts, significant at ≥100 mg/kg/day, decreases in hemoglobin and hematocrit at 300 mg/kg/day, and increased MCV and MCH at ≥10 mg/kg/day. Female data were generated in both the main and repeated studies. The concentrations at which effects became statistically significant varied, but in general, the results were consistent with males showing decreases in erythrocytes, hemoglobin, and hematocrit. MCV and MCH were increased in study 5, but these changes were not reproducible. Erythrocytes and hematocrit remained decreased after the 14-day recovery. Changes in the leukocytes and platelets counts occurred in both sexes; however, the authors conclude these cells "were not targeted by D4". No significant differences in absolute lymphocyte or phenotype were seen in the males. In peripheral blood, WBC counts were significantly decreased at ≥100 mg/kg-day, and B-cells were decreased at the same dose. As percent values, there were significant reductions in B-cells, T-cells, and CD4 T-cells at 300 mg/kg/day. The main study in females (study 5) showed statistically significant decreases in the absolute values of B-cells, and in CD4 and CD8 T-cells, compared with controls; the effects were dose-related and became significant at ≥100 mg/kg/day. In the repeat study, only a decrease in the percent, but not absolute values of B-cells was observed. During repeat studies, a more reliable antibody for B-cells became available and the previous results were confirmed. The repeat study, however, showed a non-dose-related decrease in total T-cells, but not changes in absolute values of CD4 or CD8 T cells. No significantly relevant changes in cell-mediated immunity were seen as measured by one-way mixed lymphocyte (MLR) response and NK cell activity of splenocytes and peripheral blood lymphocytes compared to control. Positive controls responded as expected. No author-reported toxicity values were provided. A LOAEL of 10 mg/kg/day was determined based on increased absolute and relative liver weights in both sexes and RBC-related hematological changes.

[35] 5887620: A collection of similar studies focused on assessing the potential for octamethylcyclotetrasiloxane (D4) mediated immunotoxicity in rats were conducted over a two-year period. Studies on male and female rats were done separately. Repeat studies were conducted at later time points to test the reproducibility of observed effects, and also to assess the potential for recovery. This form corresponds to studies related to macrophage function as measured by the vascular clearance and phagocytic uptake of 51Cr sheep red blood cell (sRBC) and includes studies 2 (male), 4 (female), 10 (repeat of study 4) and 10rec (recovery experiment), 11 (repeat of study 2) and 11rec (recovery experiment) as specified in the PDF. For all of the studies, Fisher 344 rats (10 females [studies 4, 10, and 10rec] or males [study 2, 11, 11rec] group) were administered 0, 10, 30, 100 or 300 mg/kg/day of octamethylcyclotetrasiloxane (D4) in corn oil via gavage for 28 days. Recovery experiments were done with control and the high dose groups only. Rats were evaluated for mortality, clinical signs of toxicity, body weight (days 1, 8, 15, 22, and 29 and also on days 36 and 43 in the recovery group), and food intake (studies 2 and 4 only) two times a week. On day 29 rats were injected with 51Cr-labeled sheep erythrocytes. Clearance of labelled sheep erythrocytes from the blood was determined over the first 30 minutes to determine phagocytic index and half-life. Animals were sacrificed after 60 minutes. Organ weights (liver, spleen, lung, thymus, and kidney) and distribution of the labeled sheep erythrocyte were determined. In the recovery experiments, at the end of recovery on day 43, animals were injected with 51Cr-labeled sheep erythrocytes. Endpoints described in the main study were evaluated.A positive control for the functional activity of RES was included; animals were injected with maleic vinyl ether (5mg/ml) via i.v. 24 hours prior to the evaluation of the RES.No compound-related deaths occurred. No overt signs of toxicity were seen compared to control. In groups 2 and 4, no biologically significant changes in body weights, body weight gains or terminal body weights were seen throughout the study period. In the repeat study, no body weight effects were seen in females; in males, body weight gain over the course of the study was significantly decreased 32%, with terminal body weight significantly decreased (9%) at 300 mg/kg/day compared to control. Food intake was significantly increased in the 300 mg/kg/day females throughout the study (except for week 1, which was decreased), and in the 100 mg/kg/day females during the second half of the study; no differences were seen in males. Gross pathology was not reported. Significant increases in absolute liver weights were seen in females (19 to 81%) at ≥30 mg/kg/day in group 4 and in the repeat study (18 to 56%) at ≥100 mg/kg/day. Only liver and thymus weight changes were consistent across studies. In males, significant increases in absolute liver weights (11 to 52%) were seen at ≥30 mg/kg/day in group 2, and in the repeat study (27%) at 300 mg/kg/day, compared with controls. In females, significant increases in absolute (19 to 81%) liver weights occurred at ≥30 mg/kg/day in study 4, and at ≥100 mg/kg/day in the repeat study 10. Absolute thymus weights were significantly decreased (17 and 18%) in study 2 and 11 males, respectively, at 300 mg/kg/day. Absolute thymus weights were also significantly decreased (22%) in females in study 12 at 300 mg/kg/day, but not in study 4. Absolute lung weights were significantly increased at ≥30, in study 2 males, but not in the repeat study. No dose-related changes were seen in other organs. After recovery, the only organ weight that remained changed was an increase in liver weights (15%) in males at 300 mg/kg/day. In males, a non-significant dose-related decrease in the half-life of labeled erythrocytes in the blood was seen (significantly decreased only at 100 mg/kg/day in the repeat study). A significant increase in the percentage of uptake by the liver (32.2% in the repeat study; non-significant 10% in group 2) was seen; percent uptake in the thymus, lung and kidney were significantly decreased. In the recovery group, liver uptake remained significantly increased (32%) and kidney uptake remained significantly decreased. In females, a non-significant dose-related decrease in the half-life of labeled erythrocytes in the blood was seen. Unlike in males, the decrease was not associated with liver uptake, but a significant decrease in splenic uptake (decreased splenic phagocytosis). After the recovery period, splenic phagocytosis decreased, albeit not significantly compared to control. Macrophage function as measured by vascular clearance and phagocytic uptake of radiolabeled sRBC was not considered by the study authors to be related to the test substance but rather to liver size and, thus, liver blood volumes in males. These changes were not seen in females. In females, splenic phagocytosis is decreased which may be affecting vascular clearance. No author-reported toxicity values were provided.A NOAEL of 10 mg/kg/day and a LOAEL of 30 mg/kg/day was determined based on increased absolute liver weights in male and female rats.

[36] 6835125: In a study focused on characterizing the protein expression levels and activities of microsomal CYP450 enzymes following exposure, groups of Sprague-Dawley rats (3-4/sex/group) were administered D4 (purity not reported) at 0 (vehicle control), 1, 5, 20, or 100 mg/kg-day for 4 consecutive days, via gavage in corn oil. A group of positive control animals were administered phenobarbital injections over 4 consecutive days. Animal body weights were recorded daily. At the end of dosing, animals were sacrificed, and livers were excised, weighed, and homogenated for microsome extraction. Microsomal fractions were evaluated for CYP450 protein expression and incubated with PRF and ERF as substrates to determine PROD and EROD activities, respectively. No body weight gain changes in treated animals were observed, compared with controls. Quantitative data for body weights were not provided. Relative liver weights in females were significantly increased at 20 and 100 mg/kg-day, although the change was not clearly dose-responsive. The magnitude of change at 100 mg/kg-day was reported to be a 19% increase. A 10% increase in relative liver weights of high-dose males was not statistically significant. Absolute liver weights were not reported. Increases in PROD and EROD activities occurred at ≥5 mg/kg-day and at ≥20 mg/kg-day, respectively. Male rats showed significant induction of CYP2B1/2 at ≥5 mg/kg-day, and at CYP3A1/2 at 100 mg/kg-day. Female rats showed significant induction CYP2B1/2 in all treatment groups and CYP3A1/2 at ≥20 mg/kg-day. No induction to CYP1A1/2 was observed in either sex. NADPH reductase was significantly induced in high-dose females but showed no changes in males. No author-reported toxicity values were provided. A NOAEL of 5 mg/kg-day and a LOAEL of 20 mg/kg-day were identified based on significantly increased relative liver weights in female rats.

Octamethylcyclotetrasiloxane (D4)- Parent compound - Subchronic (>30-91 days)

Guideline and Animal Species, Strain, Sex	Exposure Route and Exposure Duration	Study-wide POD and Dose/ Concentration(s)	Summary	Major Limitations	Principal Target Organs/Systems and OQD*	HERO ID
No guidelines or adherence to GLP conditions were reported. It was stated that the study was not in compliance with GLP. Rat-Sprague-Dawley - [rat]-Both	Inhalation-Vapor-Duration: Subchronic (>30-90 days)-5-6-5-week(s) 6 hours/day 5 days/week 5 week(s) Animals were exposed for 6 hrs/day, 5 days/week for 5 weeks (or a total of 28 days)	**POD: 10 ppm (in air, water, or food) (NOAEC) -Increased liver weights** n= 10 Dose= 0, n= 10 Dose= 10, n= 10 Dose= 705, ppm (in air, water, or food)	See footnotes for full summary [1]	The study was limited in scope. High concentration was > 700 ppm.	Hepatic/Liver-Absolute and relative liver weights (inhalation study); liver histopathology and liver enzymes (7-ethoxycoumarin deethylase [EOD]; 7-ethoxyresorufin deethylase [EOR]; aldrin epoxidase [ALD]; epoxide hydrolase [EH]; Glutathione-s-transferase [GST]; and UDP-Glucuronyl transferase [GLU-T]); oral study; High	Dow Corning, 2001 5884201
No guidelines or adherence to GLP conditions were reported. It was stated that the study was not in compliance with GLP. Mouse-CD-1 - [mouse]-Both	Inhalation-Vapor-Duration: Subchronic (>30-90 days)-5-6-5-week(s) 6 hours/day 5 days/week 5 week(s) Animals were exposed for 6 hrs/day, 5 days/week for 5 weeks (or a total of 28 days)	**POD: 10 ppm (in air, water, or food) (NOAEC) -increased liver weights** n= 10 Dose= 0, n= 10 Dose= 10, n= 10 Dose= 705, ppm (in air, water, or food)	See footnotes for full summary [2]	The study was limited in scope. The high concentration was > 700 ppm.	Hepatic/Liver-Absolute and relative liver weights (inhalation study); liver histopathology and liver enzymes (7-ethoxycoumarin deethylase [EOD]; 7-ethoxyresorufin deethylase [EOR]; aldrin epoxidase [ALD]; epoxide hydrolase [EH]; Glutathione-s-transferase [GST]; and UDP-Glucuronyl transferase [GLU-T]); oral study; High	Dow Corning, 2001 5884201

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Octamethylcyclotetrasiloxane (D4)- Parent compound - Subchronic (>30-91 days)

Guideline and Animal Species, Strain, Sex	Exposure Route and Exposure Duration	Study-wide POD and Dose/ Concentration(s)	Summary	Major Limitations	Principal Target Organs/Systems and OQD*	HERO ID
No guidelines or adherence to GLP conditions were reported. It was stated that the study was not in compliance with GLP. Rabbit-New Zealand White - [rabbit]-Both	Inhalation-Vapor-Duration: Subchronic (>30-90 days)-5-6-5-week(s) 6 hours/day 5 days/week 5 week(s) Animals were exposed for 6 hrs/day, 5 days/week for 5 weeks (or a total of 28 days)	**POD: ppm (in air, water, or food) (Other) -Not suitable for POD determination** n= 10 Dose= 0, n= 10 Dose= 10, n= 10 Dose= 705, ppm (in air, water, or food)	See footnotes for full summary [3]	The study was limited in scope	Hepatic/Liver-Absolute and relative liver weights (inhalation study); liver histopathology and liver enzymes (7-ethoxycoumarin deethylase [EOD]; 7-ethoxyresorufin deethylase [EOR]; aldrin epoxidase [ALD]; epoxide hydrolase [EH]; Glutathione-s-transferase [GST]; and UDP-Glucuronyl transferase [GLU-T]); oral study; High	Dow Corning, 2001 5884201
No guidelines or adherence to GLP conditions were reported. It was stated that the study was not in compliance with GLP. Guinea pig-Hartley - [guinea pig]-Both	Inhalation-Vapor-Duration: Subchronic (>30-90 days)-5-6-5-week(s) 6 hours/day 5 days/week 5 week(s) Animals were exposed for 6 hrs/day, 5 days/week for 5 weeks (or a total of 28 days)	**POD: ppm (in air, water, or food) (Other) -Not suitable for POD determination** n= 10 Dose= 0, n= 10 Dose= 10, n= 10 Dose= 705, ppm (in air, water, or food)	See footnotes for full summary [4]	The study was limited in scope	Hepatic/Liver-Absolute and relative liver weights (inhalation study); liver histopathology and liver enzymes (7-ethoxycoumarin deethylase [EOD]; 7-ethoxyresorufin deethylase [EOR]; aldrin epoxidase [ALD]; epoxide hydrolase [EH]; Glutathione-s-transferase [GST]; and UDP-Glucuronyl transferase [GLU-T]); oral study; High	Dow Corning, 2001 5884201

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Octamethylcyclotetrasiloxane (D4)- Parent compound - Subchronic (>30-91 days)

Guideline and Animal Species, Strain, Sex	Exposure Route and Exposure Duration	Study-wide POD and Dose/ Concentration(s)	Summary	Major Limitations	Principal Target Organs/Systems and OQD*	HERO ID
No guidelines or adherence to GLP conditions were reported. It was stated that the study was not in compliance with GLP. Hamster, Syrian-Other (Golden)-Both	Inhalation-Vapor-Duration: Subchronic (>30-90 days)-5-6-5-week(s) 6 hours/day 5 days/week 5 week(s) Animals were exposed for 6 hrs/day, 5 days/week for 5 weeks (or a total of 28 days)	**POD: 10 ppm (in air, water, or food) (NOAEC) -increased liver weights** n= 10 Dose= 0, n= 10 Dose= 10, n= 10 Dose= 705, ppm (in air, water, or food)	See footnotes for full summary [5]	The study was limited in scope. High concentration was > 700 ppm.	Hepatic/Liver-Absolute and relative liver weights (inhalation study); liver histopathology and liver enzymes (7-ethoxycoumarin deethylase [EOD]; 7-ethoxyresorufin deethylase [EOR]; aldrin epoxidase [ALD]; epoxide hydrolase [EH]; Glutathione-s-transferase [GST]; and UDP-Glucuronyl transferase [GLU-T]); oral study; High	Dow Corning, 2001 5884201
The study was conducted under GLP conditions.. Rat-Other (Crl:CD(SD) BR)-Female	Inhalation-Vapor-Duration: Subchronic (>30-90 days)-1-F0- premating (28)-F0-mating (15)-F0 - gestation (GD19) "Overall phase" -Females were exposed 28 days prior to mating, during mating (up to 15 days) and until GD 19	**POD: 301 ppm (in air, water, or food) (NOAEL) - Decreased viable fetuses, implantation sites, and corpora lutea** n= 24 Dose= 0, n= 24 Dose= 72, n= 24 Dose= 301, n= 24 Dose= 503, n= 24 Dose= 698, ppm (in air, water, or food)Total # of generations: 1 Female Exposure: F0- premating, 28, F0- mating, 15, F0 - gestation, GD19	See footnotes for full summary [6]	No major limitations.	Mortality-Mortality-Nutritional/Metabolic-Body weight and food consumption-Other (please specify below) (Clinical signs)-Clinical signs-Other (please specify below) (Endocrine)-Adrenal gland and thyroid weight-Reproductive/Developmental-Pre-coital interval, mating index, fertility index. Gravid uteri weight. Ovarian weight. Uteri and ovaries were examined for numbers of fetuses, early and late resorptions, total implantations, implantation sites, pre-implantation loss, post-implantation loss and number of viable fetuses.; High	Dow Corning, 1998 5887452

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Octamethylcyclotetrasiloxane (D4)- Parent compound - Subchronic (>30-91 days)

Guideline and Animal Species, Strain, Sex	Exposure Route and Exposure Duration	Study-wide POD and Dose/ Concentration(s)	Summary	Major Limitations	Principal Target Organs/Systems and OQD*	HERO ID
The study was conducted under GLP conditions.. Rat-Other (Crl:CD(SD) BR)-Female	Inhalation-Vapor-Duration: Short-term (>1-30 days)-1-F0- premating (28) "Overall phase" -Females were exposed 28 days prior to mating, during mating (up to 15 days) and until GD 19	**POD: 702 ppm (in air, water, or food) (NOAEL) - Reproductive/developmental effects** n= 30 Dose= 0, n= 60 Dose= 702, ppm (in air, water, or food)Total # of generations: 1 Female Exposure: F0- premating, 28, F0- mating, 15, F0 - gestation, GD19	See footnotes for full summary [7]	Data are highly variable with SD equal to and greater than the mean.	Mortality-Mortality-Nutritional/Metabolic-Body weight and food consumption-Other (please specify below) (Clinical signs)-Clinical signs-Reproductive/Developmental-Pre-coital interval, mating index, fertility index. Gravid uteri weight. Ovarian weight. Uteri and ovaries were examined for numbers of fetuses, early and late resorptions, total implantations, implantation sites, pre-implantation loss, post-implantation loss and number of viable fetuses.; High	Dow Corning, 1998 5887452

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Octamethylcyclotetrasiloxane (D4)- Parent compound - Subchronic (>30-91 days)

Guideline and Animal Species, Strain, Sex	Exposure Route and Exposure Duration	Study-wide POD and Dose/ Concentration(s)	Summary	Major Limitations	Principal Target Organs/Systems and OQD*	HERO ID
The study was conducted under GLP conditions.. Rat-Other (Crl:CD(SD) BR)-Female	Inhalation-Vapor-Duration: Short-term (>1-30 days)-1-F0- premating (3)-F0-mating (2)-F0 - gestation (3) "Overall phase" -Females were exposed 28 days prior to mating, during mating (up to 15 days) and until GD 19	**POD: 696 ppm (in air, water, or food) (LOAEL) -Maternal toxicity (decreased body weight) and reproductive end-points.** n= 30 Dose= 0, n= 60 Dose= 696, ppm (in air, water, or food)Total # of generations: 1 Female Exposure: F0- premating, 28, F0- mating, 15, F0 - gestation, GD19	See footnotes for full summary [8]	Mating interval was different for control and exposed groups precluding evaluation of pre-coital interval, mating, and fertility indices. Some data are highly variable with SD equal to and greater than the mean.	Mortality-Mortality-Nutritional/Metabolic-Body weight and food consumption-Other (please specify below) (Clinical signs)-Clinical signs-Reproductive/Developmental-Pre-coital interval, mating index, fertility index. Gravid uteri weight. Ovarian weight. Uteri and ovaries were examined for numbers of fetuses, early and late resorptions, total implantations, implantation sites, pre-implantation loss, post-implantation loss and number of viable fetuses.; High	Dow Corning, 1998 5887452

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Octamethylcyclotetrasiloxane (D4)- Parent compound - Subchronic (>30-91 days)

Guideline and Animal Species, Strain, Sex	Exposure Route and Exposure Duration	Study-wide POD and Dose/ Concentration(s)	Summary	Major Limitations	Principal Target Organs/Systems and OQD*	HERO ID
The study was conducted under GLP conditions. Rat-Other (Crl:CD(SD) BR)-Female	Inhalation-Vapor-Duration: Short-term (>1-30 days)-1-F0- premating-F0- mating-F0 - gestation (GD 2-5) "Overall phase" -Females were exposed 28 days prior to mating, during mating (up to 15 days) and until GD 19	**POD: 702 ppm (in air, water, or food) (NOAEL) -** n= 24 Dose= 0, n= 24 Dose= 702, ppm (in air, water, or food)Total # of generations: 1 Female Exposure: F0- premating, 28, F0- mating, 15, F0 - gestation, GD19	See footnotes for full summary [9]	One concentration studied.	Mortality-Mortality-Nutritional/Metabolic-Body weight and food consumption-Other (please specify below) (Clinical signs)-Clinical signs-Reproductive/Developmental-Pre-coital interval, mating index, fertility index. Gravid uteri weight. Ovarian weight. Uteri and ovaries were examined for numbers of fetuses, early and late resorptions, total implantations, implantation sites, pre-implantation loss, post-implantation loss and number of viable fetuses.; High	Dow Corning, 1998 5887452

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Octamethylcyclotetrasiloxane (D4)- Parent compound - Subchronic (>30-91 days)

Guideline and Animal Species, Strain, Sex	Exposure Route and Exposure Duration	Study-wide POD and Dose/ Concentration(s)	Summary	Major Limitations	Principal Target Organs/Systems and OQD*	HERO ID
No guideline was specified. The study was conducted under GLP conditions. Rat-Sprague-Dawley - [rat]-Both	Inhalation-Vapor-Duration: Subchronic (>30-90 days)-7-6-13-week(s) 6 hours/day 7 days/week 13 week(s)	**POD: 51 ppm (in air, water, or food) (LOAEC) - Increased absolute and relative liver weights.** n= 40 Dose= 0, n= 20 Dose= 51, n= 20 Dose= 301, n= 40 Dose= 700, ppm (in air, water, or food)	See footnotes for full summary [10]	No major limitations.	Mortality-Mortality-Nutritional/Metabolic-Body weight, body weight gains, and food intake-Immune/Hematological-Hematology (RBC count, hematocrit, hemoglobin concentration, platelet count, and total and differential WBC counts);Spleen weight and histology; histology on lymph nodes and thymus-Hepatic/Liver-Liver weight and histology; serum levels of ALT, AST, GGT, LDH, total bilirubin-Other (please specify below) (Endocrine)-Adrenal weight; histology on adrenal glands, pancreas, pituitary, and thyroid/parathyroid. Gross necropsy.; High	Dow Corning, 1989 7310563

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Octamethylcyclotetrasiloxane (D4)- Parent compound - Subchronic (>30-91 days)

Guideline and Animal Species, Strain, Sex	Exposure Route and Exposure Duration	Study-wide POD and Dose/ Concentration(s)	Summary	Major Limitations	Principal Target Organs/Systems and OQD*	HERO ID
OECD TG 413 and U.S. EPA TG 40 CFR1 798.2450; and EC Directive 87/302 (Appendix Ij -:0 the Directive EC 67/54B, OfficialJournal of the European Communities No Ll33 'of May 30, 1988, chapter 5, page 20: Sub-chronic inhalation toxicity study: 90-day repeated inhalation-dose study using rodent species; GLP compliant. Rat-Fischer 344 - [rat]-Both	Inhalation-Vapor-Duration: Subchronic (>30-90 days)-5-6-13-week(s) 6 hours/day 5 days/week 13 week(s) Animals were exposed nose-only for 6hrs/day, 5 days/week for 13 weeks	**POD: 420 mg/m^3 (NOAEC) - Interstitial inflammation in the lungs** n= 60 Dose= 0, n= 40 Dose= 420, n= 40 Dose= 1480, n= 40 Dose= 5910, mg/m^3	See footnotes for full summary [11]	No major limitations were identified.	Mortality-Mortality-Hepatic/Liver-Organ weights, gross necropsy, histopathology, clinical chemistry (serum glucose, bilirubin, total cholesterol, triglycerides, phospholipids, AST, ALT, LDH, LDH, ALP, GGT, total protein, albumin, globulin, A/G ratio))-Lung/Respiratory-Organ weights; gross necropsy; histopathology (nasal cavities, larynx, lungs, trachea)-Reproductive/Developmental-Organ weights (ovaries, testes); gross necropsy; histopathology (epididymides, ovaries, prostate, seminal vesicles, testes, uterus, vagina); estrous cycle stage at time of sacrifice; High	RCC, 1995 7309971

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Octamethylcyclotetrasiloxane (D4)- Parent compound - Subchronic (>30-91 days)

Guideline and Animal Species, Strain, Sex	Exposure Route and Exposure Duration	Study-wide POD and Dose/ Concentration(s)	Summary	Major Limitations	Principal Target Organs/Systems and OQD*	HERO ID
OECD TG 413 and U.S. EPA TG 40 CFR1 798.2450; and EC Directive 87/302 (Appendix Ij -:0 the Directive EC 67/54B, OfficialJournal of the European Communities No Ll33 'of May 30, 1988, chapter 5, page 20: Sub-chronic inhalation toxicity study: 90-day repeated inhalation-dose study using rodent species; GLP compliant. Rat-Fischer 344 - [rat]-Both	Inhalation-Aerosol-Duration: Subchronic (>30-90 days)-5-6-13-week(s) 6 hours/day 5 days/week 13 week(s) Animals were exposed nose-only for 6hrs/day, 5 days/week for 13 weeks	**POD: mg/m^3 (Other) -** n= 60 Dose= 0, n= 60 Dose= 10870, mg/m^3	See footnotes for full summary [12]	The study did use a proper control. At the concentration tested, an aerosol should have been used as a control.	nan; Uninformative	RCC, 1995 7309971

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Octamethylcyclotetrasiloxane (D4)- Parent compound - Subchronic (>30-91 days)

Guideline and Animal Species, Strain, Sex	Exposure Route and Exposure Duration	Study-wide POD and Dose/ Concentration(s)	Summary	Major Limitations	Principal Target Organs/Systems and OQD*	HERO ID
The study was GLP compliant. Rat-Sprague-Dawley - [rat]-Male	Inhalation-Vapor-Duration: Subchronic (>30-90 days)-1-F0- premating (70) Rats were exposed for 70 days prior to mating and throughout mating (up to 15 days)	**POD: 300 ppm (in air, water, or food) (NOAEC) - Increased absolute and relative liver weights** n= 22 Dose= 0, n= 22 Dose= 71, n= 22 Dose= 300, n= 22 Dose= 492, n= 22 Dose= 694, ppm (in air, water, or food)Total # of generations: 1 Male Exposure: F0-premating, 70	See footnotes for full summary [13]	No major limitations.	Mortality-Mortality-Other (please specify below) (Clinical signs)-Clinical signs-Hepatic/Liver-Liver weight and histology-Reproductive/Developmental-Weight: epididymides (total and cauda), prostate, seminal vesicles with coagulating glands (with accessory fluids), and testes; Histology: Epididymis, penis, prepuce, preputial gland, prostate, and testis,Sperm motility and morphology;Reproductive parameters (days between pairing and coitus, mating indices, fertility indices, and duration of gestation and parturition); litter size, sex, gross malformation in pups, pup body weight, survival, pup behavior, necropsy at PND 4; High	WIL Research, 1997 7310463

* Overall Quality Determination

[1] 5884201: A series of experiments were conducted in multiple species to assess differences in liver responses to inhalation exposure to D4 vapor. The following endpoints were assessed: Induction of liver enzymes in rats and guinea pigs (Experiment 1: 5/sex/group, exposure to 0 or 700 ppm for 5 days); urinary metabolite excretion in rats, mice, guinea pigs, rabbits, and hamsters (Experiment 2; 5/sex/group, exposure to 0, 10, or 700 ppm for 28 days); and liver cell replication in rats (10/sex/group, exposure to 0 or 700 ppm for 3 or 5 days). Only experiment 2 (urinary metabolite group) measured apical endpoints; therefore the other experiments were not evaluated. Experiment 2: In a study primarily focused on measuring urinary metabolites, groups of Sprague Dawley rats (5/sex/group) were exposed to D4 vapor (purity >99%) at target concentrations of 0, 10, or 700 ppm (mean measured: 0, 10, or 705 ppm) for 28 days. Animals were observed for mortality and clinical signs of toxicity. Body weights were recorded at study initiation and at terminal sacrifice. At the end of exposure, all animals were necropsied, and absolute and relative liver weights were recorded. As part of an aqueous silanol functionality test (ASFT), animals were placed in metabolism cages overnight and urine samples were collected on study days 1, 3, 5, 12, 19, and 25. The samples were pooled by sex and to determine the extent of Si-CH3 bond cleavage, the metabolites methyltris(trimethylsiloxy silane (T) and octamethyltrisiloxane (D) were quantified for cross-species comparisons. Results from sampling days 3 and 25 were reported. No animals died. There were no clinical signs that were attributed to exposure (data not shown). The body weights of treated animals were comparable to controls. Significant increases in absolute liver weights were observed in males (32% and 28%) and females (41% and 43%), respectively. No author-reported toxicity values were provided. A NOAEC of 10 ppm and a LOAEC of 705 ppm (measured) were identified based on increased absolute and relative liver weights.

[2] 5884201: A series of experiments were conducted in multiple species to assess differences in liver responses to inhalation exposure to D4 (vapor). The following endpoints were assessed: Induction of liver enzymes in rats and guinea pigs (Experiment 1; 5/sex/group, exposure to 0 or 700 ppm for 5 days); urinary metabolite excretion in rats, mice, guinea pigs, rabbits, and hamsters (Experiment 2; 5/sex/group, exposure to 0, 10, or 700 ppm for 28 days); and liver cell replication in rats (10/sex/group, exposure to 0 or 700 ppm for 3 or 5 days). All of the experiments presumably assessed mortality and performed clinical observations. Only experiment 2 (urinary metabolite group) measured apical endpoints; therefore the other experiments were not evaluated. Experiment 2: In a study primarily focused on measuring urinary metabolites, groups of CD-1 mice (5/sex/group) were exposed to D4 vapor (purity >99%) at target concentrations of 0, 10, or 700 ppm (mean measured: 10 and 705 ppm) for 28 days. Animals were observed for mortality and clinical signs of toxicity. Body weights were recorded at study initiation and at terminal sacrifice. At the end of exposure, all animals were necropsied and absolute and relative liver weights were recorded. As part of an aqueous silanol functionality test (ASFT), animals were placed in metabolism cages overnight and urine samples were collected on study days 1, 3, 5, 12, 19, and 25. The samples were pooled by sex and to determine the extent of Si-CH3 bond cleavage, the metabolites methyltris(trimethylsiloxy silane (T) and octamethyltrisiloxane (D) were quantified for cross-species comparisons.. Results from sampling days 3 and 25 were reported. No animals died. There were no clinical signs that were attributed to exposure (data not shown). The body weights of treated animals were comparable to controls. Significant increases in absolute liver weights were observed in males (65% and 64%) and females (83% and 82%), respectively. No author-reported toxicity values were provided. A NOAEC of 10 ppm and a LOAEC of 705 ppm (measured) were identified based on increased absolute and relative liver weights.

[3] 5884201: A series of experiments were conducted in multiple species to assess differences in liver responses to inhalation exposure to D4 vapor. The following endpoints were assessed: Induction of liver enzymes in rats and guinea pigs (Experiment 1; 5/sex/group, exposure to 0 or 700 ppm for 5 days); urinary metabolite excretion in rats, mice, guinea pigs, rabbits, and hamsters (Experiment 2; 5/sex/group, exposure to 0, 10, or 700 ppm for 28 days); and liver cell replication in rats (10/sex/group, exposure to 0 or 700 ppm for 3 or 5 days). All of the experiments presumably assessed mortality and performed clinical observations. Only experiment 2 (urinary metabolite group) measured apical endpoints; therefore the other experiments were not evaluated. Experiment 2: In a study primarily focused on measuring urinary metabolites, groups of New Zealand White rabbits (5/sex/group) were exposed to to D4 vapor (purity >99%) at target concentrations of 0, 10, or 700 ppm (mean measured: 10 and 705 ppm) for 28 days. Animals were observed for mortality and clinical signs of toxicity. Body weights were recorded at study initiation and at terminal sacrifice. At the end of exposure, all animals were necropsied and absolute and relative liver weights were recorded. As part of an aqueous silanol functionality test (ASFT), animals were placed in metabolism cages overnight and urine samples were collected on study days 1, 3, 5, 12, 19, and 25. The samples were pooled by sex and to determine the extent of Si-CH3 bond cleavage, the metabolites methyltris(trimethylsiloxy silane (T) and octamethyltrisiloxane (D) were quantified for cross-species comparisons. Results from sampling days 3 and 25 were reported. No animals died. There were no clinical signs that were attributed to exposure (data not shown). The body weights and liver weights of treated animals were comparable to controls. No author-reported toxicity values were provided. Although no changes in body weights and liver weights were observed, the scope of the study is too narrow to confidently derive an NOAEC.

[4] 5884201: A series of experiments were conducted in multiple species to assess differences in liver responses to inhalation exposure to D4 vapor. The following endpoints were assessed: Induction of liver enzymes in rats and guinea pigs (Experiment 1; 5/sex/group, exposure to 0 or 700 ppm for 5 days); urinary metabolite excretion in rats, mice, guinea pigs, rabbits, and hamsters (Experiment 2; 5/sex/group, exposure to 0, 10, or 700 ppm for 28 days); and liver cell replication in rats (10/sex/group, exposure to 0 or 700 ppm for 3 or 5 days). All of the experiments presumably assessed mortality and performed clinical observations. Only experiment 2 (urinary metabolite group) measured apical endpoints; therefore the other experiments were not evaluated. Experiment 2: In a study primarily focused on measuring urinary metabolites, groups of Dunkin Hartley guinea pigs (5/sex/group) were exposed to D4 vapor (purity >99%) at target concentrations of 0, 10, or 700 ppm (mean measured: 10 and 705 ppm) for 28 days. Animals were observed for mortality and clinical signs of toxicity. Body weights were recorded at study initiation and at terminal sacrifice. At the end of exposure, all animals were necropsied and absolute and relative liver weights were recorded. As part of an aqueous silanol functionality test (ASFT), animals were placed in metabolism cages overnight and urine samples were collected on study days 1, 3, 5, 12, 19, and 25. The samples were pooled by sex and to determine the extent of Si-CH3 bond cleavage, the metabolites methyltris(trimethylsiloxy silane (T) and octamethyltrisiloxane (D) were quantified for cross-species comparisons.. Results from sampling days 3 and 25 were reported. No animals died. There were no clinical signs that were attributed to exposure (data not shown). The body weights and liver weights of treated animals were comparable to controls. No author-reported toxicity values were provided. Although no changes in body weights and liver weights were observed, the scope of the study is too narrow to confidently derive an NOAEC.

[5] 5884201: A series of experiments were conducted in multiple species to assess differences in liver responses to inhalation exposure to D4 vapor. The following endpoints were assessed: Induction of liver enzymes in rats and guinea pigs (Experiment 1; 5/sex/group, exposure to 0 or 700 ppm for 5 days); urinary metabolite excretion in rats, mice, guinea pigs, rabbits, and hamsters (Experiment 2; 5/sex/group, exposure to 0, 10, or 700 ppm for 28 days); and liver cell replication in rats (10/sex/group, exposure to 0 or 700 ppm for 3 or 5 days). All of the experiments presumably assessed mortality and performed clinical observations. Only experiment 2 (urinary metabolite group) measured apical endpoints; therefore the other experiments were not evaluated. Experiment 2: In a study primarily focused on measuring urinary metabolites, groups of Syrian hamsters (5/sex/group) were exposed to D4 vapor (purity >99%) at target concentrations of 0, 10, or 700 ppm (mean measured: 10 and 705 ppm) for 28 days. Animals were observed for mortality and clinical signs of toxicity. Body weights were recorded at study initiation and at terminal sacrifice. At the end of exposure, all animals were necropsied and absolute and relative liver weights were recorded. As part of an aqueous silanol functionality test (ASFT), animals were placed in metabolism cages overnight and urine samples were collected on study days 1, 3, 5, 12, 19, and 25. The samples were pooled by sex and to determine the extent of Si-CH3 bond cleavage, the metabolites methyltris(trimethylsiloxy silane (T) and octamethyltrisiloxane (D) were quantified for cross-species comparisons.. Results from sampling days 3 and 25 were reported. No animals died. There were no clinical signs that were attributed to exposure (data not shown). The body weights of treated animals were comparable to controls. Significant increases in absolute liver weights were observed in males (22% and 20%) and females (33% and 27%), respectively. No author-reported toxicity values were provided. A NOAEC of 10 ppm and a LOAEC of 705 ppm (measured) were identified based on increased absolute and relative liver weights.

[6] 5887452: To study the effects of exposure during overall reproductive/developmental stages: Female Crl:CD(SD)BR rats (24/group) were exposed to 0, 72, 301, 503 or 698 ppm (analytical, corresponding to 0, 70, 300, 500, and 700 ppm nominal concentrations) of octamethylcyclotetrasiloxane (D4) vapor via whole-body inhalation (6 hours/day daily) twenty-eight days prior to mating with an unexposed male (1:1). Exposure continuing through mating and gestation until gestation day (GD) 19. Females were mated (up to 15 days) until presence of sperm in a vaginal smear or a copulation plug was seen. The day when evidence of mating occurred was considered gestation day 0. Surviving females were sacrificed on GD 20. Endpoints evaluated included clinical signs, body weight, food consumption, pre-coital interval, mating index, and fertility index. Gross necropsy was performed on the thoracic, abdominal, and pelvic cavities. The following organs were weighed: gravid uteri, brain, ovaries, adrenal glands, and thyroid glands. Uteri and ovaries were examined for numbers of fetuses, early and late resorptions, total implantations, pre-implantation loss, post-implantation loss, and corpora lutea. Implantation site sizes were also measured.All females survived until scheduled sacrifice. No compound-related clinical signs were observed compared to control. No difference in days between pairing and coitus (ranged from 2.4-2.9 days), mating indices (ranged from 95.8- 100%), or fertility indices (ranged from 91.7% to 95.8%) were seen compared to control. During the first week of exposure (premating), significant decreases in mean body weights (5%) in the 503 ppm group, and body weight gains (88-150%) at ≥301 ppm were seen compared to control. Mean body weights and body weight gains were not significantly different from control for the remainder of pre-mating period. Body weight gain was significantly decreased from GD 14-20 (23%) and GD 0-20 (14%) in the 698 ppm group compared to control. The study authors state this decrease in body weight is partly due to the decrease in viable fetuses in this group. Food consumption was significantly decreased (12-24%) during week one of exposure at ≥301 ppm but no treatment related effects were observed in any group for the remainder of the study. No significant gross pathological findings were seen at necropsy. Absolute adrenal gland weight was significantly increased (17%) at 698 ppm compared to control. No significant difference in brain, ovary, or thyroid weights were seen compared to control. Gravid uterine weight was decreased (30%) at 698 ppm compared to control. The number of corpora lutea was significantly decreased by 10%,13%, and 9%, at 301, 503, and 698 ppm respectively, compared to control; albeit not significantly at 698 ppm. The number of implantation sites was

significantly decreased (21% and 32%) at 503 and 698 ppm, respectively. Pre-implantation loss was significantly increased 23% at 698 ppm compared to control. Post-implantation loss was increased at 698 ppm (16.6%), albeit not statistically significantly, compared to control (7.8%) and historical controls (2.2-13.5%); this was considered by study authors to be compound-related. Due to the decreased numbers of corpora lutea and increased pre-implantation loss, the number of viable fetuses were significantly decreased by 24% and 36% at 503 and 698 ppm, respectively, compared to control. The decrease in viable fetuses is most likely responsible for the decreased gravid uterine weight. A NOAEL of 301 ppm and a LOAEL of 501 ppm were determined based on decreased viable fetuses, implantation sites, and corpora lutea.

[7] 5887452: To study effects of exposure during the ovarian phase: Female Crl:CD(SD)BR rats were exposed to 0 (n=30) or 702 ppm (n=60) of octamethylcyclotetrasiloxane (D4) vapor via whole-body inhalation for 6 hours/day, daily for 28 days (31 days prior to the start of mating and stopped 3 days before mating started). Females were mated with unexposed males (1:1) for up to 10 days. Endpoints evaluated included clinical signs, body weight, food consumption, pre-coital interval, mating index, and fertility index. The following organs were weighed: gravid uteri, brain, ovaries, adrenal glands, and thyroid glands. Uteri and ovaries were examined for numbers of fetuses, early and late resorptions, total implantations, pre-implantation loss, post-implantation loss, and corpora lutea. All females survived until scheduled sacrifice. No compound-related clinical signs were observed compared to control. No difference in mean days between pairing and coitus (2.5 and 2.5 days), mating indices (93.3% and 85%), or fertility indices (86.7% and 83.3%) were seen in control and 702 ppm, respectively. Significantly decreased body weight (4-5%) was seen transiently in during weeks 2 and 3 of exposure; body weight gain was significantly decreased the first week and then increased the third week of exposure compared to control. Body weights during gestation were not significantly different from control. Food consumption was significantly decreased (11-18%) during the first two weeks of exposure compared to control. Food consumption was slightly increased during gestation, but this was not considered a toxicological effect. No significant difference in maternal organ weights (brain, ovary, adrenal gland, or thyroid) were seen compared to control. Mean gravid uterine weight was not significantly different from control. No significant difference in number of corpora lutea, implantation sites, pre-implantation loss, resorptions, post-implantation loss, or viable fetuses were seen. A NOAEL of 702 ppm for reproductive/developmental effects was determined.

[8] 5887452: To study effects of exposure during the fertilization phase: Female Crl:CD(SD)BR rats were exposed to 0 (n=30) or 696 ppm (n=60) of octamethylcyclotetrasiloxane (D4) via whole-body inhalation 6 hours/day daily from 3 days prior to the start of the mating interval, with exposures continuing through the mating interval until gestation day 3. Females were mated with unexposed males (1:1). The mating interval was 5 days for the control and 2 days for the exposed group. Endpoints evaluated included clinical signs, body weight and food consumption The following organs were weighed: gravid uteri, brain, ovaries, adrenal glands, and thyroid glands. Uteri and ovaries were examined for numbers of fetuses, early and late resorptions, total implantations, pre-implantation loss, post-implantation loss, and corpora lutea. All females survived until scheduled sacrifice. No compound-related clinical signs were observed compared to control. Pre coital interval, mating index, and fertility index could not be compared since the number of days that animals were allowed to mate was different between the groups. Body weights were significantly decreased on GD 4 (5%) and GD 20 (7%) compared to control. Body weight gain was significantly decreased during GD 0-4 (24%) at 696 ppm compared to control. When exposure ended, body weights recovered for 3 days and were similar to controls until the last week of gestation when they were reduced. Body weights during GD0-20 were decreased by 12% in the 696 ppm group, compared to control. Food consumption was significantly decreased during the 3-day pre-mating exposure and GD 0-4 compared to control. No significant compound-related difference in brain, adrenal gland or thyroid weights were seen compared to control. Absolute ovarian weight was significantly decreased (10%) compared to control. Significant decreases in the number of corpora lutea (15%), implantation sites (31%), and gravid uterine weight (43%) were seen in the 696 ppm group, compared to control. Significant increases in pre-implantation loss (19% per litter), early resorption (12%), and post-implantation loss (12%) were seen at 696 ppm, compared to control. The number of viable fetuses was significantly decreased 39% compared to control. A LOAEL of 696 ppm was determined for maternal toxicity (decreased body weight) and reproductive endpoints.

[9] 5887452: To study effects of exposure during implantation phase: Female Crl:CD(SD)BR rats were mated with males (1:1). Mated females (24/group) were then exposed to 0 or 702 ppm of octamethylcyclotetrasiloxane (D4) vapor via whole-body inhalation for 6 hours/day daily from gestation day 2 through gestation day 5. Endpoints evaluated included clinical signs, body weight, food consumption, pre-coitus interval, mating index, and fertility index. The following organs were weighted: gravid uteri, brain, ovaries, adrenal glands, and thyroid glands. Uteri and ovaries were examined for numbers of fetuses, early and late resorptions, total implantations, pre-implantation loss, post-implantation loss, and corpora lutea. No compound-related deaths were seen. One control female died from an undetermined cause on post mating day 2. No compound-related clinical signs were observed compared to control. Mean body weights were significantly decreased (5%) on GD 6 compared to control but no significant effects on body weights throughout gestation were observed. Food consumption was decreased 38% in the 702-ppm group from GD 2-6 compared to control. No significant difference was seen from GD 0-20. No significant difference in maternal organ weights of brain, ovary, adrenal gland, or thyroid gland were seen compared to control. The percentage of gravid females was 100% and 95.8% in the control and exposed groups, respectively. No significant difference in body weight gain during gestation was seen compared to control. No significant differences in number of corpora lutea or implantation sites, pre-implantation loss, post-implantation loss, resorptions, gravid uterine weight, or number of viable fetuses were seen. A NOAEL of 702 ppm was determined based on no effects observed at the only concentration.

[10] 7310563: Sprague-Dawley rats (10/sex/group) were exposed to actual mean concentrations of 0, 51, 301, or 700 ppm of octamethylcyclotetrasiloxane (D4) 6 hours/day, 7 days/week, for 13 weeks. Satellite recovery groups of 10/sex/group exposed to either 0 or 703 ppm of D4 for 13 weeks as described above but were allowed to recover for 28 days prior to sacrifice. Animals were observed for mortality, clinical signs (respiratory, dermal, behavior, nasal or ocular changes), body weight, body weight gain, and food consumption changes during exposure. Eyes were examined using an ophthalmoscope before treatment period began and at termination. Endpoints evaluated at sacrifice included hematology (RBC count, hematocrit, hemoglobin concentration, platelet count, and total and differential WBC counts), clinical chemistry (ALT, AST, ALP, GGT, LDH, total bilirubin, creatinine, total protein, albumin, BUN, globulin, calcium, chloride, potassium, sodium, phosphorus) , urinalysis (urine collected in metabolism cage overnight), gross pathology (main group animals only), organ weights (liver, brain, heart, kidneys, adrenals, testes, ovaries, lungs, and spleen), and histology on a complete set of 42 tissues and organs in control and high dose animals. The lungs, nasal passages, larynx, and trachea were also examined in animals in the other exposure groups.No animals died during treatment. No clinical signs of toxicity were seen compared to control. Body weights and body weight gains were not significantly different from control. In the 700 ppm females, slight, non-significant decreases in terminal body weight (7%) and body weight gain (21%) were noted. No treatment-related effects on food consumption were seen in males. In 700 ppm females, food consumption was significantly decreased (15%) during the first week, but then returned to control levels for the remainder of the study. No biologically relevant changes in hematological or clinical chemistry were seen compared to control. Slight, yet significant, increases in RBC count, hemoglobin, and hematocrit in the 700 ppm females were not considered by the authors to be biologically significant. Values for these endpoints were significantly decreased in recovery females. No significant differences in urinalysis values were seen compared to control. Absolute and relative liver weights were significantly increased in males at 51 ppm (24%, 15%), 301 ppm (17%, 9%) and 700 ppm (27%, 22%), respectively, compared to controls. In females, significant increases in relative liver weight (11%) were seen at 301 ppm and absolute (20%) and relative (31%) liver weights at 700 ppm, compared to controls. After recovery, liver weights returned to control values in males; however, in females at 701 ppm, relative liver weight remained significantly increased (11%). Absolute adrenal weights were significantly decreased in females at 700 ppm (18%) compared to control but returned to control levels after recovery. No other treatment-related significant changes in organ weights were seen. No treatment-related gross or histopathological changes were observed.A LOAEC of 51 ppm was identified for increased absolute and relative liver weights. A NOAEC was not identified. The liver weight changes occurred in the absence of supporting clinical chemistry or histopathology changes.

[11] 7309971: In a subchronic study reported in HERO ID 7309971 (unpublished study) and HERO ID 6833996 (published report). Groups of Fischer 344 rats (CDF F-344/CrlBR, SPF) (20/sex/group) were exposed via nose-only inhalation to oxtamethylcyclotetrasiloxane (purity >99.42%) at mean analytical concentrations of 0, 0.42, 1.48, 5.91, and 10.87 mg/L (420, 1,480, 5,910, and 10,870 mg/m3) for 6 hours/day, 5 days/week, for 13 weeks.

An additional 10/sex were included in the control and high exposure groups; these animals were held for a 1-month post-exposure recovery period. Since 10,870 mg/m3 is greater than the vapor saturation concentration, an atmospheric mixture of vapor and aerosol would have been formed. A proper control for this highest concentration would have been a vapor/aerosol exposure. Therefore, the highest concentration group is evaluated on a separate form. Animals were observed for mortality and clinical signs of toxicity. Ophthalmoscopic examinations were conducted before the start of the study and at the end of the treatment and recovery phases. Other endpoints included body weights, weight gain, food consumption, hematology, coagulation parameters, clinical chemistry, urinalysis, complete necropsy, select organ weights, and comprehensive histological examinations on >25 tissues and organs. No deaths were observed. No other exposure-related clinical signs were observed. Body weight gain fluctuations in all animals, including controls, were thought to be related to the restraint during exposure. Exposed animals consumed more food than controls, but the effects were not dependent on concentration. Hematological changes included slight, but significant decreases in RBC and HB in males increases in MCV in both sexes at 5,910 mg/m3. The most notable clinical chemistry changes were moderately increased in GGT activity in females at 5,910 mg/m3 and decreased total bilirubin in females and decreased triglycerides in both sexes at ≥1,480 mg/m3. Other significant changes in both sexes included increased ALT primarily in high-exposure animals and increased total protein at 5,910 mg/m3. Increases in total cholesterol in females and decreases in phospholipids and creatinine kinase in males were not exposure concentration related. The authors did not consider any urinalysis changes to be exposure-related, although urine-specific gravity and osmolality in females were significantly increased at 5,910 mg/m3.Organ weight changes in males generally did not show any clear relation to exposure (e.g., changes were not concentration-dependent). Organ weight changes in females included significant increases in absolute (20%) and relative (22%) liver weights at 5,910 mg/m3. Also in females, significant decreases in absolute and relative thymus and increases in adrenal weights were seen at 5,910 mg/m3.There were no notable gross macroscopic findings. Histopathological changes were reported differently in the unpublished study report (HERO 7309971) and in the peer-reviewed published study (HERO 683396). For example, the unpublished report included the following lung lesions: congestion, alveolar macrophages, mononuclear cells, hemorrhage, mineralization, osseous metaplasia, and chronic interstitial inflammation. Incidences were reported in separate tables for control and high-exposure animals and for the lower-exposure group animals. The unpublished study summary tables included no measures of severity, but the severity of lesions was discussed in the test and reported with individual animal data. The published study reports limited histopathological data focused on the upper respiratory system including incidences and measures of severity of alveolar macrophage accumulation, interstitial inflammation, and leukocyte infiltration, which had not been included in the unpublished version. The data presented in the published study are the consensus of a Pathology Working Group (PWG) review. For the two lesions shared between the reports, starting with alveolar macrophages the incidences were 4/20 (controls), 2/20, 3/20, and 4/20 in the unpublished version vs. 4/20 (controls), 3/20, 6/20, and 10/20 in the published version for males, and 1/20 (controls), 1/20, 12/20, and 11/20 in the unpublished version vs. 3/20 (controls), 6/20, 18/20, 18/20 in the published documents for females at 420, 1,480, 5,910 mg/m3, respectively. For (chronic) interstitial inflammation reported in the unpublished and published versions respectively, incidences were 2/20 (controls), 3/20, 2/20, 9/20 and 3/20 (controls), 3/20, 4/20, 5/20 for males, and 0/20 (controls), 4/20, 6/20, 15/20 and 1/20 (controls), 3/20, 7/20, 12/20, for females in the 0, 420, 1,480, and mg/m3 groups, respectively. Leukocyte infiltration, which was reported in the published, but not the unpublished study was not visible in the controls or exposure groups. No increased incidences of vaginal mucification in the unpublished or published report were seen compared to control.No histopathological changes were observed in the liver. Despite differences in incidence counts between the unpublished and published study reports, overall, the levels of statistical significance were generally consistent. No author-reported toxicity values were provided. In the unpublished report, the authors noted that effects considered to be toxicologically relevant were restricted to the 5,910 groups. Based on the available data, a NOAEC of 420 mg/m3 and a LOAEC of 1,480 mg/m3 was identified based on significantly increased incidences of interstitial inflammation in the lungs of exposed male and female rats and incidences of alveolar macrophages in females. However, the authors in the published study indicated that the toxicological significance of the pulmonary findings are unclear and may be an exacerbation of "spontaneous nonspecific background inflammation" that had been described previously.

[12] 7309971: A total of 5/30 females in the 10,870 mg/m3 group died. Three died between treatment days 2 and 3, one during week 7, and another during week 12. The causes of death could not be determined and no other deaths were observed. During the first week, exposed females showed signs of hunched posture and one female had a slightly stiff gait; no other exposure-related clinical signs were observed. Mean body weights of exposed animals were generally decreased in a significant manner throughout the study period when compared to controls. However, the reductions were low in magnitude; at week 13, high-exposure male and female body weights were significantly decreased by 5% and 4%, respectively. Body weight gain fluctuations in all animals, including controls, were thought to be related to the restraint during exposure. However, weight gain reductions were more pronounced in epxosed animals, and the authors considered this to be exposure, rather than restraint, related. Significant decreases in food consumption of exposed animals (males and females) were transient; primarily occurring within the first 10 days. Hematological changes included slight, but significant decreases in RBC and HB in males increases in MCV in both sexes at 10,870 mg/m3, and decreased MCHC in both males and females at 10,870 mg/m3. The most notable clinical chemistry changes were moderately increased in GGT activity in males and females at 10,870 mg/m3, decreased total bilirubin in females and decreased triglycerides in both sexes at 10,870 mg/m3. Other significant changes in both sexes included increased ALT and increased total protein at 10,870 mg/m3. In recovery males, ALT remained elevated. The authors did not consider any urinalysis changes to be exposure-related, although urine-specific gravity and osmolality in females were significantly increased at 10,870 mg/m3.Organ weight changes in males generally did not show any clear relation to exposure (e.g., changes were not concentration-dependent). Relative, but not absolute lung and liver (both increased 16%) weights in males were increased at 10,870 mg/m3. Organ weight changes in females included significant increases in absolute (25%) and relative (28%) liver weights at 10,870 mg/m3. Also in females, significant decreases in absolute and relative thymus and increases in adrenal weights were seen at 10,870 mg/m3, along with increases in absolute and relative lung and marked decreases in absolute and relative ovary weights (38% and 36%, respectively) at 10,870 mg/m3. The reductions in ovary weights were reported to be marked. There were no notable gross macroscopic findings. Histopathological changes were reported differently in the unpublished study report (HERO 7309971) and in the peer-reviewed published study (HERO 683396). For example, the unpublished report included the following lung lesions: congestion, alveolar macrophages, mononuclear cells, hemorrhage, mineralization, osseous metaplasia, and chronic interstitial inflammation. Incidences were reported in separate tables for control and high-exposure animals and for the lower-exposure group animals. The unpublished study summary tables included no measures of severity, but the severity of lesions was discussed in the test and reported with individual animal data. The published study reports limited histopathological data focused on the upper respiratory system including incidences and measures of severity of alveolar macrophage accumulation, interstitial inflammation, and leukocyte infiltration, which had not been included in the unpublished version. The data presented in the published study are the consensus of a Pathology Working Group (PWG) review. For the two lesions shared between the reports, starting with alveolar macrophages the incidences were 4/20 (controls) and 9/20 in the unpublished version vs. 4/20 (controls) and 18/20 in the published version for males, and 1/20 (controls) and 10/20 in the unpublished, and 3/20 (controls) and 18/20 in the published version for females. For (chronic) interstitial inflammation reported in the unpublished and published versions respectively, incidences were 2/20 (controls), and 17/20 and 3/20 (controls) and 14/20 for males, and 0/20 (controls) and 17/20 and 1/20 (controls) and 16/20, for females in the 0 and 10,870 mg/m3 groups, respectively. Leukocyte infiltration, which was reported in the published, but not the unpublished study was visible in exposed males (11/20) and females (16/20) only, with no incidences in the controls or lower exposure groups. Non-respiratory lesions described in the unpublished report also included increased incidences of ovarian congestion and atrophy and vaginal mucification that were significant at 10,870 mg/m3. The PWG further characterized the ovarian and vaginal lesions. The ovaries of high-exposure females showed diffuse hypoactivity, characterized by the absence of corpora lutea. Incidences of vaginal mucification in the unpublished report were 0/20 (controls) and 17/20 at 0 and 10,870 mg/m3, respectively, and were 9/20 and 19/20, respectively, in the published report. The published report also showed a significantly increased incidence of high-exposure animals in diestrous, compared with controls. No histopathological changes were observed in the liver. Despite differences in incidence counts between the unpublished and published study reports, overall, the levels of statistical significance were generally consistent. No author-reported toxicity values were provided. In the unpublished report, the authors noted that effects considered to be toxicologically relevant were restricted to the 10,870 mg/m3 group. Although changes in females reproductive tract and histopathology in the respiratory system were seen, a NOAEL/LOAEL could not be determined because the control group was not appropriate.

[13] 7310463: In a reproductive toxicity study, male Crl:CD (SD)BR rats (22/group) were exposed to octamethylcyclotetrasiloxane (D4) at mean measured concentrations of 0, 71, 300, 492, and 694 ppm to via whole-body inhalation 6 hours/day for at least 70 consecutive days prior to mating, and throughout the mating interval. Males were mated with females exposed to filtered air only in a 1:1 ratio until the presence of a copulatory plug or

sperm in a vaginal smear was noted (up to 15 days). Females were exposed to filtered air through GD20. Animals were observed twice a day for mortality and clinical signs. Body weights of both sexes were assessed weekly before mating and maternal body weights were assessed on gestational days (GDs) 0, 7, 10, 14, and 20 and post-natal days (PNDs) 1 and 4. Food consumption was measured before mating, during gestation and lactation. Females were allowed to deliver naturally. F0 dams that delivered were necropsied at PND 4; F0 females that did not deliver were necropsied 25 days after breeding. F0 males were sacrificed at either week 12 (10/group; 1-2 days after exposure ended) or at week 16 (all remaining males; one month after exposure ended). Endpoints evaluated in F0 males included organ weights (adrenals, brain, epididymides, heart, kidneys, liver, lungs, pituitary, prostate, seminal vesicles with coagulating glands, testes, spleen thymus, and thyroid), gross necropsy, histology (adrenals, brain-hypothalamus, epididymis, liver, penis, pituitary, prepuce, preputial gland, prostate, spleen, testis, thymus, all gross lesions), and in the 0, 492 and 694 ppm groups, sperm motility, and sperm morphology. Reproductive parameters (days between pairing and coitus, mating indices, fertility indices, and duration of gestation and parturition) were assessed. The numbers of stillborn and live pups were recorded. F1 pups were examined daily for changes in appearance or behavior, body weights on PND 1 and 4, sex on PND 0 and 4, litter size, postnatal survival, and necropsy for external and internal abnormalities. No increase in mortality was seen compared to controls. One male and one female in the 694-ppm group died but deaths were not considered treatment-related. Clinical signs observed included increased incidences of red material around the nose of males after an hour of exposure to 694 ppm, and exposure-related increases in the number of ejaculatory plugs in all exposure groups. No significant differences in male or female body weights, body weight gains, or food consumption were seen, compared to controls. In F0 males, significant increases in absolute and relative liver weight (16-21%) kidney (21-26%) and thyroid (29-40%) weights were seen at 694 ppm, compared to controls. Significant increases in absolute and relative liver weights (9-14%) were seen at 492 ppm, compared to controls. Relative organ weights were calculated as relative to final body weight and brain weights. After a one-month recovery, organ weights were not different from controls. No significant differences in other organ weights were observed. No notable gross necropsy findings or exposure-related histological effects were seen in exposed males, compared to controls. No changes in sperm motility or sperm morphology were observed. Reproductive parameters (male mating indices ranged from 90.0-100%; female mating indices ranged from 95.5-100%; fertility indices ranged from 90.9% to 100%) were unaffected by exposure. No differences in the numbers of uterine implantation sites, pups born, or implantation sites unaccounted for by offspring were seen. There were no significant differences between the mean number of pups/litter, live litter size, sex ratio, or physical condition of the pups of exposed males and controls. Pup survival (% per litter) at 694 ppm was non-statistically significantly reduced on PND0 (95.2% vs. 99.2% in controls) and from birth to PND4; however, the authors noted that the data were confounded by two litters with increased numbers of dead pups at birth. Pup body weights in the 694 ppm group were significantly decreased on PND 1(12%) and PND 4 (8%) compared to the concurrent control group but were within the range of historical control data. No exposure-related findings were seen in PND 4 pups at necropsy.A parental (male) NOAEC of 300 ppm and a LOAEC of 492 ppm was identified for increased absolute and relative liver weight.A developmental NOEC of 492 ppm and a LOEC of 694 ppm were determined, based on decreased pup body weights; these changes were not likely adverse because the pup body weights remained within the provided historical control values.

Octamethylcyclotetrasiloxane (D4)- Parent compound - Chronic (>91 days)

Guideline and Animal Species, Strain, Sex	Exposure Route and Exposure Duration	Study-wide POD and Dose/ Concentration(s)	Summary	Major Limitations	Principal Target Organs/Systems and OQD*	HERO ID
No guidelines or adherence to GLP practices were specified. Rat-Other (Albino FDRL)-Both	Oral-Diet-Duration: Chronic (>90 days)-7-52-week(s) 7 days/week 52 week(s) Dietary exposure were food was provided ad libitum	**POD: 1 % (in water or food) (NOAEL) -No effects were observed for any endpoint throughout the study.** n= 5 Dose= 0, n= 5 Dose= 1, % (in water or food)	See footnotes for full summary [1]	The test substance purity is not reported and there is substantial ambiguity about how the test substance was formulated and prepared, making the true administered dose difficult to determine. There are also serious flaws with sample size and ambiguity with statistical analysis.	nan; Low	FDRL, 1966 5889837
No guidelines or adherence to GLP practices were specified. Rabbit-Not specified-Both	Oral-Diet-Duration: Chronic (>90 days)-7-36-week(s) 7 days/week 36 week(s) Exposed in the diet for 36 weeks.	**POD: % (in water or food) (Other) -** n= 12 Dose= 0, n= 6 Dose= 1, % (in water or food)	See footnotes for full summary [2]	Insufficient details on the test material, uncertainties in the dose (e.g. apparent inhalation of some of the powdered diet, lack of measurements of feed intake), and other confounding variables (e.g., infection)	Other (please specify below) (Clinical signs)-Observations for changes in appearance and behavior; Uninformative	FDRL, 1965 5889936
Followed OPPTs guideline 870.4300; GLP compliant Rat-Fischer 344 - [rat]-Both	Inhalation-Vapor-Duration: Chronic (>90 days)-5-6-12-month(s) 6 hours/day 5 days/week 12 month(s) 12 month chronic toxicity	**POD: 30 ppm (in air, water, or food) (NOAEC) -increased absolute and relative liver weights** n= 10 Dose= 0, n= 10 Dose= 10, n= 10 Dose= 30, n= 10 Dose= 150, n= 10 Dose= 700, ppm (in air, water, or food)	See footnotes for full summary [3]	No major limitations were identified	Hepatic/Liver-clinical chemistry, liver weights, histology-Reproductive/Developmental-uterus, vagina, ovary, cervix, mammary gland, testes, seminal vesicles, prepuce, preputial gland,prostate, penis histology-Renal/Kidney-clinical chemistry, kidney weights, necropsy and histology (kidney, and bladder)-Lung/Respiratory-Lung weights and histology of all respiratory tissues including nasal tissues.; High	Jean et. al 2017 6833979

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Octamethylcyclotetrasiloxane (D4)- Parent compound - Chronic (>91 days)

Guideline and Animal Species, Strain, Sex	Exposure Route and Exposure Duration	Study-wide POD and Dose/ Concentration(s)	Summary	Major Limitations	Principal Target Organs/Systems and OQD*	HERO ID
Followed OPPTs guideline 870.4300; GLP compliant Rat-Fischer 344 - [rat]-Both	Inhalation-Vapor-Duration: Chronic (>90 days)-5-6-12-month(s) 6 hours/day 5 days/week 12 month(s) 12 months exposure followed by 12 months unexposed recovery.	**POD: 150 ppm (in air, water, or food) (NOAEC) -Increased testes weights** n= 20 Dose= 0, n= 20 Dose= 10, n= 20 Dose= 30, n= 20 Dose= 150, n= 20 Dose= 700, ppm (in air, water, or food)	See footnotes for full summary [4]	No major limitations were identified	Hepatic/Liver-clinical chemistry, liver weights, histology-Reproductive/Developmental-uterus, vagina, ovary, cervix, mammary gland, testes, seminal vesicles, prepuce, preputial gland,prostate, penis histology-Renal/Kidney-clinical chemistry, kidney weights, necropsy and histology (kidney, and bladder)-Lung/Respiratory-Lung weights and histology of all respiratory tissues including nasal tissues.; High	Jean et. al 2017 6833979

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Octamethylcyclotetrasiloxane (D4)- Parent compound - Chronic (>91 days)

Guideline and Animal Species, Strain, Sex	Exposure Route and Exposure Duration	Study-wide POD and Dose/ Concentration(s)	Summary	Major Limitations	Principal Target Organs/Systems and OQD*	HERO ID
Followed OPPTs guideline 870.4300; GLP compliant Rat-Fischer 344 - [rat]-Both	Inhalation-Vapor-Duration: Chronic (>90 days)-5-6-24-month(s) 6 hours/day 5 days/week 24 month(s) 24 month cancer	**POD: 10 ppm (in air, water, or food) (NOAEC) -Nasal lesions and chronic nephropathy in females** n= 60 Dose= 0, n= 60 Dose= 10, n= 60 Dose= 30, n= 60 Dose= 150, n= 60 Dose= 700, ppm (in air, water, or food)	See footnotes for full summary [5]	No major limitations were identified	Cancer/Carcinogenesis-Examinations for tumors.-Hepatic/Liver-clinical chemistry, liver weights, histology-Reproductive/Developmental-uterus, vagina, ovary, cervix, mammary gland, testes, seminal vesicles, prepuce, preputial gland,prostate, penis histology-Mortality-Survival-Renal/Kidney-clinical chemistry, kidney weights, necropsy and histology (kidney, and bladder)-Lung/Respiratory-Lung weights and histology of all respiratory tissues including nasal tissues.; High	Jean et. al 2017 6833979

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Octamethylcyclotetrasiloxane (D4)- Parent compound - Chronic (>91 days)

Guideline and Animal Species, Strain, Sex	Exposure Route and Exposure Duration	Study-wide POD and Dose/ Concentration(s)	Summary	Major Limitations	Principal Target Organs/Systems and OQD*	HERO ID
No guideline or adherence to GLP was specified. Rat-Fischer 344 - [rat]-Female	Inhalation-Vapor-Duration: Chronic (>90 days)-5-6-14-month(s) 6 hours/day 5 days/week 14 month(s) 6hrs/day, 5 days/week from 11 through 24 months of age.	**POD: 704 ppm (in air, water, or food) (LOAEC) -reproductive effects; increased liver weights** n= 50 Dose= 0, n= 50 Dose= 704, ppm (in air, water, or food)	See footnotes for full summary [6]	The concentration tested was high and not representative of expected exposure levels. The concentration tested was near the point of vapor saturation leading to uncertainty that the entirety is a vapor. The animal strain selected was unique, and the results cannot be translated to other strains and may not be relevant to humans.	Reproductive/Development-Estrous cyclicity, serum hormones (prolactin, progesterone, estradiol, corticosterone), FSH and estradiol and metabolite profiles, organ weights (uterus, ovaries and oviducts), histopathology of reproductive organs, including corpora lutea subclassification, number of healthy and atretic antral follicles and primordial follicles; gross necropsy-Hepatic/Liver-Liver weight; gross necropsy; Medium	Jean et. al 2017 4166321

* Overall Quality Determination

[1] 5889837: In a 52-week chronic feeding study, the commercial product F-6060 (purity and composition unknown) was added to the basal diets of albino FDRL strain rats (5/sex/group, 10/sex/group for controls) yielding a dietary concentration of 1% D4 in food. The control group received the basal diet. Animals had access to food ad libitum. Animals were monitored for survival and clinical signs daily. Body weights and food consumption were recorded weekly for the first 12 weeks; and then body weights were measured bi-weekly for the remaining 40 weeks. Limited hematology (hemoglobin, hematocrit, red cell fragility, total and differential leukocyte counts), and urinalysis (pH, specific gravity, albumin, glucose, acetone, bile salts, pigments, and microscopic analysis of sediments) were measured at 3, 6, and 12 months. Serum chemistry measurements at 12 months included BUN, total cholesterol, ALP, and glutamic pyruvic transaminase activity. At the end of the exposure period, animals were sacrificed and subjected to gross necropsy. Select organs were taken to measure relative organ weights (liver, kidneys, spleen, heart, gonads, adnexa, adrenals, thyroids, brain, pituitary and lungs) and to perform histopathology (liver, spleen, stomach, small intestines, large intestines, pancreas, kidneys, bladder, adrenals, gonads, thyroids, pituitary, thymus, esophagus, mediastinal and mesenteric lymph nodes, heart and aorta, lungs, bone marrow, skin, skeletal muscle with peripheral nerve, spinal cord, brain, uterus or seminal vesicles and prostate. 2/5 males exposed to D4, and 1/10 controls of both sexes died during the study. No clinical signs were reported. No differences in body weights nor food consumption were reported. No significant differences in hematological parameters, blood serum chemistry or urinalysis were observed. No significant differences in organ weights nor histopathology were observed. A NOAEL of 1.0% for all measured endpoints was determined as a result of no effects observed during the study. The authors reported a NOAEL of 1% D4 in the diet.

[2] 5889936: In an 8-month (36-week) chronic feeding study, the commercial product F-6060 (purity and composition unknown) was added to the basal diets of albino rabbits (3/sex; 6/sex controls), yielding a dietary concentration of 1% D4 in food. Animals were observed for mortality and behavioral changes. Body weights were recorded weekly. There were unsuccessful attempts to record food intake, efforts were discontinued after a few weeks. Limited hematology (hemoglobin, hematocrit, red cell fragility, total and differential leukocyte counts), and urinalysis (pH, specific gravity, albumin, glucose, acetone, bile salts, pigments, and microscopic analysis of sediments) were measured at 0, 4, and 8 months. Serum chemistry measurements at 8 months included BUN, total cholesterol, ALP, and glutamic pyruvic transaminase activity. Animals were subjected to gross necropsy, organ weights (liver, spleen, kidneys, heart, lung, brain, gonads and adnexa, adrenals, and thyroids) were recorded. Histopathology was done on ~25 organs/tissues. No animals died and there were no notable changes in appearance or behavior that could be attributed to treatment. All animals, including controls, showed evidence of nasal and ocular irritation within the first two hours after eating. This was attributed to insufflation of the powdered test material, which was the likely cause of respiratory infections that were noted in the majority of animals. Transient body weight loss was noted in all groups; controls showed small net weight losses throughout the study. Treated animals showed net growth overall, and no significant body weight changes between treated and control rats. No treatment-related hematological, urinalysis, or clinical chemistry changes were observed. There were no treatment-related organ weight changes. Gross and microscopic findings were sporadic or attributed to respiratory or parasitic infections. The authors reported a NOAEL of 1% D4 in the diet. However, due to the significant uncertainty in the actual administered dose, a reliable toxicity value cannot be determined.

[3] 6833979: As part of a combined chronic/carcinogenicity study, groups of Fisher 344 rats (10/sex/group) were exposed to the test substance at concentrations of 0, 10, 30, 150, or 700 ppm for 6 hours a day, 5 days a week for 12 months. Endpoints evaluated include mortality, clinical signs of toxicity, body weights, body weight gain, ophthalmoscopy (control and high exposure group), hematology (prothrombin time and activated partial thromboplastin time only), complete gross necropsy, and complete histological examinations (control and high exposure group). Microscopic examinations of the liver, lungs, kidney, uteri, spleen, adrenal, nasal cavities, and any gross lesions were conducted on animals from all groups.No mortality occurred in any animals. No exposure-related clinical signs, ophthalmological, body weights, or body weight gain. Kidney weights (absolute and relative to body weights) were significantly increased in males at 700 ppm. Absolute kidney weights were also increased in females at 700 ppm, but the magnitude of change was small (5%). Liver weights were significantly increased at ≥150 ppm (absolute 16-30%) and ≥30 ppm (relative; 8-29%) in males and at ≥150 ppm (absolute; 14-30% and relative (10-26%) in females. Relative, but not absolute testes weights were increased in males at 700 ppm. In the nasal cavity dorsal meatus, and olfactory and respiratory epithelium, increased incidences of intracytoplasmic eosinophilic globules were observed at 700 ppm in both sexes (10/10 M, 10/10 F) compared to controls (5/10 M, 7/10 F). At 0, 10, 30, 150, 700 ppm, respectively, incidences of goblet cell hyperplasia in the respiratory epithelium was 0/10, 1/10, 0/10, 0/10, 10/10 in males and 1/10, 1/10, 0/10, 2/10, 8/10 in females and squamous cell epithelial hyperplasia in the mucosa was 0/10, 0/10, 1/10, 0/10, 10/10 in males and 0/10, 1/10, 1/10, 1/10, 9/10 in females. Both had dose-related increases in severity. Increased incidences of suppurative inflammation in males was significant at 700 ppm. Significantly increased incidences of centrilobular hepatocellular hypertrophy were observed in males at 700 ppm. A focused review of hormone-sensitive tissues showed a small increase in the proportion of females with a prolonged cycle at 700 ppm. No author-reported toxicity values were provided. Based on the data provided, a NOAEC of 30 ppm and a LOAEC of 150 ppm was determined based on statistically and biologically relevant (>10% change) increases in absolute and relative liver weights in male and female rats.

[4] 6833979: As part of a combined chronic/carcinogenicity study separate groups of Fisher 344 rats (20/sex/group) were used to assess recovery. Rats exposed to the test substance at concentrations of 0, 10, 30, 150, or 700 ppm for 6 hours a day, 5 days a week for 12 months followed by a 12 month untreated recovery period. Endpoints evaluated include mortality, clinical signs of toxicity, body weights, body weight gain, hematology and clinical chemistry at 3, 6, 9 (clinical chemistry only), and 12 months, gross necropsy, organ weights, and complete histological examinations (control and high exposure group). Microscopic examinations of the liver, lungs, kidney, uteri, spleen, adrenal, nasal cavities, and any gross lesions were conducted on animals from all groups.Survival in exposed animals after 24 months was comparable to controls. No treatment related effects were observed on clinical signs, ophthalmology, body weights, body weight gain, or urinalysis. Increased white blood cell counts and lymphocytes were observed at 700 ppm in both sexes in a time-related, but not dose-related manner (observed at 3, 6 and 12 months). Treatment related changes in clinical chemistry include increased total protein and decreased creatinine, CK, and LDH in both sexes primarily in the two highest exposure groups. Other changes (decreased ALP, ALT, AST) are not considered to be toxicologically significant. Kidney weights (absolute and relative to body weights) were significantly increased at 700 ppm in females but not in males; however, the magnitudes of change were small (<10%). Absolute and relative liver weights were increased at 150 and 700 ppm in both sexes after 12 month exposure, but no effect remained after the recovery period. Testes weights (68% absolute and 323% relative) were increased in males at 700 ppm after 12 months exposure and the recovery period. Testes weights were increased in males at 150 ppm (25% absolute and relative), but the results were not statistically significant. Incidences of stromal polyps in the uterus were increased in all treatment groups, but there was no clear relation to exposure concentration (1/20, 6/20, 4/10, 6/20, and 6/20 at 0, 10, 30, 150, or 700 ppm, respectively). These lesions were not observed in animals sacrificed after treatment and the effect was not discussed by the study authors; the toxicological relevance is therefore unclear. Squamous epithelial cell hyperplasia in the cervix was The only other histopathological lesions observed in recovery animals was a small, but significant increase in incidences of goblet cell hyperplasia in the respiratory epithelium of male rats (3/20 vs. 0/20 in controls). No author-reported toxicity values were provided. Based on the data provided, a NOAEC of 150 ppm and a LOAEC of 700 ppm was determined for increased testes weights in male rats exposed to D4 vapors.

[5] 6833979: Groups of Fisher 344 rats (60/sex/group) were exposed to the test substance at concentrations of 0, 10, 30, 150, or 700 ppm for 6 hours a day, 5 days a week for 24 months. Endpoints evaluated include mortality, clinical signs of toxicity, body weights, body weight gain, ophthalmoscopy, hematology, clinical chemistry, gross necropsy, organ weights, histology and evaluation of hyperplasia and neoplastic lesions.Males of the 700 ppm group had reduced survival (38% compared to 58% in controls). There were no other effects on survival in other exposure groups. No treatment related effects were observed on clinical signs, ophthalmology, body weights, body weight gain, or urinalysis. Surviving animal kidney weights (absolute and relative to body weights) were significantly increased at 700 ppm in both sexes. Significantly increased absolute kidney weights in females at 150 ppm were low in magnitude (<10%). Absolute and relative liver weights were increased at 150 and 700 ppm in females and at 700 ppm in males. Absolute and relative uterine weights were increased in females at 700 ppm. Testes weights (relative, but not absolute) were increased in males at 700 ppm. Significant non-neoplastic changes in the nasal cavity included increased incidences of eosinophilic globules in females at ≥30 ppm and in males at 700 ppm, goblet cell hyperplasia of the respiratory epithelium in males at ≥150 ppm in males and at 700 ppm in females, and hyperplasia of the squamous epithelium in males at 700 ppm. In the lungs, increased incidences of hemorrhages were observed in females at 700 ppm and subleural chronic inflammation was increased at 10, 30, and 700 ppm. Incidences of interstitial cell hyperplasia were increased in male testes at ≥150 ppm along with concentration-related increases in severity. Centrilobular hepatocellular hypertrophy was observed in males at 700 ppm. Chronic nephropathy was noted in females at concentrations ≥ 30 ppm with exposure related increases in severity. Other lesions in females included increased incidences of hematopoietic proliferation in spleens, hyperplasia of the endometrial epithelium and cervical squamous epithelium and stromal hyperplasia at 700 ppm. The increased incidences of uterine cystic endometrial hyperplasia were observed as cystically dilated endometrial glands with increased collagen in the stroma, and neutrophils in the gland. No increased incidences of any neoplasms were statistically significant, compared with controls. Endometrial adenomas were observed in 4/60 females at 700 ppm compared with 0/60 on controls, but the increased incidence was not statistically significant; however, a positive trend was observed.No author reported toxicity values were provided. The carcinogenicity potential of D4 is unclear. For non-neoplastic effects, a NOAEC of 10 ppm and a LOAEC of 30 ppm were determined for nasal lesions and chronic nephropathy in female rats.

[6] 4166321: In a study focused on investigating effects on reproductive senescence, female Crl:CD(Fischer 344) BR VAF/Plus rats (50/group; aged 49-50 weeks at initiation) were exposed, whole body, to target D4 vapors (>99% purity) of 0 (air only) or 700 ppm for 6 hours/day, 5 days/week, from age 11 to 24 months (~14 months). The analytical concentration was 704 ± 22 ppm. Separate groups of animals were exposed to decamethylcyclopentasiloxane (D5; not reviewed herein), and to pergolide mesylate (PM), known to produce dopamine-like agonist effects on estrous cyclicity (positive control). Prior to exposure, circulating prolactin

levels were measured. Animals with normal prolactin levels (mean ± 2) were allocated into groups using a body weight-stratified randomization procedure. Each group also contained 4-5 animals with abnormal prolactin levels. Animals were monitored for mortality and clinical signs of toxicity. Other endpoints included body weights, weight gain, food consumption, daily estrous cycle monitoring, serum levels of prolactin, progesterone, estradiol, and corticosterone (monthly), select organ weights, detailed gross necropsy, and microscopic examinations with a focus on reproductive tissues (ovary, uterine horn, uterine body with cervix, vagina). There were no exposure-related effects on mortality or clinical signs. Changes to body weights and food consumption were inconsistent (e.g., sometimes increased and sometimes decreased) and intermittent. There was a significant increase in the cumulative number of estrogenic days per 45-day interval and in the percentage of days in an estrous predominant state. The range of % estrogen-predominant days was 20.4-61.2% compared to 12.5 – 34.9% in controls. There were no differences between treated and control rats in the timing of the two transition points that show shifts in the percentages of days in estrous as normal rats enter senescence. However, the within-cycle duration of the proestrus – estrus phase was significantly increased (2.4 – 3.5 days/cycle cs. 1-2 days/cycle in controls). There were no differences in serum prolactin levels; however, inter-group variability was high. Circulating progesterone concentrations were significantly increased during weeks 2, 6, and 10 in D4 exposed animals. Estradiol levels and estradiol:progesterone ratios were significantly decreased at nearly all time points throughout the study. From weeks 2 – 51, corticosterone concentrations were significantly increased 10-30% over controls. Organ weight changes included significant increases in absolute and relative liver (35% and 33%) and kidney (10% and 8%) weights, respectively. Other changes were considered to be incidental. No significant gross findings were observed. Total incidences of cystic endometrial hyperplasia (14/35 vs. 8/37 in controls) were significantly increased, and there was a 37% decrease in antral-size atretic follicles. There was an increase in the severity of epithelial thickness of vaginal tissue, compared with controls, and incidences of mucification was slightly lower. No increases in incidences of tumors in reproductive tissues were observed. A LOAEC of 704 ppm was identified based on effects on reproductive effects and increased liver weights in F344 female rats.

Octamethylcyclotetrasiloxane (D4)- Parent compound - Reproductive/Developmental

Guideline and Animal Species, Strain, Sex	Exposure Route and Exposure Duration	Study-wide POD and Dose/ Concentration(s)	Summary	Major Limitations	Principal Target Organs/Systems and OQD*	HERO ID
Non-guideline study; GLP not specified. Rabbit-New Zealand White - [rabbit]-Female	Oral-Gavage-Duration: Reproductive/Developmental-F0 - gestation (Unclear) Pregnant dams were either dosed from GD 5-16 or 5-18. There is a discrepancy in the report.	**POD: mg/kg (Other) -** Dose= 100, mg/kg Female Exposure: F0 - gestation, Unclear	In a study aimed at determining a maximum tolerated dose (MTD), groups of pregnant New Zealand white rabbits were dosed with undiluted PDMS/D4 fluid (95.9% D4, 4% decamethylcylcopentasiloxane, and 0.1% hexamethylcyclotrisoloxane in PDMS) at 100 mg/kg/day (reported as mg/kg), via “oral ingestion” from GD 5-18. It was not specified whether oral exposure was via gavage or through the diet, but gavage was implied. A gavage volume was not reported, but doses were adjusted according to body weight, suggestive of gavage. A control group was not described in the text; however, a data table lists a control group but reports a dose of 2,000 mg/kg-day. It is unclear what this concentration is referring to. The sacrifice time was not specified. Animals were observed daily for clinical signs of toxicity. Body weights were measured on GDs 5, 12, 16, and 19, and food consumption was measured on days GDs 16 and 20. This suggests that animals were maintained at least through GD20. Animals were subjected to gross necropsy. No fetal examinations were conducted. No statistical analysis was described.Mortality was not listed as an endpoint, and no results specifying survival or death were reported. No abnormal clinical signs were observed. There were no effects on body weight or food consumption. All animals were pregnant. No gross lesions on any internal organs were observed. No effects (of the limited endpoints evaluated) were observed in rabbits dosed orally with 100 mg/kg-day PDMS/D4 fluid. The text described a similar previous study in which death, weight loss, and reductions in food consumption occurred at 225 mg/kg D4.	Major limitations include a reporting discrepancy in the study duration and a significant amount of missing data (number of animals per group, control details, method of oral exposure, test substance purity and source).	nan; Uninformative	Dow Corning, 1983 5888421

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Octamethylcyclotetrasiloxane (D4)- Parent compound - Reproductive/Developmental

Guideline and Animal Species, Strain, Sex	Exposure Route and Exposure Duration	Study-wide POD and Dose/ Concentration(s)	Summary	Major Limitations	Principal Target Organs/Systems and OQD*	HERO ID
No compliance to any guidance documents is stated. Rat-Sprague-Dawley - [rat]-Female	Oral-Gavage-Duration: Reproductive/Developmental-1-F0 - gestation (GD 12-20)	**POD: 5 mg/kg-bw/day (NOAEL) -Mechanistic NOAEL: increased EROD and PROD activity, CYP2B1/2 and CYP3A1/2 protein expression in pregnant dams and increased CYP2B1/2 mRNA expression in fetal livers.** n= 4 Dose= 0, n= 0 Dose= 1, n= 4 Dose= 5, n= 4 Dose= 20, n= 4 Dose= 100, mg/kg-bw/dayTotal # of generations: 1 Female Exposure: F0 - gestation, GD 12-20	See footnotes for full summary [1]	There are some errors and discrepancies in the text as well as data omissions. The methods state a 1 mg/kg-day group was included, but this dose is not specified in the study abstract, and no data for a 1 mg/kg-day group was reported. The text refers to Table 1 for PROD activity; however, these data are in Table 2. The study reports relative liver weights without providing absolute weights or body weight data. There are some concerns regarding sample size.	Reproductive/Developmental-Fetal body weight, fetal relative liver weight. Mechanistic endpoints in fetal livers: PROD activity, CYP2B1/2 mRNA expression.; Medium	Falany et. al-2005 99288
"'This study was conducted in conformance with the Good Laboratory Practice Standards." Rabbit-New Zealand White - [rabbit]-Female	Inhalation-Vapor-Duration: Reproductive/Developmental-1-F0 - gestation (GD 6-18) Inseminated females were exposed from GD 6-18	**POD: 300 ppm (in air, water, or food) (NOAEL) -Reduced food consumption** n= 15 Dose= 0, n= 14 Dose= 100, n= 17 Dose= 300, n= 13 Dose= 501, ppm (in air, water, or food)Total # of generations: 1 Female Exposure: F0 - gestation, GD 6-18	See footnotes for full summary [2]	The number of pregnant females examined was below the OECD guideline 414 recommendation of 20 /group.	Mortality-Mortality-Nutritional/Metabolic-Body weight and food intake-Reproductive/Developmental-Gravid uteri were weighed, fetuses were removed and uteri assessed for location of viable and nonviable fetuses, early and late resorptions, and number of total implantations and corpora lutea. Individual fetuses were weighed, sexed, and examined for internal (visceral and skeletal) and external malformations.; Medium	IRDC, 1993 5885492

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Octamethylcyclotetrasiloxane (D4)- Parent compound - Reproductive/Developmental

Guideline and Animal Species, Strain, Sex	Exposure Route and Exposure Duration	Study-wide POD and Dose/ Concentration(s)	Summary	Major Limitations	Principal Target Organs/Systems and OQD*	HERO ID
"This study was conducted in accordance with the protocol as approved by the Sponsor and in compliance with the Standard Operating Procedures of International Research and Development Corporation (IRDC)." Rabbit-New Zealand White - [rabbit]-Female	Inhalation-Vapor-Duration: Reproductive/Developmental-1-F0 - gestation (GD 6-18) Inseminated females were exposed 6 hours/day from gestational days 6-18.	**POD: 301 ppm (in air, water, or food) (NOAEC) - slight reductions in maternal body weight gain and food intake** n= 6 Dose= 0, n= 6 Dose= 10, n= 6 Dose= 101, n= 6 Dose= 301, n= 6 Dose= 700, ppm (in air, water, or food)Total # of generations: 1 Female Exposure: F0 - gestation, GD 6-18	See footnotes for full summary [3]	The number of animals used for a developmental study was lower than current OECD recommendations. The study evaluated only a limited number of developmental endpoints.	Nutritional/Metabolic-Maternal body weight, adjusted body weights, body weight gain, and food intake; Medium	IRDC, 1993 5889424
The authors state that they followed SOP for the International Research and Development Corporation and that their protocol was approved by the sponsor. The study was conducted under GLP conditions. Rabbit-New Zealand White - [rabbit]-Female	Oral-Gavage-Duration: Reproductive/Developmental-1-F0 - gestation (GD 7-19)	**POD: 50 mg/kg-bw/day (NOAEL) -Decreased body weight gain and food consumption** n= 12 Dose= 0, n= 12 Dose= 50, n= 12 Dose= 100, n= 12 Dose= 500, n= 12 Dose= 1000, mg/kg-bw/dayTotal # of generations: 1 Female Exposure: F0 - gestation, GD 7-19	See footnotes for full summary [4]	Spontaneous abortions in the 500 and 1,000 mg/kg/day groups precluded the ability to assess some of the endpoints at those doses.	Nutritional/Metabolic-Body weights, food consumption-Reproductive/Developmental-Number and location of viable and nonviable fetuses, early and late resorptions, number of total implantations and corpora lutea. Gravid uterine weight.; High	IRDC, 1993 5889449

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Octamethylcyclotetrasiloxane (D4)- Parent compound - Reproductive/Developmental

Guideline and Animal Species, Strain, Sex	Exposure Route and Exposure Duration	Study-wide POD and Dose/ Concentration(s)	Summary	Major Limitations	Principal Target Organs/Systems and OQD*	HERO ID
No guideline was cited; conducted under GLP conditions Rat-Other (Crl:CD)-Female	Inhalation-Vapor-Duration: Reproductive/Developmental-1-F0 - gestation (GD 6-15) Once daily, for 6 h/day, on GDs 6-15	**POD: 301 ppm (in air, water, or food) (NOAEL) -Decreased body weight gain** n= 6 Dose= 0, n= 6 Dose= 10, n= 6 Dose= 101, n= 6 Dose= 301, n= 6 Dose= 700, ppm (in air, water, or food)Total # of generations: 1 Female Exposure: F0 - gestation, GD 6-15	See footnotes for full summary [5]	Respiratory rates were not measured and there is potential for respiratory irritation for this test substance.	Nutritional/Metabolic-Body weight, body weight gain, food consumption; Medium	IRDC, 1993 5889493

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Octamethylcyclotetrasiloxane (D4)- Parent compound - Reproductive/Developmental

Guideline and Animal Species, Strain, Sex	Exposure Route and Exposure Duration	Study-wide POD and Dose/ Concentration(s)	Summary	Major Limitations	Principal Target Organs/Systems and OQD*	HERO ID
GLP FDA 21 CFE Part 58, EOA 40 CFR Parts 160 and 792, EPA OPPTS Health Effects TGs (870.3800, Reproduction and Fertility Effects (Draft), 1996), EPA FIFRA Pesticide Assessment Guidelines (Subdivision F, Addendum 10, Series 83-6; Developmental Neurotoxicity Study). Rat-Other (CRL:CD (SG)IGS BR)-Both	Inhalation-Vapor-Duration: Reproductive/Developmental-2-F0- premating (70 days)-F0- mating (Up to 14 days)-F0 - gestation (GD 0 - 20)-F0- lactation (PND 5 - 21)-F1- premating (70)-F1- mating (Up to 14 days)-F1 - gestation (GD 0 - 20)-F1- lactation (PND 5 - 21)-F0- premating (70)-F0- mating (Up to 14 days)-F1- premating (70)-F1- mating (Up to 14 days) F0 animals were exposed 6hrs/day, 7days/week for 70 days prior to mating, and throughout mating and gestation until PND 21 (weaning); Exposure in females was paused on GD20 through PND 4. F1 females were exposed from weaning (PND 22) through two mating and gestation periods through GD20 of the F2b litter. F1 males were exposed from weaning (PND22) through three matings and sacrificed after mating.	**POD: 70 ppm (in air, water, or food) (NOAEC) - Increased absolute and relative liver weights in F0 female rats** n= 60 Dose= 0, n= 60 Dose= 70, n= 60 Dose= 298, n= 60 Dose= 502, n= 60 Dose= 700, ppm (in air, water, or food)Total # of generations: 2 Male Exposure: F0- premating, 70, F0- mating, Up to 14 days, F1- premating, 70, F1- mating, Up to 14 days Female Exposure: F0- premating, 70 days, F0- mating, Up to 14 days, F0 - gestation, GD 0 - 20, F0- lactation, PND 5 - 21, F1- premating, 70, F1- mating, Up to 14 days, F1 - gestation, GD 0 - 20, F1- lactation, PND 5 - 21	See footnotes for full summary [6]	The study authors noted that the advanced age of some females used for breeding may confound some of the results.	Reproductive/Developmental: F0 adults: sperm morphology and production rate, ovarian primordial follicle and corpora lutea counts, ejaculatory plugs, dystocia, litter size, fertility index, histopathology (uterus, ovaries, clitoral gland, vagina, mammary gland, testis, prostate, penis, prepuce, preputial gland, seminal vesicles, vas deferens, epididymis), organ weights (epididymides (total and cauda), ovaries, prostate, seminal vesicles, testes, uterus) estrous cycle timing, reproductive performance and senescence, gross necropsyF1 offspring: Balanopreputial separation, vaginal patency, mean number of pups, % of males per litter, gross and skeletal malformations, anogenital distance, pup neurobehavior (motor activity, startle response, biel maze), body weight of pups on PND 1, 4, 7, 14 and 21, clinical signs, gross necropsyF1 adults: sperm morphology and production rate, ovarian primordial follicle and corpora lutea counts, dystocia, litter size, histopatholgoy (cervix, coagulating gland, epididymis	WIL Research, 2001 5884077

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Octamethylcyclotetrasiloxane (D4)- Parent compound - Reproductive/Developmental

Guideline and Animal Species, Strain, Sex	Exposure Route and Exposure Duration	Study-wide POD and Dose/ Concentration(s)	Summary	Major Limitations	Principal Target Organs/Systems and OQD*	HERO ID
"This study was conducted in compliance with the Good Laboratory Practice Regulations for Nonclinical Laboratory Studies of the United States Food and Drug Administration (21 CPR Part 58) and Environmental Protection Agency (40 CPR Parts 160 and 792) and the Standard Operating Procedures of WIL Research Laboratories, Inc." Rat-Sprague-Dawley - [rat]-Female	Inhalation-Vapor-Duration: Reproductive/Developmental-F0- premating (6 hours) Females were exposed for a single 6-hour duration either 1, 2, 3, or 4 days prior to a successful mating.	**POD: 700 ppm (in air, water, or food) (LOAEC) -Decreased pregnancy rates when exposed one day before mating** n= 25 Dose= 0, n= 125 Dose= 700, ppm (in air, water, or food) Female Exposure: F0- premating, 6 hours	See footnotes for full summary [7]	A control group was allowed to mate up to 5 days after exposure. All data for this group were combined; data on different days to mate was not parsed out and compared to respective test groups.	Reproductive/Development: Number of corpora lutea on each ovary, total number of implantation sites; uterus and ovary weight and histopathology;; High	WIL Research, 1999 5884342
"This study was conducted in compliance with the Good Laboratory Practice Regulations for Nonclinical Laboratory Studies of the United States Food and Drug Administration (21 CPR Part 58) and Environmental Protection Agency (40 CPR Parts 160 and 792) and the Standard Operating Procedures of WIL Research Laboratories, Inc." Rat-Sprague-Dawley - [rat]-Female	Inhalation-Vapor-Duration: Reproductive/Developmental-F0- premating (3 days) Females were exposed for a single 6-hour duration either 1, 2, 3, or 4 days prior to a successful mating.	**POD: 700 ppm (in air, water, or food) (NOAEC) -No adverse effects** n= 25 Dose= 0, n= 125 Dose= 700, ppm (in air, water, or food) Female Exposure: F0- premating, 6 hours	See footnotes for full summary [8]	There were differences in the exposure timing for the control group (6 hours, the day prior to mating) compared with the exposure group (6 hours/day for 3 days prior to mating).	Nutritional/Metabolic-Body weight, body weight gain, and food consumption; High	WIL Research, 1999 5884342

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Octamethylcyclotetrasiloxane (D4)- Parent compound - Reproductive/Developmental

Guideline and Animal Species, Strain, Sex	Exposure Route and Exposure Duration	Study-wide POD and Dose/ Concentration(s)	Summary	Major Limitations	Principal Target Organs/Systems and OQD*	HERO ID
"This study was conducted in compliance with the Good Laboratory Practice Regulations for Nonclinical Laboratory Studies of the United States Food and Drug Administration (21 CPR Part 58) and Environmental Protection Agency (40 CPR Parts 160 and 792) and the Standard Operating Procedures of WIL Research Laboratories, Inc." Rat-Sprague-Dawley - [rat]-Female	Inhalation-Vapor-Duration: Reproductive/Developmental-F0- premating (3 days)-F0-mating (1-2 days)-F0 - gestation (GD0 - GD3) Females were exposed for a single 6-hour duration either 1, 2, 3, or 4 days prior to a successful mating.	**POD: 700 ppm (in air, water, or food) (LOAEC) - Decreased number of corpora lutea, an increased number of small implantation sites, and decreased uterine weights.** n= 25 Dose= 0, n= 70 Dose= 700, ppm (in air, water, or food) Female Exposure: F0- premating, 6 hours	See footnotes for full summary [9]	The negative control group was only exposed for 6 hours whereas the test group was exposed for 6 hours/day for 7-8 days.	Nutritional/Metabolic-Body weight, body weight gain, and food consumption-Reproductive/Developmental-Number of corpora lutea on each ovary, total number of implantation sites; uterus and ovary weight and histopathology;; High	WIL Research, 1999 5884342
"This study was conducted in compliance with the Good Laboratory Practice Regulations for Nonclinical Laboratory Studies of the United States Food and Drug Administration (21 CPR Part 58) and Environmental Protection Agency (40 CPR Parts 160 and 792) and the Standard Operating Procedures of WIL Research Laboratories, Inc." Rat-Sprague-Dawley - [rat]-Female	Inhalation-Vapor-Duration: Reproductive/Developmental-F0 - gestation (6 hours) Females were exposed for a single 6-hour duration either 1, 2, 3, or 4 days prior to a successful mating.	**POD: 700 ppm (in air, water, or food) (NOAEC) -No adverse effects** n= 25 Dose= 0, n= 155 Dose= 700, ppm (in air, water, or food) Female Exposure: F0- premating, 6 hours	See footnotes for full summary [10]	Difference in timing of control group's exposure to air (GD 0) compared to two of the test groups (GD 1 and GD2).	Reproductive/Developmental-Number of corpora lutea on each ovary, total number of implantation sites; uterus and ovary weight and histopathology;; High	WIL Research, 1999 5884342

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Octamethylcyclotetrasiloxane (D4)- Parent compound - Reproductive/Developmental

Guideline and Animal Species, Strain, Sex	Exposure Route and Exposure Duration	Study-wide POD and Dose/ Concentration(s)	Summary	Major Limitations	Principal Target Organs/Systems and OQD*	HERO ID
"This study was conducted in compliance with the Good Laboratory Practice Regulations for Nonclinical Laboratory Studies of the United States Food and Drug Administration (21 CPR Part 58) and Environmental Protection Agency (40 CPR Parts 160 and 792) and the Standard Operating Procedures of WIL Research Laboratories, Inc." Rat-Sprague-Dawley - [rat]-Female	Inhalation-Vapor-Duration: Reproductive/Developmental-F0 - gestation (GD 0- GD 2) Females were exposed for a single 6-hour duration either 1, 2, 3, or 4 days prior to a successful mating.	**POD: 700 ppm (in air, water, or food) (LOAEC) -decreased body weight gain and food consumption** n= 25 Dose= 0, n= 155 Dose= 700, ppm (in air, water, or food) Female Exposure: F0- premating, 6 hours	See footnotes for full summary [11]	There was a difference in the timing of the control group's exposure to air (GD 0 for 6 hours) compared to the compound group's exposure (GD 0-2).	Nutritional/Metabolic-Body weight, body weight gain, and food consumption; High	WIL Research, 1999 5884342
GLP 21 CFR Part 58 and EPA 40 CFR Parts 160 and 792) Rat-Sprague-Dawley - [rat]-Male	nan Males were exposed for at least 70 days before mating, and then until study 113. Females were not exposed.	**POD: 500 ppm (in air, water, or food) (NOAEC) -Decreased body weight gain and food consumption.** n= 40 Dose= 0, n= 40 Dose= 500, n= 40 Dose= 693, ppm (in air, water, or food)Total # of generations: 1 Male Exposure: F0- premating, 70 days, F0- mating, 43 days	See footnotes for full summary [12]	The lack of measurement of respiratory rate may be concerning due to D4's potential as a respiratory irritant. While the study is generally well constructed. The 5- week recovery period was not justified and may have contributed to the negative results for terminal endpoints.	Nutritional/Metabolic-Body weights, food consumption; High	WIL Research, 1997 5887603

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Octamethylcyclotetrasiloxane (D4)- Parent compound - Reproductive/Developmental

Guideline and Animal Species, Strain, Sex	Exposure Route and Exposure Duration	Study-wide POD and Dose/ Concentration(s)	Summary	Major Limitations	Principal Target Organs/Systems and OQD*	HERO ID
GLP for Nonclinical Laboratory Studies of the FDA (21 CFR Part 58) and EPA (40 CFR Parts 160 and 792). Rat-Sprague-Dawley - [rat]- Both	Inhalation-Vapor-Duration: Reproductive/Developmental-1-F0- premating (28 days)-F0- mating-F0 - gestation (GD 0-20)-F0- premating (28 days)-F0- mating Males sacrificed after mating, females sacrificed on PND 4	**POD: 700 ppm (in air, water, or food) (LOAEC) -Repro/Dev: Decreased litter size, number of pups born, pup viability and increased pre-implantation loss and increased pup weight.Nutritional/Metabolic: Decreased body weights in females.** n= 44 Dose= 0, n= 44 Dose= 0, n= 44 Dose= 700, ppm (in air, water, or food)Total # of generations: 1 Male Exposure: F0- premating, 28 days, F0- mating Female Exposure: F0- premating, 28 days, F0- mating, F0 - gestation, GD 0-20	See footnotes for full summary [13]	Limitations include the lack of additional test substance concentrations and the lack of performing an independent analytical verification of the test substance purity.	Nutritional/Metabolic-Body weights, body weight gain, food consumption-Reproductive/Developmental-F0 mating and fertility indices, length of gestation, sperm numbers and sperm production rate. F1 litter viability/survival, number of pups, sex ratio, gross malformations, pup gross necropsy, clinical signs, body weights, F0 organ weights (epididymides, prostate, testes, ovaries), F0 histopathology (epididymides, testes, ovaries); High	WIL Research, 1996 5887777

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Octamethylcyclotetrasiloxane (D4)- Parent compound - Reproductive/Developmental

Guideline and Animal Species, Strain, Sex	Exposure Route and Exposure Duration	Study-wide POD and Dose/ Concentration(s)	Summary	Major Limitations	Principal Target Organs/Systems and OQD*	HERO ID
The authors do not cite a specific guideline but indicate that the study was conducted "in accordance with current GLP regulations for nonclinical laboratory studies of the US FDA and EPA, SOP of WIL Research Laboratories Inc, and the Sponsor's protocol and protocol amendments". Rat-Sprague-Dawley - [rat]-Female	Inhalation-Vapor-Duration: Reproductive/Developmental-1-F0- premating (70 days)-F0- mating-F0 - gestation (GD 1-21)-F0- lactation (PND 5-21) Exposure was paused from PND 1 to PND 4.	**POD: 300 ppm (in air, water, or food) (LOAEC) -Increased relative maternal liver weights.** n= 22 Dose= 0, n= 22 Dose= 300, n= 22 Dose= 500, n= 22 Dose= 700, ppm (in air, water, or food)Total # of generations: 1 Female Exposure: F0- premating, 70 days, F0- mating, F0 - gestation, GD 1-21, F0- lactation, PND 5-21	See footnotes for full summary [14]	No major limitations were identified.	Nutritional/Metabolic-Body weights, body weight gain, food consumption-Reproductive/Developmental-Mating and fertility indices, estrous cyclicity, days between mating and coitus, duration of gestation, timing of parturition, F0 organ weights (ovaries, uterus), F0 gross necropsy and histopathology (mammary gland, ovaries, uterus, vagina), F0 corpora lutea and oocyte counts, litter viability/survival, F1 body weights, food consumption, sex ratio, organ weights (liver, ovaries, testes), F1 gross necropsy and histopathology (adrenals, aorta, bone with marrow, brain, clitoral gland, eyes with optic nerve, gastrointestinal tract, heart, kidneys, liver, lungs, lymph nodes, mammary gland, ovaries, pancreas, penis, peripheral nerve, pituitary, prepuce, preputial gland, prostate, salivary gland, seminal vesicles, skeletal muscle, skin, spinal cord, spleen, testes, thymus, thyroid gland, trachea, urinary bladder, uterus with vagina, gross lesions).-Hepatic/Liver-Organ weights (Liver), histopathology (Liver); High	WIL Research, 1997 5887799

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Octamethylcyclotetrasiloxane (D4)- Parent compound - Reproductive/Developmental

Guideline and Animal Species, Strain, Sex	Exposure Route and Exposure Duration	Study-wide POD and Dose/ Concentration(s)	Summary	Major Limitations	Principal Target Organs/Systems and OQD*	HERO ID
GLP EPA and FDA 21 CFR Part 58 and EPA 40 CFR Parts 160 and 792 Rat-Sprague-Dawley - [rat]-Both	Inhalation-Vapor-Duration: Reproductive/Developmental-1-F0- premating (28 days)-F0- mating (~2-weeks)-F0 - gestation (GD 1-20)-F0-lactation (LD 5-21)-F1-post-natal (PND 21-28)-F0-premating (28 days)-F0-mating (~2-weeks)-F1-post-natal (PDN 21-28) Exposure paused in females between GD 21-LD 4	**POD: 70 ppm (in air, water, or food) (NOAEC) -Repro/Dev: Decreased litter size and number of implantation sitesMaternal: Decreased body weights and food consumption in females** n= 40 Dose= 0, n= 40 Dose= 70, n= 40 Dose= 700, ppm (in air, water, or food)Total # of generations: 1 Male Exposure: F0-premating, 28 days, F0- mating, ~2-weeks, F1- post-natal, PDN 21-28 Female Exposure: F0- premating, 28 days, F0- mating, ~2-weeks, F0 - gestation, GD 1-20, F0- lactation, LD 5-21, F1- post-natal, PND 21-28	See footnotes for full summary [15]	No major limitations were identified. The systemic endpoints in parental animals were limited; however, the study was specified to be a screening study.	Nutritional/Metabolic-Body weights. body weight gain, and food consumption-Reproductive/Developmental-F0: Mating and fertility indices, time to coitus, gestation length, number of implantation sites. F1: litter viability and survival, litter clinical signs, sex ratio, body weights (PND 1, 4, 7, 14, 21 and 28), gross lesions, skeletal anomalies; Medium	WIL Research, 1996 5888075

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Octamethylcyclotetrasiloxane (D4)- Parent compound - Reproductive/Developmental

Guideline and Animal Species, Strain, Sex	Exposure Route and Exposure Duration	Study-wide POD and Dose/ Concentration(s)	Summary	Major Limitations	Principal Target Organs/Systems and OQD*	HERO ID
EPA GLP 40 CFR Part 160m 40 CFR Part 792, EPA TG OPPTS 870.3800, Reproduction and Fertility Effects Rat-Other (Crl: SD (SD) IGD BR)-Female	Inhalation-Vapor-Duration: Reproductive/Developmental-2-F0- premating (7 days)-F0- mating (during mating)-F0 - gestation (GD 0-20)-F0- lactation (LD 5-20)-F1- premating (70 days)-F1- mating (during mating)-F1 - gestation (GD 0-21 (two mating periods))-F1- lactation (LD 5-20 (two mating periods)) 700/700-D22 ppm: Author reported name for this experiment group	**POD: 704 ppm (in air, water, or food) (LOAEC) -Repro/Dev: reproductive toxicity and histopathology in ovaries, uterus and mammary gland in the F1 generation and decreased litter size and survival in the F2a generationNutritional/Metabolic: decreased body weights and food consumption** n= 30 Dose= 0, n= 30 Dose= 704, ppm (in air, water, or food)Total # of generations: 2 Female Exposure: F0- premating, 7 days, F0- mating, during mating, F0 - gestation, GD 0-20, F0- lactation, LD 5-20, F1- premating, 70 days, F1- mating, during mating, F1 - gestation, GD 0-21 (two mating periods), F1- lactation, LD 5-20 (two mating periods)	See footnotes for full summary [16]	The authors could have taken more steps to minimize observational bias for some endpoints as well as confounding bias.	Nutritional/Metabolic-Body weights, food consumption-Reproductive/Developmental-Repro/Dev-: F0: Estrous cycle timing, fertility and mating indices, gestation length, histopathology in females (mammary tissue, ovary, uterus, vagina), organ weights (ovary, uterus). Gross necropsy (ovaries, vagina, mammary gland, uterus).F1 and F2 generations: sex ratio, litter viability, gross malformations, skeletal variations and malformations, pup weights (on PND 1, 4, 5, 14 and 21), live litter size, postnatal survival between birth or PND 4, postnatal survival for all other intervals. In F1 generation only: histopathology in females (mammary tissue, ovary, pituitary, uterus, vagina, gross lesions), organ weights in females (ovary, pituitary, uterus), serum hormone analysis (estradiol, prolactin, progesterone).; High	WIL Research, 2005 7310330

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Octamethylcyclotetrasiloxane (D4)- Parent compound - Reproductive/Developmental

Guideline and Animal Species, Strain, Sex	Exposure Route and Exposure Duration	Study-wide POD and Dose/ Concentration(s)	Summary	Major Limitations	Principal Target Organs/Systems and OQD*	HERO ID
EPA GLP 40 CFR Part 160m 40 CFR Part 792, EPA TG OPPTS 870.3800, Reproduction and Fertility Effects Rat-Other (Crl: SD (SD) IGD BR)-Female	Inhalation-Vapor-Duration: Reproductive/Developmental-2-F0- premating (7 days)-F0- mating (during mating)-F0 - gestation (GD 0-20)-F0- lactation (LD 5-20)-F1- premating (70 days)-F1- mating (during mating)-F1 - gestation (GD 0-21 (two mating periods))-F1- lactation (LD 0-20 (two mating periods)) 700/700-D22 ppm: Author reported name for this experiment group	**POD: 704 ppm (in air, water, or food) (LOAEC) -Repro/Dev: reproductive toxicity and histopathology in ovaries and mammary gland in the F1 generation and decreased litter size and survival in the F2a generationNutritional/Metabolic: decreased body weights and food consumption** n= 30 Dose= 0, n= 30 Dose= 704, ppm (in air, water, or food)Total # of generations: 2 Female Exposure: F0- premating, 7 days, F0- mating, during mating, F0 - gestation, GD 0-20, F0- lactation, LD 5-20, F1- premating, 70 days, F1- mating, during mating, F1 - gestation, GD 0-21 (two mating periods), F1- lactation, LD 5-20 (two mating periods)	See footnotes for full summary [17]	The authors could have taken more steps to minimize observational bias for some endpoints as well as confounding bias.	Nutritional/Metabolic-Body weights, food consumption-Reproductive/Developmental-Repro/Dev-: F0: Estrous cycle timing, fertility and mating indices, gestation length, histopathology in females (mammary tissue, ovary, uterus, vagina), organ weights (ovary, uterus). Gross necropsy (ovaries, vagina, mammary gland, uterus).F1 and F2 generations: sex ratio, litter viability, gross malformations, skeletal variations and malformations, pup weights (on PND 1, 4, 5, 14 and 21), live litter size, postnatal survival between birth or PND 4, postnatal survival for all other intervals. In F1 generation only: histopathology in females (mammary tissue, ovary, pituitary, uterus, vagina, gross lesions), organ weights in females (ovary, pituitary, uterus), serum hormone analysis (estradiol, prolactin, progesterone).; High	WIL Research, 2005 7310330

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Guideline and Animal Species, Strain, Sex	Exposure Route and Exposure Duration	Study-wide POD and Dose/ Concentration(s)	Summary	Major Limitations	Principal Target Organs/Systems and OQD*	HERO ID
EPA GLP 40 CFR Part 160m 40 CFR Part 792, EPA TG OPPTS 870.3800, Reproduction and Fertility Effects Rat-Other (Crl: SD (SD) IGD BR)-Female	Inhalation-Vapor-Duration: Reproductive/Developmental-2-F0- premating (7 days)-F0- mating (during mating)-F0 - gestation (GD 0-20)-F0- lactation (LD 5-20)-F1- premating (70 days)-F1- mating (during mating)-F1 - gestation (GD 0-21 (two mating periods))-F1- lactation (LD 5-20 (two mating periods)) 700/700-D22 ppm: Author reported name for this experiment group	**POD: 704 ppm (in air, water, or food) (LOAEC) -Repro/Dev: reproductive toxicity and histopathology in the mammary glands in F1 femalesNutritional/Metabolic: decreased body weights and food consumption** n= 30 Dose= 0, n= 30 Dose= 704, ppm (in air, water, or food)Total # of generations: 2 Female Exposure: F0- premating, 7 days, F0- mating, during mating, F0 - gestation, GD 0-20, F0- lactation, LD 5-20, F1- premating, 70 days, F1- mating, during mating, F1 - gestation, GD 0-21 (two mating periods), F1- lactation, LD 5-20 (two mating periods)	See footnotes for full summary [18]	The authors could have taken more steps to minimize observational bias for some endpoints as well as confounding bias.	Nutritional/Metabolic-Body weights, food consumption-Reproductive/Developmental-Repro/Dev-: F0: Estrous cycle timing, fertility and mating indices, gestation length, histopathology in females (mammary tissue, ovary, uterus, vagina), organ weights (ovary, uterus). Gross necropsy (ovaries, vagina, mammary gland, uterus).F1 and F2 generations: sex ratio, litter viability, gross malformations, skeletal variations and malformations, pup weights (on PND 1, 4, 5, 14 and 21), live litter size, postnatal survival between birth or PND 4, postnatal survival for all other intervals. In F1 generation only: histopathology in females (mammary tissue, ovary, pituitary, uterus, vagina, gross lesions), organ weights in females (ovary, pituitary, uterus), serum hormone analysis (estradiol, prolactin, progesterone).; High	WIL Research, 2005 7310330

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Octamethylcyclotetrasiloxane (D4)- Parent compound - Reproductive/Developmental

Guideline and Animal Species, Strain, Sex	Exposure Route and Exposure Duration	Study-wide POD and Dose/ Concentration(s)	Summary	Major Limitations	Principal Target Organs/Systems and OQD*	HERO ID
EPA GLP 40 CFR Part 160m 40 CFR Part 792, EPA TG OPPTS 870.3800, Reproduction and Fertility Effects Rat-Other (Crl: SD (SD) IGD BR)-Female	Inhalation-Vapor-Duration: Reproductive/Developmental-2-F1- premating (70 days)-F1- mating (during mating)-F1 - gestation (GD 0-20 (two mating periods))-F1- lactation (LD 0-20 (two mating periods)) 700/700-D22 ppm: Author reported name for this experiment group	**POD: 704 ppm (in air, water, or food) (LOAEC) -Repro/Dev: reproductive toxicity and histopathology in ovaries, uterus and mammary gland in the F1 generation and decreased litter size and survival in the F2a generation** n= 30 Dose= 0, n= 30 Dose= 704, ppm (in air, water, or food)Total # of generations: 2 Female Exposure: F0- premating, 7 days, F0- mating, during mating, F0 - gestation, GD 0-20, F0- lactation, LD 5-20, F1- premating, 70 days, F1- mating, during mating, F1 - gestation, GD 0-21 (two mating periods), F1- lactation, LD 5-20 (two mating periods)	See footnotes for full summary [19]	The authors could have taken more steps to minimize observational bias for some endpoints as well as confounding bias.	Nutritional/Metabolic-Body weights, food consumption-Reproductive/Developmental-Repro/Dev-: F0: Estrous cycle timing, fertility and mating indices, gestation length, histopathology in females (mammary tissue, ovary, uterus, vagina), organ weights (ovary, uterus). Gross necropsy (ovaries, vagina, mammary gland, uterus).F1 and F2 generations: sex ratio, litter viability, gross malformations, skeletal variations and malformations, pup weights (on PND 1, 4, 5, 14 and 21), live litter size, postnatal survival between birth or PND 4, postnatal survival for all other intervals. In F1 generation only: histopathology in females (mammary tissue, ovary, pituitary, uterus, vagina, gross lesions), organ weights in females (ovary, pituitary, uterus), serum hormone analysis (estradiol, prolactin, progesterone).; High	WIL Research, 2005 7310330

* Overall Quality Determination

[1] 99288: Pregnant Sprague-Dawley rats (4/group) with a history of 2-previous litters were exposed to 0, 5, 20 or 100 mg/kg/day of octamethyltetracyclosiloxane (D4) via gavage in corn oil vehicle for 8 consecutive days from GD 12-20. A 1 mg/kg/day group was mentioned once in the study text; however, no data were reported and it is presumed to be reported in error. Body weights were measured daily but were not reported in the results. On GD 20, animals were sacrificed, and maternal livers, fetuses and fetal livers were extracted and weighed. Relative liver weights, fetal body weights and fetal relative liver weights were reported. Several mechanistic endpoints, including microsomal pentoxyresorufin O-deethylation (PROD) and 7-ethoxyresorufin O-deethylation (EROD) activity and CYP1A1/2, CYP2B1/2, CYP3A1/2 protein expression and CYP2B1/2 mRNA expression were also measured in the liver tissue of pregnant dams, with PROD and CYP2B1/2 mRNA expression additionally measured in maternal and fetal liver tissue.No significant differences in relative liver weights were observed in pregnant dams. Significantly decreased fetal body weights and fetal relative liver weights were observed at 100 mg/kg/day. Significantly increased EROD and PROD activity, CYP2B1/2 and CYP3A1/2 protein expression, and CYP2B1 mRNA expression were observed in pregnant dams at $\geq$20 mg/kg/day. In fetal liver tissue, PROD activity was significantly increased at 100 mg/kg/day whereas CYP2B1/2 mRNA expression was increased at $\geq$20 mg/kg/day.No author-reported toxicity values were provided. Based on the available data, A NOAEL of 20 mg/kg/day and LOAEL of 100 mg/kg/day and for apical reproductive/developmental endpoints were determined based on decreased fetal body weights and fetal relative liver weights. A NOAEL of 5 mg/kg/day and LOAEL of 20 mg/kg/day and for mechanistic hepatic/liver and reproductive/developmental effects were determined based on increased EROD and PROD activity, CYP2B1/2 and CYP3A1/2 protein expression in pregnant dams and increased CYP2B1/2 mRNA expression in fetal livers.

[2] 5885492: Inseminated New Zealand White SFF female rabbits (20/group) were exposed to mean measured concentrations of 0, 100, 300, or 501 ppm of octamethylcyclotetrasiloxane (D4) (purity >99%) for 6 hours/day on gestation days 6-18. Animals were sacrificed on GD 29 and cesarean sections were performed. Endpoints evaluated included maternal mortality, clinical signs, body weight (GD 0, 6, 9, 12, 15, 19, 24, and 29), weight gain, and food consumption (GD 0-6, 6-9, 9-12, 12-15, 15-19, 19-24, 24-29, 6-19, and 0-29). On GD 29, sacrificed females were evaluated for any gross morphological changes in the abdominal or thoracic cavities (including organs). Uteri were excised and pregnancy status was determined. Gravid uteri were weighed, fetuses were removed, and uteri were assessed for location of viable and nonviable fetuses, early and late resorptions, and number of total implantations and corpora lutea. Individual fetuses were weighed, sexed, and examined for internal (visceral and skeletal) and external malformations.All animals survived the entirety of the experiment. No clinical signs of toxicity were observed. The number of pregnant females was 15, 14, 17, and 13 in the control, 100, 300, and 501 ppm groups, respectively. Only confirmed pregnant females were included in body weight and food intake analysis. No significant changes in maternal body weight or body weight gains were seen, compared with controls, despite a significant decrease in maternal food consumption at 501 ppm (22% from GD 6-9; 17% from GD 9-12, compared with controls). No significantly increased incidences of gross abnormalities were seen in the does. Mean post-implantation loss (resorption) was slightly increased in the 501 ppm group compared to controls; however, the authors indicated that the loss was within historical control ranges (not provided). No differences in the number of viable fetuses per doe or mean fetal body weights were seen relative to controls. There was no compound-related developmental toxicity or increases in internal or external malformations or variations. A maternal NOAEL of 300 ppm was determined by study authors based on reduced food consumption at 501 ppm. The author reported NOAEL for developmental toxicity was >501 ppm, based on the absence of observable effects. The reduction in maternal food consumption occurred in the absence of significant changes in body weight or weight gain and did not appear to impact any developmental outcomes. The adversity of decreased food consumption should be reconsidered, and 501 ppm is a suggested NOAEL for maternal toxicity.

[3] 5889424: In a range-finding study, inseminated New Zealand White SFF female rabbits (6/group) were exposed to 0, 10, 101, 301 or 700 ppm of octamethylcyclotetrasiloxane (D4) for 6 hours/day on gestation days 6-18. Animals were sacrificed on GD 29 and cesarean section was performed. Endpoints evaluated included maternal mortality, clinical signs, body weight (GD 0, 6, 9, 12, 15, 19, 24, and 29), and food consumption (GD 1-6, 6-9, 9-12, 12-15, 15-19, 19-24, 24-29, 6-19, and 1-29). On GD 29, sacrificed females were evaluated for any gross morphological changes in the abdominal or thoracic cavities (including organs). Uteri were excised and pregnancy status was determined. The placenta and gravid uteri were weighed and adjusted maternal body weights were determined. Fetuses were removed, and the uteri were assessed for the location of viable and nonviable fetuses, early and late resorptions, number of total implantations and corpora lutea, and fetal weights. No additional fetal examinations were included. Mean-adjusted maternal body weight changes were recorded. Maternal animals survived the entirety of the experiment. Clinical signs observed included non-concentration-related incidences of decreased defection, soft stool, anogenital staining, and hair loss. No significant changes in body weights were seen, compared with controls. Body weight gain was significantly decreased at 700 ppm on GD 15-19 and overall, from GD 6-19, but was significantly increased on GD 19-24 (after exposure ended); no significant difference was seen overall from GD 0-29. Food consumption was significantly decreased on GD 15-19 (72%) in the 700-ppm group compared to control. No significant gross lesions at necropsy were seen. No significant differences in number of corpora lutea, implantation sites, post-implantation loss, pre-implantation loss, viable fetuses, uterine weight, fetal sex ratio, or fetal weight were seen compared to control. No author-derived toxicity values were reported. A NOAEC of 301 ppm and a LOAEC of 700 ppm were identified based on slight, but significant reductions in maternal body weight gain and food intake. No screening-level developmental effects were observed.

[4] 5889449: In a range-finding developmental toxicity study, pregnant New Zealand White SPF rabbits (6/group) were exposed to 0, 50, 100, 500, or 1,000 mg/kg/day of octamethylcyclotetrasiloxane (D4), via gavage in methocel vehicle, each day between gestational day (GD) 7-19. Exposures were paused after day 19, but animals were kept alive until GD 29. Animals were monitored twice daily for mortality and clinical signs of overt toxicity. Body weights were measured on days 0, 7-19, 23, 26 and 29, with food consumption measured between study days: 0-7, 7-19, 23-26 and 0-29. On GD 29, animals were euthanized, and the uterus was examined for the number and location of viable and nonviable fetuses, early and late resorptions, number of total implantations and corpora lutea. Dams were examined for gross morphological changes and the gravid uterus was weighed. The liver was isolated and weighed. No additional fetal examinations were conducted.One animal died at 500 mg/kg/day on GD26; no deaths occurred in any other treatment group, including at 1,000 mg/kg/day. Observed clinical signs included increased incidences of anogenital staining and hair loss at 1000 mg/kg/day, mucoid stool at ≥500 mg/kg/day, and decreased defection at doses ≥100 mg/kg/day. Significantly decreased body weights and body weight gains were observed at ≥100 mg/kg/day. Significant decreases in food consumption were observed at 50 mg/kg/day over a single day (between GD 12-13), at 100 mg/kg-day between GD11-14, and at 500 and 1,000 mg/kg/day from GD 7-19 and 0-29. By GD13 some animals in the 500 and 1,000 mg/kg/day groups were reported to be eating less than 20g/day or not at all. Significantly increased numbers of abortions, 5 and 4, occurred at 500 and 1000 mg/kg/day, respectively. Due to attrition and abortions in the 500 mg/kg/day group, uterine examination endpoints did not have sufficient data for statistical analysis and were omitted from the analysis, and contents from only 2 animals were available for examination in the 1,000 mg/kg/day group. Single abortions occurred at 50 and 100 mg/kg/day. The authors claimed these were not treatment-related, but correlated with the severely decreased food consumption of these animals. Significantly increased post-implantation loss, decreased number of fetuses and gravid uterine weight were observed at 1,000 mg/kg/day. Uterine examinations in the 50 and 100 mg/kg/day groups were comparable with controls. Absolute liver weights were significantly decreased at 100 and 1,000 mg/kg/day; no liver weight data was collected for the 500 mg/kg/day due to abortions and the single death in that dose group. No changes in relative liver weights were observed, suggesting the reductions in absolute weights were likely due to the decreases in body weights. No treatment-related necropsy findings were observed. No author-reported toxicity values were provided. The significant decrease in food consumption on a single day at 50 mg/kg/day in the absence of a significant changes in body weights or other observed effects was not considered for this review to be adverse. A NOAEL of 50 mg/kg/day and a LOAEL of 100 mg/kg/day were determined based on reduced body weights, body weight gain, and food consumption.

[5] 5889493: In a range-finding study for a developmental toxicity study, mated Charles River Crl:CD female rats (6/group) were exposed to the test substance, D4, at target exposure levels of 0 (control, filtered air only), 10, 100, 300, and 700 ppm by whole-body inhalation for 6 hours/day on gestation days (GD) 6-15. Corresponding mean measured concentrations for the test substance-exposed groups were 10, 101, 301, and 700 ppm, respectively. Animals were observed twice daily for mortality and overt changes in appearance and behavior. Clinical signs were recorded once daily on GDs 6 to 20. Individual body weights and food consumption were recorded on GDs 0, 6, 9, 12, 16, and 20 and body weight change and food consumption were calculated for GD intervals 0-6, 6-9, 9-12, 12-16, 16-20, 6-16, and 0-20. All animals were sacrificed on GD 20 and uterine examinations were performed. The number of animals with viable fetuses and resorptions, and numbers of corpora lutea and implantation sites, pre- post-implantation loss, number of resorptions (early, late, and total), numbers of dead and live fetuses, gravid uterine weight, and relative fetal weight (calculated as mean uterine weight/mean number of live fetuses) were determined.No mortalities occurred during the study. No clinical signs of toxicity were observed. No significant difference in body wights were seen compared to control. Mean body weight gain of maternal animals for GD 0-20 adjusted weight ("GD 0-20 Adj" = GD 20 body weight – gravid uterine weight) was significantly decreased at 700 ppm (-27%) compared to the control group. No significant changes in food consumption were observed compared to control. No significant changes in any of the uterine/fetal parameters were observed. A POD was not reported by the study authors. The NOAEL (determined by the reviewer) is 301 ppm based on decreased body weight gain in maternal animals at 700 ppm; the LOAEL is 700 ppm.

[6] 5884077: Virgin F0 Crl:CD (SD)IGS BR rats (30/sex/group) were exposed to 0, 71, 298, 502 or 700 ppm analytical vapor concentrations of octamethyltetracyclosiloxane (D4) (99.70% purity) via whole-body inhalation for 6 hours/day for at least 70 days prior to mating, through weaning of F1 pups on postnatal day (PND 21). Exposure in females was suspended from GD21 through PD4 to allow for parturition. One F1 litter per F0 pair was produced. On PND 22, F1 offspring (30/sex/group) were exposed to the identical target concentrations to their corresponding F0 parents (with analytical concentrations being 0, 71, 301, 502 and 702 ppm) for 70 days prior to mating and during mating/gestation/lactation to produce the F2a litter. Thirty days after the weaning of the F2a pups, the F1 animals were mated again via the same breeding pairs to produce an F2b litter (with continuous exposure as described for producing the F2a generation). F1 males were then paired with unexposed F0 females to produce an F2c litter. F0 animals were euthanized at selection of the F1 generation-breeding pairs, mated F1 males were euthanized following breeding with unexposed females, and mated F1 females were euthanized on PND4 after completion of the second breeding. F1 pups not selected for mating were necropsied on PND

21 or 28. Some F2a pups were euthanized on PND 11 for brain weight measurements and neuropathological examinations. Thirty F2a offspring/sex/group were euthanized on PND 70 after measurement of developmental landmarks. Excess F2a pups were sacrificed on PND21. Pups from F2b and F2c were euthanized on PND 4.Standard systemic endpoints assessed in F0 and F1adult animals included monitoring for mortality and clinical signs and body weights and food consumption were measured weekly. At necropsy, organ weights (epididymides [total and cauda], ovaries, prostate, seminal vesicles, testes, uterus, brain, kidneys, liver, lungs, spleen, thymus, heart, adrenals, pituitary, thyroid) were weighed, animals were grossly examined, and histopathology as conducted on >35 organs or tissues. F1 females were also subjected to functional observational battery (FOB) on GD10 and PND20 following the first mating. Reproductive endpoints included standard evaluations of reproductive performance, as well as sperm morphology and production rate, ovarian primordial follicle and corpora lutea counts, ejaculatory plugs, dystocia, and fertility index. The litter sizes, sex ratio, mean number of pups, and postnatal survival were recorded for all litters. F1, as well as F2a offspring, underwent measurements of body weights on PND 1, 4, 7, 14, and 21, anogenital distance on PND1, and the day of vaginal patency and timing of balanopreputial separation were recorded. F2a animals underwent additional FOB neurobehavioral tests on PND 20, 42, and 69, as well as motor activity observations, auditory startle tests, and biel maze swimming trials. Brain organ weights and dimensions were also recorded for select F2a offspring on PND70. Subsets of the animals underwent nervous system histopathological examinations (for brain, spinal cord, gasserian ganglion, lumbar dorsal root ganglion/fibers, cervical dorsal root ganglion/fibers, optic nerves, sciatic nerves, sural nerves, tibial nerves, peroneal nerves, eyes) and brain morphometry evaluations, or underwent gross necropsy on PND70. F2b and F2c animals were observed and weighed on PND 1 and 4. Mortality in the F0 generation occurred in one control male, 1/30 males at 502 and 700 ppm, and 4/30 females at 700 ppm within weeks 1 to 16. Another male in the 700 ppm group was also sacrificed in extremis. Observed clinical signs attributed to test chemical exposure included increased ejaculatory plugs in males. Moribund animals that either died or were euthanized in extremis had clinical signs prior to death that included misaligned incisors, labored breathing, hypoactivity, decreased defecation and urination, lurching, unkempt appearance, red material around the nose or genitals. No other significant clinical signs were observed in animals that survived until sacrifice. No statistically significant differences in weekly F0 body weights were observed, but there was a statistically significant decrease in body weight gain between exposure week 0 and week 1 for females at 502 ppm and in both sexes at 700 ppm. Significantly decreased body weight changes in females were also observed from GD 14-20 at 700 ppm but were attributed to fewer developing pups in this group. Isolated changes in food consumption or food efficacy were observed in both sexes but did not correlate with any significant changes in body weights. Dose-dependent organ weight changes in F0 animals included: significantly increased absolute (8-11%) and relative (7-14%) kidney weights in males at ≥502 and ≥298 ppm, respectively, increased absolute (10-30%) and relative (13-33%) liver weights in females at ≥298 ppm, and increased absolute (16%) and relative (9-19%) liver weights at 700 and ≥ 298 ppm, respectively, in males. All other organ weight changes did not show dose-response changes nor other significant changes attributed to exposure. No notable macroscopic changes were described. Dose-related histopathological changes in F0 animals included increased incidences of tubular mineralization in the kidneys of males and alveolar histiocytosis females which both reached statistical significance at 700 ppm. No other exposure-related histopathological findings were observed in exposed F0 animals. No significant differences in any F0 reproductive endpoints were observed although 2/30 and 3/30 dams at 502 and 700 ppm, respectively, had extended parturition and dystocia, which the authors considered to be exposure-related. No test article-related effects that were adverse were noted for spermatogenic endpoints in F0 males. Significant F1 litter effects included dose-related decreases in F1 litter size and the number of F1 pups born at ≥502 ppm. Some reductions in pup survival were noted from birth to PND 4 (by 23.7%) at 502 ppm which the authors stated may be "potentially indicative of a test article-related effect", but no effects on survival occurred at 700 ppm. Decreases at 298 ppm also occurred but did not reach statistical significance. Increased F1 pup mean body weights were observed on PND 1 and 4 at 700 ppm and were attributed to the decreased litter size. Pup body weights were not altered on PND 7, 14, 21 or 28. No organ weight changes were observed in F1 weanlings euthanized on PND 21. Dose-related decreases in absolute and relative spleen weights were observed in males at ≥298 ppm (by >11%) and in females at ≥500 ppm (by >10%) in F1 weanlings euthanized on PND 28. At the scheduled necropsies (PND21 and PND28) of the F1 weanlings not selected for mating, no notable macroscopic findings were observed. Measured developmental landmarks showed no differences in balanopreputial separation or vaginal patency. No exposure-related effects on mortality, clinical signs, or weekly body weights were observed in F1 adult animals during re-exposure, or at any time point during mating or gestation. There were significant reductions in body weight gains during GD 14-20 and 0-20, and during lactation (PND 7-14) following the first mating. During lactation, this corresponded with a significant reduction in food efficacy. Otherwise, food consumption and efficacy were generally unaffected, though there were some temporary, but statistically significant increases in food consumption at >500 ppm in both males and females during the pre-mating period. No exposure-related differences in home-cage/handling and open-field tests were observed. Notable organ weight changes observed in adult F1 males included: significant increases in absolute (12%) and relative (10-16%) liver weights at 702 and ≥502 ppm, respectively, and increased relative (10-11%) kidney weights at ≥502 ppm. In adult F1 females absolute (18-32%) and relative (14-27%) liver weights were significantly increased at ≥502 ppm, and absolute (13%) and relative (9%) kidney weights were increased at 702 ppm. No exposure-related changes in gross necropsy were observed. Dose-related histological changes observed in F1 animals included: increased incidences of tubular mineralization in the kidneys, pigmented liver, liver hyperplasia, centrilobular hepatocellular hypertrophy, and alveolar histiocytosis in males, and alveolar histiocytosis in females, all reaching significance in males at 702 ppm. Incidences of centrilobular hepatocellular hypertrophy in females were statistically significantly increased at ≥502 ppm.There were no differences observed for mean ovarian primordial follicle counts, but reduced corpora lutea counts were observed at 702 ppm. For the first mating, F1 Male and female mating indices were decreased at >700 ppm; the reduction was significant for females. Fertility indices for both sexes were significantly decreased at the same concentration. Estrous cycle length was significantly increased at 702 ppm, compared with controls. During the second mating, significant decreases in the mating indices occurred in high-exposure males and females, and fertility indices were decreased in both sexes at ≥502 ppm. Dystocia was observed in 2 and 3 females in the 502 and 702 ppm groups, which the authors considered to be test-article related; dystocia was the cause of death in 2/3 high-exposure females. For F1 males paired with unexposed females, no differences in reproductive performance were observed. Sperm parameters were not significantly affected by D4 exposure in F1 males.F2 litter effects included significant reductions in F2a litter size and number of pups born at ≥502 and 702 ppm, respectively, and significant increases in F2a male and female pup body weights on PND 1, 4, and 7. Reductions in F2b litter sizes were observed but were not responsive to exposure concentration. Reduced pup survival was observed for F2b at 702 ppm. Body weights of F2 offspring were not affected by exposure. FOB handling observations (PND70) identified an increased incidence palpebral closure, reductions in fecal pellets at 702 ppm. There was also a reduction in drooping eyelids in F2 animals exposed to ≥502 ppm. No other neurobehavioral effects were observed in the selected offspring tested. There were no effects on balanopreputial separation or vaginal patency, or on organ weights in sacrificed offspring. Some malformations were observed in all litters (typically in 1-2 pups/litter), but these findings were considered developmental variations that were not attributed to parental exposure and did not occur in a dose-dependent manner. Absolute forebrain weights of F2 female offspring were significantly increased on PND11 at 702 ppm, and on PND70, absolute female brain weights were significantly increased at ≥ 502 ppm.No author-derived toxicity values were reported. Based on the available data, a study-wide NOAEC of 70 ppm and a LOAEC of 298 ppm was determined based on increased absolute and relative liver weights in F0 female rats. At the LOAEL, male relative liver weights were also statistically, but not biologically (9%) increased. Histopathological changes in the liver were also evident, becoming significant at higher exposure levels. Reproductive and developmental effects including reductions in fertility indices, litter size, and the number of pups were observed at the LOAEL, but statistical significance was not reached until ≥502 ppm. Note: two linked references were also reviewed during this evaluation: 7002248 (amendment to report) and 4924646 (corresponding journal article).

[7] 5884342: Virgin female Crl:CD(SD)IGS BR rats were exposed to 700 ppm (n=125 total) octamethylcyclotetrasiloxane (D4) for 6 hours via whole body inhalation one, two, three, or four days prior to mating. A single control group (n = 25) was exposed for 6 hours one day prior to mating. Females were then mated 1:1 with unexposed male rats for a maximum of 4 days and examined daily for evidence of mating (presence of sperm in vaginal smear or copulatory plug). The day evidence of mating was identified (deemed gestational day 0), females were removed and housed individually. Controls were allowed to mate for a maximum of 5 days. In the control group, 22 females had evidence of mating and were assigned to Group 1. Exposed females with evidence of mating one day following exposure were assigned to Group 2 (Day -1; n=17); females with evidence of mating two days following exposure were assigned to Group 3 (Day -2; n=22); females with evidence of mating three days following exposure were assigned to Group 4 (Day -3; n=40); and females with evidence of mating four days following exposure were assigned to Group 5 (Day -4; n=23). Females were sacrificed on GD 8. Endpoints evaluated included mortality, clinical signs (appearance and behavior; during exposure, one hour after and daily beginning on GD0), body weights on GD 0, 4, and 8, and food consumption on GD 0, 4 and 8. At necropsy, gross abnormalities were noted. The uterus and ovaries were weighed. The number of corpora lutea on

each ovary and the total number of, and position of implantation sites were recorded. Histopathological examination was performed on the uterus, ovaries (Group 2 only), and all small implantation sites.All females survived the entirety of the experiment. No significant clinical signs were noted. Reduced pregnancy rates (gravid females/females with evidence of mating) were seen in females exposed one day (Day -1) prior to mating, compared to controls. The pregnancy rates were as follows: control (95.5%), Day -1 (64.7%), Day -2 (100%), Day -3 (100%) and Day -4 (95.7%). No treatment-related changes in body weight or body weight gains were seen. In the Day -2 group, a statistically significant decrease in body weight was seen on GD 8 (6%) and body weight gain (GD 4-8; 26%), however, these changes were attributed to biological variation by the study authors and not related to the compound. No significant difference in food consumption was seen compared to controls. No significant maternal gross abnormalities were seen. No changes in the numbers of corpora lutea, implantation sites, or pre-implantation loss were seen relative to controls. No significant biologically relevant differences in uterine or ovarian weights (absolute or relative) were observed in any group. Ovaries from Day -1 females (group 2) had a normal complement of corpora lutea; ovaries from other groups were not examined microscopically. A LOAEL of 700 ppm was determined based on decreased pregnancy rates in rats exposed one day before mating.

[8] 5884342: Virgin female Crl:CD(SD)IGS BR rats (n = 125 total) were exposed to 700 ppm of octamethylcyclotetrasiloxane (D4) via whole body inhalation 6 hours/day for 3 consecutive days prior to mating. Control rats (n = 25) were exposed to filtered air for 6 hours the day before mating. D4 exposed females were mated 1:1 with unexposed male rats for one day and examined for evidence of mating (presence of sperm in vaginal smear or copulatory plug). Forty presumed pregnant D4-exposed females were assigned to the study; all others were euthanized. Controls were allowed to mate for a maximum of 5 days; 22 control females had evidence of mating and were assigned to the study. The day evidence of mating was identified (deemed gestational day 0), and females were removed and housed individually. Females were sacrificed on GD 8. Endpoints evaluated included mortality, clinical signs (appearance and behavior), body weights on GD 0, 4, and 8, and food consumption on GD 0, 4 and 8. At necropsy, gross abnormalities were noted. The uterus and ovaries were weighed and the number of corpora lutea on each ovary and the total number of, and position of implantation sites were recorded. Histopathological examination was performed on the uterus and all small implantation sites. All females survived the entirety of the experiment. No significant clinical signs were noted. No significant difference in pregnancy rates (gravid females/females with evidence of mating) was seen in exposed rats (97.5%) compared to control (95.5%). Mean body weights were significantly, but only slightly decreased (5%) on GD0 compared with controls, but were similar to controls on GD 4 and GD 8. Mean body weight gains were increased compared to control on days 0-4 (64%) and 0-8 (28%) compared with control. No effects on food consumption were observed. No significant differences in the mean number of corpora lutea (14.9 in the exposed group vs 16.0 in controls), pre-implantation loss, or the number of small implantation sites were seen, compared to controls. Uterine or ovarian weights were comparable across groups. A NOAEL of 700 ppm was determined based on the lack of statistically and biologically significant changes.

[9] 5884342: Virgin female Crl:CD(SD)IGS BR rats were exposed to 700 ppm (n=70) of octamethylcyclotetrasiloxane (D4) via whole body inhalation 6 hours/day for 3 consecutive days prior to mating, throughout mating (a maximum of two days for mating), and through gestation day 3. Controls (n=25) were exposed to filtered air for 6 hours one day prior to mating. Females were mated 1:1 with unexposed male rats (2-5 days) and examined for evidence of mating (presence of sperm in vaginal smear or copulatory plug). Forty presumed pregnant females exposed to D4 were assigned to the study; all others were euthanized. Controls were allowed to mate for a maximum of 5 days; 22 control females had evidence of mating and were assigned to the study. Females were sacrificed on GD 8. Endpoints evaluated included mortality, clinical signs (appearance and behavior; during exposure, one hour after and daily beginning on GD0), body weights on GD 0, 4, and 8, food consumption on GD 0, 4 and 8. Gross abnormalities were noted, the uterus and ovaries were weighed. The number of corpora lutea on each ovary and total number of, and position of implantation sites were recorded. Histopathological examination was performed on the uterus and all small implantation sites.All females survived the entirety of the experiment. No significant clinical signs were noted during or following exposure. No significant difference in pregnancy rates (gravid females/females with evidence of mating) were seen in exposed rats (90.0%) compared with controls (95.5%). Mean body weights were not significantly different from controls on GD 0, 4, or 8. Mean body weight gains were significantly decreased from GD 0-4 (35%) and then increased from GD 4-8 (37%) compared with control; however, no significant difference was seen when the entire gestation period was evaluated GD 0-8. Food consumption significantly decreased GD 0-4 (25%) and overall, from GD 0-8 (10%) compared with controls. A significant decrease in the mean number of corpora lutea was observed (13.9) vs control (16.0). The number of implantation sites was also decreased (12.1) vs control (13.8) although this decrease was not statistically significant. No significant change in pre-implantation loss was seen. A compound-related increase in the number of small implantation sites (22 in 10 exposed females) was seen compared with controls (1 in 1 female). Significant decreases in the absolute (20%) and relative (21%) uterine weights were seen compared with control; this may be partially due to the observed small implantation sites. No differences in ovarian weights were observed. A LOAEC of 700 ppm was determined based on a decreased number of corpora lutea, an increased number of small implantation sites, and decreased uterine weights.

[10] 5884342: Fourteen-week-old virgin female Crl:CD(SD)IGS BR rats (n=155) were paired 1:1 with males and examined daily for evidence of mating (presence of sperm in vaginal smear or copulatory plug). The day evidence of mating was observed was considered gestation day 0. Presumed pregnant females were divided into a control group (n=25) and three exposure groups (n=25/group). Exposure groups were exposed to 700 ppm of octamethylcyclotetrasiloxane (D4) for 6 hours via whole-body inhalation on either GD 0, GD 1 or GD 2. The control group was exposed to air for 6 hours on GD 0. Females were sacrificed on GD 8. Endpoints evaluated included mortality, clinical signs (appearance and behavior), body weights and food consumption on GD 0, 4, and 8. Gross abnormalities were noted at the time of sacrifice. The uterus and ovaries were weighed and the number of corpora lutea on each ovary and the total number of, and position of implantation sites were recorded. Histopathological examination was performed on the uterus, and all small implantation sites.All females survived the entirety of the experiment. No clinical signs of toxicity were noted. The pregnancy rate (gravid females/females with evidence of mating) was slightly decreased in the rats exposed on GD 2; however, this was not considered to be treatment-related. The pregnancy rates were 96% (control), 92% (GD 0), 92% (GD 1) and 88% (GD 2). No significant difference in body weight or body weight gains was seen compared to controls. Slight changes in food consumption observed were not considered to be compound-related. No significant differences in mean numbers of corpora lutea, implantation sites, pre-implantation loss, or small implantation sites were seen compared to controls. There were no changes in uterine or ovarian weights and no exposure-related histological changes in the uteri or implantation sites.A NOAEC of 700 ppm was determined for the lack of observed effects.

[11] 5884342: Fourteen-week-old virgin female Crl:CD(SD)IGS BR rats (n=155 total) were paired 1:1 with males and examined daily for evidence of mating (presence of sperm in vaginal smear or copulatory plug). The day evidence of mating was observed was considered gestation day 0. Presumed pregnant females were divided into a control group (n=25) or an exposure group (n=25/group). The exposure groups were exposed to 700 ppm of octamethylcyclotetrasiloxane (D4) for 6 hours via whole-body inhalation from GD 0 through GD 2. Controls were exposed for 6 hours on GD 0. The remaining females were used for other exposure durations (separate extraction). Females were sacrificed on GD 8. Endpoints evaluated included mortality, clinical signs (appearance and behavior), and body weights and food consumption on GD 0, 4, and 8. Gross abnormalities were noted at the time of sacrifice. The uterus and ovaries were weighed. The number of corpora lutea on each ovary and total number of, and position of implantation sites were recorded. Histopathological examination was performed on the uterus, ovaries, and all small implantation sites. All females survived the entirety of the experiment. No clinical signs of toxicity were noted. The pregnancy rate (gravid females/females with evidence of mating) was slightly decreased (88%) in exposed rats compared to control (96%); however, this was not considered to be treatment related. No significant differences in body weights were seen on GD 0, 4 or 8, although body weight gain was significantly decreased from GD 0-4 in conjunction with decreases in food consumption from GD 0-4 and GD 0-8, compared with controls. No significant difference in mean numbers of corpora lutea, implantation sites, pre-implantation loss, or small implantation sites was found between exposed and control animals. No significant changes in uterine or ovarian weights and no notable histological changes were observed.A LOAEL of 700 ppm was determined based on decreases in body weight gain and food consumption

[12] 5887603: Male Sprague-Dawley rats (40/group) were exposed to 0, 500 or 693 ppm of octamethylcyclotetrasiloxane (D4) for 6 hours/day for at least 70 days prior to mating with sham-air exposed females. Exposures of the F0 males continued through mating for 43 additional days until study day 113. Males were then allowed to recover for 5-weeks before being sacrificed. Females were additionally exposed to sham-air during gestation

days (GD) 0-21 and lactation (postnatal day 4-21). All animals were monitored daily for mortality and clinical signs of toxicity. Body weights were recorded weekly prior to mating (both sexes); females body weights were recorded on GD 0, 7, 10, 14 and 20 and PND 1, 4, 7, 14 and 21. Female food consumption was measured prior to mating, during gestion, and during lactation. F0 dams were sacrificed on PND 21 if they delivered litters, or on PND 25 if they failed to deliver litters. Pups were sacrificed on PND 21. Endpoints assessed included F0 gross necropsy, F0 male organ weights (adrenals, brain, epididymides, heart, kidneys, liver, lungs, pituitary, prostate, seminal vesicles with coagulating glands, testes, spleen, thymus, thyroid); and F0 male histopathology (adrenals, aorta, bone with marrow, brain, eyes with optic nerve, gastrointestinal tract, heart, kidneys, liver, lungs, lymph nodes, pancreas, penis, peripheral nerve, pituitary, prepuce, preputial gland, prostate, salivary gland, seminal vesicles, skeletal muscle, skin, spinal cord, spleen, testes with epididymides, thymus, thyroid gland, trachea, urinary bladder, and gross lesions). Reproductive parameters (mating and fertility indices, dystocia, prolonged/delayed labor, ejaculatory plugs), and developmental parameters (litter viability/survival, number of pups, sex ratio, skeletal malformations, pup gross necropsy, clinical signs, body weights on PND 1, 4, 7, 14, and 21) were measured.Only one F0 male died during the exposure period in the 693-ppm group, but the study authors considered this death not to be related to D4 exposure. The only notable exposure related clinical sign was dried red material around the nose at 693 ppm. Significantly reduced mean body weight gain and food consumption in males during week 0-1 was observed at 693 ppm but was not affected throughout the remainder of the study; no significant differences in females were seen. No significant findings for organ weights nor histopathology were reported in F0 males. No exposure related differences in reproductive performance were observed. No significant differences in litter size, number of pups, sex ratio of offspring, pup survival, malformations, pup weight or pup gross necropsy at PND21 were observed. A LOAEC of 693 ppm and NOAEC of 500 ppm for nutritional/metabolic effects was determined based on decreased body weight gain and food consumption in F0 males. A NOAEC of $>$ 693 ppm for reproductive/developmental effects was also determined.

[13] 5887777: Sprague-Dawley rats (22/sex/group) were exposed to 0 or 700 ppm octamethylcyclotetrasiloxane (D4) via whole-body inhalation for 6 hours/day, 7 days/week for at least 4 weeks prior to mating and during the mating period. Males were sacrificed after breeding and females were additionally exposed from gestational day (GD) 0-20 and sacrificed on either post-natal day (PND) 4 or post-mating day 25. Two sham-air control groups of 22 animals were included in the study design. Animals were monitored for clinical signs of toxicity and mortality over the study period and body weights, and food consumption were measured weekly (and on GD 0, 7, 10, 14 and 20 and PND 1 and 4 in females). Body weight gain was also recorded. Other endpoints assessed in F0 animals included: mating and fertility indices, sperm number and production rate, gross necropsy, organ weights and histopathology (for epididymides, prostate, testes, ovaries), length of gestation, pre-implantation loss, and implantation sites/corpora lutea number. Endpoints assessed in F1 animals included: litter viability, litter size, gross malformations, clinical observations, sex ratio, and body weights.2 control group and 2 700 ppm group females were sacrificed early due to failing to deliver litters and 2 other 700 ppm dams had total litter loss. Observed clinical signs at 700 ppm included red material around the noise and yellow staining in the urogenital area. Compared to controls, significantly decreased body weights (from weeks 1-3 pre-mating and during the entirety of gestation were observed in treated F0 females; however, the magnitudes of change were small $<$10%. Body weight gain was reduced during the first week of exposure, and during gestation (days 10-14, 14-2-, and 0-20) in F0 females. No body weight or body weight changes occurred during lactation, or in males. Food consumption of treated females was significantly, but slightly decreased during weeks 1, 2, and 5 pre-mating, and during the first week of gestation. Significantly increased gestation length was observed at 700 ppm but was not considered to be biologically significant by the study authors. Significantly reduced litter sizes and viability (PNDs 1 and 4) were observed at 700 ppm, while pup body weights were significantly increased on PND1 and 4 (10 and 11%, respectively, compared with controls). Decreases in the mean number of implantation sites, number of pups born, number of corpora lutea, and increases in pre-implantation loss and numbers of implantation sites unaccounted for were observed in treated females, compared with controls. No malformations were reported. No exposure-related findings were observed during gross necropsy, testis and epididymis weights or histopathology in F0 males, and there were no effects of D4 on sperm number or production rate. No exposure-related findings were observed for organ weights nor histopathology in F0 females.A LOEC of 700 ppm for maternal effects was determined based on slight decreases in body weights and food consumption in F0 females. A LOAEC of 700 ppm for developmental/reproductive effects was determined based on reduced litter size, number of pups born, pup viability, and increased pre-implantation loss and pup weight. A NOAEC could not be determined.

[14] 5887799: Female Sprague-Dawley rats (22/group) were exposed to 0, 300, 500 or 700 ppm (72, 302, 498, and 700 ppm analytical) of octamethylcyclotetrasiloxane (D4) via whole body inhalation for 6 hours/day for 70 days prior to mating with unexposed males. Exposure to females continued during mating, through gestation day (GD) 1-21 and lactation day (LD) 5-21; exposure ws discontinued from GD 21- LD4 F1 animals were additionally exposed to D4 following weaning in 6 hours/day exposures from PND 21-28. Parental females were euthanized on postnatal day (PND) 25 and select pups were necropsied on PND 28. F0 females were monitored for mortality, clinical signs, body weight, weight gain, and food consumption over the study period. Other endpoints evaluated in F0 females included estrous cycle timing, days between pairing and coitus, mating and fertility indices, duration of gestation, timing of parturition, organ weights (ovaries, uterus, adrenals, pituitary, thyroid, brain, heart, liver, kidney, lungs, spleen, thymus), gross necropsy, and histopathology (ovaries, uterus, mammary gland, vagina, adrenals, hypothalamus, pituitary, brain, heart, kidney, liver, lungs, spleen, thymus). Litter and pup viability was recorded and pups were observed during lactation. Other endpoints assessed in F1 animals included pup body weights, food consumption, sex ratio, organ weights (liver, ovaries, testes), macroscopic observations (10 pups/sex/group), and histopathology (adrenals, aorta, bone with marrow, brain, clitoral gland, eyes with optic nerve, gastrointestinal tract, heart, kidneys, liver, lungs, lymph nodes, mammary gland, ovaries, pancreas, penis, peripheral nerve, pituitary, prepuce, preputial gland, prostate, salivary gland, seminal vesicles, skeletal muscle, skin, spinal cord, spleen, testes, thymus, thyroid gland, trachea, urinary bladder, uterus with vagina, gross lesions).No deaths of F0 animals occurred. Observed clinical signs included dried red material around the nose and mouth; increased incidences occurred between weeks 1 and 15 at concentrations $\geq$302 ppm. Additional dried red material around the eyes and wet red material around the nose was observed at 700 ppm. Maternal body weight gains were significantly reduced, compared with controls during weeks 1 and 3 at $\geq$ 302 ppm; however, body weights remained comparable to controls throughout the pre-mating period. During gestation, significant, but small ($<$10%) magnitude body weight reductions occurred at the highest dose on GD 14 and 20 and LDs 1, 4, 7 and 14. Body weight gains from LD14-21 and 1-21 were significantly reduced at 700 ppm (g/animal/day). Differences in food consumption included small inconsistent increases, primarily at 500 and 700 ppm during the pre-exposure period, and other directionally inconsistent or non-dose-related changes during gestation and lactation. There were no effects on reproductive performance, fertility indices, time to coitus, or oestrous cyclicity. A significantly decreased number of implantation sites was observed at 700 ppm. No difference was observed for oocyte/ovarian follicle counts. Significantly increased absolute (11- 16%) and relative (10-18%) liver weights were observed at concentrations $\geq$500 ppm and $\geq$300 ppm, respectively. No histopathological changes were reported in D4-exposed animals. Significantly reduced F1 litter sizes and number of pups born, and an increase in unaccounted-for sites were observed at 700 ppm, while pup weights, survival and sex ratio were not affected by D4 exposure. No exposure-related gross pathology or organ weight changes were observed in F1 animals. A maternal LOAEC of 300 ppm was determined based on increased and relative liver weights. A NOAEC could not be determined. A reproductive/developmental NOAEC of 500 ppm and LOAEC of 700 ppm was determined for based on decreased implantation sites and reduced F1 litter size, number of pup births, and increased unaccounted-for sites.

[15] 5888075: Sprague-Dawley Crl:CD BR rats (20/sex/group) were exposed to 0, 70 or 700 ppm of octamethylcyclotetrasiloxane (D4) vapors via whole-body inhalation for 6 hours/day from 28 days prior to mating through the two-week mating period (males), or through gestation (GD) 1-20 and lactation day (LD) 5-21 (females). F1 pups were additionally exposed to the same concentrations for 6 hours/day from postnatal day (PND) 21-28. Endpoints assessed in the F0 generation included body weights, body weight gain, and food consumption (weekly and on GD 7, 10, 14, 20 and LD 1, 4, 7, 14 and 21) and mating and fertility indices, time to coitus, gestation length, and number of implantation sites. Endpoints assessed in the F1 generation included litter viability and survival, gross lesions, skeletal anomalies, clinical signs, sex ratio, and body weights (on PND 1, 4, 7, 14, 21 and 28).No animals died over the course of the study, but three animals (one in the control, and two in the 700 ppm groups) were euthanized early due to failure to deliver litters. Increased ejaculatory plugs and some incidence of dried red material around the nose and dried clear material around the eyes were observed at 700 ppm. Significantly decreased body weights were observed in high-dose males during weeks 3-6 and in females during weeks 1-3 and GD 20 at 700 ppm; however, the magnitudes of change were small ($<$10%). Male body weight gains were significantly decreased (25-35%) during weeks 0-1 and 2-3 but were comparable to controls thereafter.

In females, body weight gains were significantly reduced during week 1 (42%), and also between GDs 14-20 and 0-20 (12-25%). There were no changes in body weights or weight gain in animals exposed to 70 ppm, or in females during the lactation period. Females at 700 ppm also showed significant reductions in food consumption during week 0-1, but food consumption was significantly increased, compared with controls, throughout gestation. During lactation, female food consumption was again reduced, significantly but only slightly, during lactation days 7-14. No clear exposure-related findings were observed in F0 males or females at necropsy.Mating and fertility indices were not affected by D4 exposure. Mean gestation length was unaffected by D4 exposure, although one 700 ppm females showed signs of dystocia. The mean number of implantation sites was decreased and the number of sites unaccounted for increased at 700 ppm. F1 litter deaths were observed at concentrations ≥70 ppm, but most of these deaths occurred from the same litter so this effect was not considered by the study authors to be exposure-related. The viability index of pups was significantly reduced on PND1 but fell within the historical control range for the performing laboratory. Survival index and sex ratio were not affected by D4 exposure. Significantly reduced litter size was observed at 700 ppm. Increased pup body weights were also observed on PND 1 and 4 at 700 ppm both before and after culling the litters. At necropsy, some pups had reddened lungs at both 70 and 700 ppm, but the statistical significance of this finding relative to control was not stated. The study authors' conclusions suggest a reproductive/developmental NOAEC of 70 ppm and LOAEC of 700 ppm based on decreased litter size and number of implantation sites, and a parental systemic NOAEC of 70 ppm and LOAEC of 700 ppm based on slightly decreased body weights, bodyweight gain, and food consumption parental animals.

[16] 7310330: Female Crl:SD (SD) IGD BR rats (30/group) were exposed to 0 or 704 ppm of octamethylcyclotetrasiloxane, (D4) for 6 hours/day for 7 days prior to mating, during mating with unexposed males, and from gestational day (GD) 0-20 and lactation day (LD) 5-20. F0 dams were euthanized on LD 25. The F1 generation (30/sex/group) was additionally exposed to 0 or 706 ppm of D4 starting at postnatal day (PND) 22 for a minimum of 70 days prior to first mating period. Exposure continued through mating and gestation as described for F0 through two mating periods to produce an F2a and F2b generation. F1 animals were euthanized without examination on PND 21 and PND 28 if not chosen for further mating. F2a animals were euthanized on PND 21 and F2b animals were euthanized on PND 4. Endpoints assessed in F0 dams included: death, body weights, food consumption, pituitary organ weights, Estrous cycle timing, fertility and mating indices, gestation length, histopathology in females (mammary tissue, ovary, uterus, vagina), and organ weights (ovary, uterus). Endpoints assessed in F1 and F2 animals included: sex ratio, litter viability, gross malformations, skeletal variations and malformations, pup weights (on PND 1, 4, 5, 14 and 21), live litter size, postnatal survival between birth or PND 4, postnatal survival for all other intervals. F1 females used for further mating were also examined for histopathology (mammary tissue, ovary, pituitary, uterus, vagina, gross lesions), organ weights (ovary, pituitary, uterus), and serum hormone analysis (estradiol, prolactin, progesterone). F0 and F1 males were discarded after mating and not examined. A pharmacokinetic analysis of D4 concentrations in the liver, plasma and fat samples of F0 and F1 animals was also performed. All F0 females survived until scheduled sacrifice; no exposure-related clinical signs of toxicity were observed. No significant differences in reproductive performance (number of days between pairing and coitus, mating indices, female fertility indices, estrous cycle length or gestation length) were seen compared to control. Significantly decreased weekly body weights and food consumption were observed in all F0 females exposed to 700 ppm during the pre-breeding period. Decreased food consumption continued during gestation but was not significantly altered during lactation. No exposure related findings were observed for gross necropsy, histopathology, or organ weights in F0 females. Significantly decreased mean number of implantation sites, number of pups and mean litter sizes were in litters born from F0 females were observed at 700 ppm. No differences in F1 sex ratio or pup survival were observed. The general physical condition of the F1 pups from PND 1-28 was similar to controls. Offspring body weights were significantly increased from PND 1-4 in all groups exposed to 700 ppm but were not significantly different on PND 14 and 21. During the exposure of pregnant F1 animals, 1/30 animals died. No exposure-related clinical signs of toxicity were observed. During the first mating, no significant differences were observed for days between pairing and coitus nor mating and fertility indices, though reduced fertility was observed due to the inability of some females to deliver offspring. During the second mating, reduced fertility rates and a decreased pre-coital interval were observed. No test substance related changes were observed for weekly body weights and food consumption in F1 females during D4 exposure or gestation during the first mating. Food consumption but not body weights were reduced during lactation of the first mating. Significantly decreased body weights and food consumption were observed in F1 females during the gestation period for the second mating but were not altered during lactation of the second mating. No significant differences were observed for gestation length during the first and second mating periods. No significant differences were observed in estradiol in F1 females, but significantly decreased mean progesterone and prolactin levels were observed at 700 ppm but was not considered to be test substance related. No exposure-related findings for gross pathology nor organ weights were observed in F1 females at the time of sacrifice. Histopathological changes observed in F1 females included: decreased basophilic new corpora lutea, increased proestrus, mammary gland duct ectasia. For F2a pups, significantly decreased number of pups born, and live litter sizes were observed at 700 ppm. Significantly decreased survival was observed in F2a pups at 700 ppm. Increased F2a body weights were observed during PND1 to PND4 but was decreased in all D4 exposed groups on PND 14 and 21. For F2b pups, significantly decreased number of pups born, and live litter sizes were observed at 700 ppm, whereas survival and body weights were not altered. No malformations or skeletal variations were observed.A LOAEC of 700 ppm for Reproductive/Developmental effects was determined based on reproductive toxicity and histopathology in ovaries, uterus and mammary gland in the F1 generation and decreased litter size and survival in the F2a generation. A LOAEL for Nutritional/Metabolic effects was also determined in F0 animals based on decreased body weights and food consumption. A NOAEC for these endpoints could not be determined.

[17] 7310330: Female Crl:SD (SD) IGD BR rats (30/group) were exposed to 0 or 704 ppm of octamethylcyclotetrasiloxane, (D4) for 6 hours/day for 7 days prior to mating, during mating with unexposed males, and from gestational day (GD) 0-20 and lactation day (LD) 5-20. F0 dams were euthanized on LD 25. The F1 generation (30/sex/group) was additionally exposed to 0 or 706 ppm starting at postnatal day (PND) 44 for a minimum of 70 days prior to the first mating period. Exposure continued through mating and gestation as described for F0 through two mating periods to produce an F2a and F2b generation. F1 animals were euthanized without examination on PND 21 and PND 28 if not chosen for further mating. F2a animals were euthanized on PND 21 and F2b animals were euthanized on PND 4. Endpoints assessed in F0 dams included: death, body weights, food consumption, pituitary organ weights, Estrous cycle timing, fertility and mating indices, gestation length, histopathology in females (mammary tissue, ovary, uterus, vagina), and organ weights (ovary, uterus). Endpoints assessed in F1 and F2 animals included: sex ratio, litter viability, gross malformations, skeletal variations and malformations, pup weights (on PND 1, 4, 5, 14 and 21), live litter size, postnatal survival between birth or PND 4, postnatal survival for all other intervals. F1 animals used for further mating were also examined for histopathology in females (mammary tissue, ovary, pituitary, uterus, vagina, gross lesions), organ weights in females (ovary, pituitary, uterus), and serum hormone analysis (estradiol, prolactin, progesterone). F0 and F1 males were discarded after mating and not examined. A pharmacokinetic analysis of D4 concentrations in the liver, plasma and fat samples of F0 and F1 animals was also performed. All F0 females survived until scheduled sacrifice; no exposure-related clinical signs of toxicity were observed. No significant differences in reproductive performance number of days between pairing and coitus, mating indices, fertility indices, estrous cycle length or gestation length) were seen compared to control. Significantly decreased weekly body weights and food consumption were observed in all F0 females exposed to 700 ppm during the pre-breeding period. Decreased food consumption continued during gestation but was not significantly altered during lactation. No exposure related findings were observed for gross necropsy, histopathology, or organ weights in F0 females Significantly decreased mean number of implantation sites, number of pups and mean litter sizes were in litters born from F0 females were observed at 700 ppm. No differences in F1 sex ratio or pup survival were observed. Offspring body weights were significantly increased from PND 1-4 at 700 ppm but were not significantly different on PND 14 and 21. During the exposure of pregnant F1 animals, 4/30 died following the first mating period, and 1/30 following the second mating period. During the first mating, no significant differences were observed for days between pairing and coitus nor, mating and fertility indices, though reduced fertility was observed in the 700/700-D22 group due to the inability of some females to deliver offspring. No test substance related changes were observed for weekly body weights and food consumption in F1 females during D4 exposure or gestation during the first mating. Food consumption but not body weights were reduced at 700 ppm during lactation of the first mating. Significantly decreased body weights and food consumption were observed in F1 females during the gestation period for the second mating but were not altered during lactation of the second mating. No significant differences were observed for gestation length during the first and second mating periods. No significant differences were observed in estradiol in F1 females, but significantly decreased mean progesterone and prolactin levels were observed at 700 ppm but were not considered to be test substance related. No exposure-related findings for gross pathology nor organ weights were observed in F1 females at the time of sacrifice. Histopathological

changes observed in F1 females included: decreased basophilic new corpora lutea and mammary gland duct ectasia. For F2a pups, significantly decreased number of pups born, and live litter sizes were observed at 700 ppm. Significantly decreased survival was observed in F2a pups at 700 ppm. Increased F2a body weights were observed during PND1 to PND4 but were decreased in on PND 14 and 21. For F2b pups, significantly decreased number of pups born, and live litter sizes were observed at 700 ppm. Decreased survival was observed in F2b pups at 700 ppm but was not statistically significant. No malformations or skeletal variations were observed. A LOAEC of 700 ppm for Reproductive/Developmental effects was determined based on reproductive toxicity and histopathology in ovaries and mammary gland in the F1 generation and decreased litter size and survival in the F2a generation. A LOAEC for Nutritional/Metabolic effects was also determined in F0 animals based on decreased body weights and food consumption. A NOAEC for these endpoints could not be determined.

[18] 7310330: Female Crl:SD (SD) IGD BR rats (30/group) were exposed to 0 or 704 ppm of octamethylcyclotetrasiloxane, (D4) for 6 hours/day for 7 days prior to mating, during mating with unexposed males, and from gestational day (GD) 0-20 and lactation day (LD) 5-20. F0 dams were euthanized on LD 25. The F1 generation was exposed to sham air continually through two mating periods to produce an F2a and F2b generation. F1 animals were euthanized without examination on PND 21 and PND 28 if not chosen for further mating. F2a animals were euthanized on PND 21 and F2b animals were euthanized on PND 4. Endpoints assessed in F0 dams included: death, body weights, food consumption, pituitary organ weights, Estrous cycle timing, fertility and mating indices, gestation length, histopathology in females (mammary tissue, ovary, uterus, vagina), and organ weights (ovary, uterus). Endpoints assessed in F1 and F2 animals included: sex ratio, litter viability, gross malformations, skeletal variations and malformations, pup weights (on PND 1, 4, 5, 14 and 21), live litter size, postnatal survival between birth or PND 4, postnatal survival for all other intervals. F1 animals used for further mating were also examined for histopathology in females (mammary tissue, ovary, pituitary, uterus, vagina, gross lesions), organ weights in females (ovary, pituitary, uterus), and serum hormone analysis (estradiol, prolactin, progesterone). A pharmacokinetic analysis of D4 concentrations in the liver, plasma and fat samples of F0 and F1 animals was also performed. All F0 females survived until scheduled sacrifice; no exposure-related clinical signs of toxicity were observed. No significant differences in reproductive performance (number of days between pairing and coitus, mating indices, fertility indices, estrous cycle length or gestation length) were seen compared to control. Significantly decreased weekly body weights and food consumption were observed in all F0 females exposed to 700 ppm during the pre-breeding period. Decreased food consumption continued during gestation but was not significantly altered during lactation. No exposure related findings were observed for gross necropsy, histopathology, or organ weights in F0 females.. Significantly decreased mean number of implantation sites, number of pups and mean litter sizes were in litters born from F0 females were observed at 700 ppm. No differences in F1 sex ratio or pup survival were observed. Offspring body weights were significantly increased from PND 1-4 at 700 ppm but were not significantly different on PND 14 and 21. No F1 animals died during the secondary sham air exposure. During the first and second mating, no significant differences were observed for days between pairing and coitus nor, mating and fertility indices for gross pathology nor organ weights were observed in F1 females at the time of sacrifice. Histopathological changes observed in F1 females included: mammary gland duct ectasia at 700 ppm. For F2a pups and F2b pups, no significant differences were observed for any measured endpoint. A LOAEC of 700 ppm for Reproductive/Developmental effects was determined based on reproductive toxicity and histopathology in the mammary glands in F1 females. A LOAEC for Nutritional/Metabolic effects was also determined in F0 animals based on decreased body weights and food consumption. A NOAEC for these endpoints could not be determined.

[19] 7310330: Female Crl:SD (SD) IGD BR rats (30/group) were exposed to filtered air for 6 hours/day for 7 days prior to mating, during mating with unexposed males, and from gestational day (GD) 0-20 and lactation day (LD) 5-20. F0 dams were euthanized on LD 25. F1 animals were exposed to 0 or 706 ppm of octamethylcyclotetrasiloxane, (D4) for 6 hours/day from weaning through two mating periods to produce an F2a and F2b generation. Animals were exposed for a minimum of 70 days prior to the first mating period. F1 animals were euthanized without examination on PND 21 and PND 28 if not chosen for further mating. F2a animals were euthanized on PND 21 and F2b animals were euthanized on PND 4. Endpoints assessed in F0 dams included: death, body weights, food consumption, pituitary organ weights, Estrous cycle timing, fertility and mating indices, gestation length, histopathology in females (mammary tissue, ovary, uterus, vagina), and organ weights (ovary, uterus). Endpoints assessed in F1 and F2 animals included: sex ratio, litter viability, gross malformations, skeletal variations and malformations, pup weights (on PND 1, 4, 5, 14 and 21), live litter size, postnatal survival between birth or PND 4, postnatal survival for all other intervals. F1 animals used for further mating were also examined for histopathology in females (mammary tissue, ovary, pituitary, uterus, vagina, gross lesions), organ weights in females (ovary, pituitary, uterus), and serum hormone analysis (estradiol, prolactin, progesterone). A pharmacokinetic analysis of D4 concentrations in the liver, plasma and fat samples of F0 and F1 animals was also performed. All F0 females survived until scheduled sacrifice; no exposure-related clinical signs of toxicity were observed. No significant differences in body weight, food consumption or reproductive performance (number of days between pairing and coitus, mating indices, fertility indices, estrous cycle length or gestation length) were seen compared to control. Significantly decreased mean number of implantation sites, number of pups and mean litter sizes were in litters born from F0 females were observed at 700 ppm. No exposure related findings were observed for gross pathology, histopathology, or organ weights in F0 females. . In the F1 animals, 1/30 females died at 700 ppm following the second mating period. During the first and second mating, no significant differences were observed for days between pairing and coitus nor, mating and fertility indices. No test substance related changes were observed for weekly body weights and food consumption in F1 females during D4 exposure or gestation during the first mating. Food consumption but not body weights were reduced at 700 ppm during lactation of the first mating. Significantly decreased body weights and food consumption were observed in F1 females during the gestation period for the second mating but were not altered during lactation of the second mating. No significant differences were observed for gestation length during the first and second mating periods. No significant differences were observed in estradiol in F1 females, but significantly decreased mean progesterone and prolactin levels were observed at 700 ppm but were not considered to be test substance related. No exposure-related findings for gross pathology nor organ weights were observed in F1 females at the time of sacrifice. Histopathological changes observed in F1 females included: decreased basophilic new corpora lutea, increased proestrus, and mammary gland duct ectasia.For F2a pups, significantly decreased number of pups born, and live litter sizes were observed at 700 ppm. Increased F2a body weights were observed during PND1 to PND4 at 700 ppm but was decreased at PND 14 and 21. For F2b pups, significantly decreased number of pups born, and live litter sizes were observed at 700 ppm. Decreased survival was observed in F2b pups at 700 ppm but was not statistically significant. Significantly increased body weights were observed in F2b pups from PND 1-4 at 700 ppm but was not altered during the rest of lactation. No malformations or skeletal variations were observed.A LOAEC of 700 ppm for Reproductive/Developmental effects was determined based on reproductive toxicity and histopathology in ovaries, uterus and mammary gland in the F1 generation and decreased litter size and survival in the F2a generation.

Octamethylcyclotetrasiloxane (D4)- Parent compound - Other (specify)

Guideline and Animal Species, Strain, Sex	Exposure Route and Exposure Duration	Study-wide POD and Dose/ Concentration(s)	Summary	Major Limitations	Principal Target Organs/Systems and OQD*	HERO ID
No guideline or adherence to GLP conditions was specified. Rabbit-Not specified-Male	Dermal-Duration: Other (specify) (Skin irritation study) Single exposure. Skin irritation study skin irritation, assessed at 24 hours	**POD: % in solvent (Dichotomous (P/N)) -Negative for skin irritation** n= 5 Dose= 0.01, n= 5 Dose= 0.1, n= 5 Dose= 1, n= 5 Dose= 10, n= 5 Dose= 100, % in solvent	In a skin irritation test, 0.01 mL of octamethylcyclotetrasiloxane (D4, purity not reported), also referred to as volatile silicone 7207, was applied uncovered to the clipped intact skin on the bellies of albino Wayne Rabbits (5/group, sex not reported) either undiluted, or as dilutions of 10, 1, 0.1, or 0.01% in an unspecified solvent. It was not specified whether animals were immobilized or housed individually to prevent possible oral exposure. Skin was examined and graded on a 10-grade scale for capillary injection, erythema, edema, or necrosis within 24-hours. No further methodological details were provided. No evidence of skin irritation was observed (Grade 1) with the undiluted test substance. The mean primary irritation score was 0.21, but it was not specified whether this was for the undiluted test substance or for one of the dilutions. The study authors report that under the conditions of this experiment, D4 was not an "irritant" by FHSA definition.	This study has significant reporting deficiencies, including missing information about the test substance and animal husbandry. The dose volume was less than guideline recommendations and the solvent was not specified.	Irritation-Skin irritation; eye irritation; Low	Carnegie Mellon University, 1972 5895941
No guideline or adherence to GLP conditions was specified. Rabbit-Not specified-Male	Ocular/ Eye-Duration: Acute (less than or equal to 24 hr) Single exposure. Skin irritation study skin irritation, assessed at 24 hours	**POD: % (Dichotomous (P/N)) -Negative for eye irritation** n= 6 Dose= 1, n= 6 Dose= 5, n= 6 Dose= 15, n= 6 Dose= 40, n= 24 Dose= 100, %	In an eye irritation study, the eyes of rabbits (presumably 6/group, strain and sex not specified) were dosed with Octamethylcyclotetrasiloxane (D4, also referred to as Silicone Y-7202). A single instillation of 0.005, 0.02, 0.1, or 0.5 ml undiluted or of 0.5 ml of 40, 15, 5, and 1% dilutions were made into the conjunctival sac. The eyes were observed immediately after instillation and 24 hours later after fluorescein staining. The authors state that all six rabbits were negative for eye irritation. They also report that under the conditions of this experiment, D4 was not an "irritant" by FHSA definition. No irritation scores were provided.	This study has significant reporting deficiencies, including missing information about the test substance and animal husbandry, limited methodological details, and only qualitative reporting of results. The dilutant was not specified.	Irritation-Skin irritation; eye irritation; Low	Carnegie Mellon University, 1972 5895941

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Octamethylcyclotetrasiloxane (D4)- Parent compound - Other (specify)

Guideline and Animal Species, Strain, Sex	Exposure Route and Exposure Duration	Study-wide POD and Dose/ Concentration(s)	Summary	Major Limitations	Principal Target Organs/Systems and OQD*	HERO ID
No guideline or adherence to GLP conditions was specified. Rabbit-Other (Albino Wayne)-Unknown	Dermal-Duration: Other (specify) (Irritation) Single exposure. Irritation Single application - dermal irritation	**POD: % (in solvent) (Dichotomous (P/N)) -Negative for skin irritation** n= 5 Dose= 100, n= 5 Dose= 10, n= 5 Dose= 1, n= 5 Dose= 0.1, n= 5 Dose= 0.01, % (in solvent)	In a skin irritation test, 0.01 mL of octamethylcyclotetrasiloxane (D4, purity not reported), also referred to as volatile silicone 7207, was applied uncovered to the clipped intact skin on the bellies of five albino Wayne Rabbits (sex not reported) either undiluted, or as dilutions of 10, 1, 0.1, or 0.01% in an unspecified solvent. It was not specified whether animals were immobilized or housed individually to prevent possible oral exposure. Skin was examined and graded on a 10-grade scale for capillary injection, erythema, edema, or necrosis within 24 hours. No further methodological details were provided. No evidence of skin irritation was observed (Grade 1) with the undiluted test substance.	This study was limited by reporting deficiencies, including a lack of details on the test substance, test model, and exposure administration.	Irritation-Skin irritation, eye irritation; Low	Carnegie Mellon University, 1978 7310549
No guideline or adherence to GLP conditions was specified. Rabbit-Other (Albino Wayne)-Unknown	Ocular/ Eye-Duration: Other (specify) (Irritation) Single exposure. Irritation Single instillation - eye irritation	**POD: mL (Dichotomous (P/N)) -Negative for eye irritation** n= 5 Dose= 0.005, n= 5 Dose= 0.02, n= 5 Dose= 0.1, n= 5 Dose= 0.5, mL	In an eye irritation study, 0.005, 0.02, 0.1, or 0.5mL of undiluted or 0.5 mL of 40, 15, 5, or 1% diluted octamethylcyclotetrasiloxane (D4, purity not reported), also referred to as volatile silicone 7207, was instilled into the conjunctival sac of five albino Wayne Rabbits (sex not reported). 24 hours after application, eyes were read unstained and stained with 5% fluorescein. Irritation was graded on a 10-grade scale. There was trace or no injury from 0.5 mL of the undiluted test substance (Grade 1),	This study was limited by reporting deficiencies, including a lack of details on the test substance, test model, and exposure administration.	Irritation-Skin irritation, eye irritation; Low	Carnegie Mellon University, 1978 7310549

* Overall Quality Determination

Octamethylcyclotetrasiloxane (D4)- Metabolite: Dimethylsilanediol (DMSD) - Short-term (>1-30 days)

Guideline and Animal Species, Strain, Sex	Exposure Route and Exposure Duration	Study-wide POD and Dose/ Concentration(s)	Summary	Major Limitations	Principal Target Organs/Systems and OQD*	HERO ID
Equivalent or similar to OECD TG 440; GLP compliant. Rat-Sprague-Dawley - [rat]-Female	Oral-Gavage-Duration: Short-term (>1-30 days)-3-day(s) 3 day(s) Animals were dosed on 3 consecutive days	**POD: 1200 mg/kg-bw/day (LOAEL) -Positive for uterotrophic response.** n= 6 Dose= 0, n= 6 Dose= 600, n= 6 Dose= 1200, mg/kg-bw/day	See footnotes for full summary [1]	It is not clear whether the study intended to identify a dose response, but the authors did conduct statistical analysis to determine whether data from both parts of the study could be combined. Because there were statistically significant differences between the vehicle and positive control groups from experimental parts 1 and 2, it was determined that the data from the two experiments could not be combined, thus precluding the ability to make comparisons across the three dose groups. No justification was provided for why the study was conducted in such a manner. Two dose groups are acceptable based on OECD TG 440. It is unclear if the third group was added as an afterthought or if the initial study design included all three dose groups.	Reproductive/Developmental; Uterotophic assay: absolute and relative uterine weight (wet and blotted); test for anti-estrogenic effects.; High	Dow Corning, 2009 9651848
Equivalent or similar to OECD TG 440; GLP compliant. Rat-Sprague-Dawley - [rat]-Female	Oral-Gavage-Duration: Short-term (>1-30 days)-3-day(s) 3 day(s) Animals were dosed on 3 consecutive days	**POD: 1000 mg/kg-bw/day (LOAEL) -Positive for uterotrophic response** n= 6 Dose= 0, n= 6 Dose= 1000, mg/kg-bw/day	See footnotes for full summary [2]	It is not clear whether the study intended to identify a dose response, but the authors did conduct statistical analysis to determine whether data from both parts of the study could be combined. Because there were statistically significant differences between the vehicle and positive control groups from experimental parts 1 and 2, it was determined that the data from the two experiments could not be combined, thus precluding the ability to make comparisons across the three dose groups. No justification was provided for why the study was conducted in such a manner. Two dose groups are acceptable based on OECD TG 440. It is unclear if the third group was added as an afterthought or if the initial study design included all three dose groups.	Reproductive/Developmental; Uterotophic assay: absolute and relative uterine weight (wet and blotted); test for anti-estrogenic effects.; High	Dow Corning, 2009 9651848

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Guideline and Animal Species, Strain, Sex	Exposure Route and Exposure Duration	Study-wide POD and Dose/ Concentration(s)	Summary	Major Limitations	Principal Target Organs/Systems and OQD*	HERO ID

* Overall Quality Determination

[1] 9651848: In a uterotrophic assay, groups of ovariectomized Crl:CD(SD)IGS BR (Sprague-Dawley) rats (6/group) were administered dimethylsilanediol (DMSD) (purity 99.3%) in corn oil at 0 (vehicle control), 60 or 1,200 mg/kg-day (part 1) or 1,000 mg/kg-day (part 2), via gavage, for three consecutive days; these animals also received subcutaneous injections of corn oil plus 10% ethanol (the vehicle for the positive controls). Positive controls received oral doses of corn oil and were subcutaneously administered ethynyl estradiol (EE) at 0.3, 1.0, or 3.0 ug/kg-day or genistein at 10, 25, or 50 mg/kg-day. Other groups of animals were co-administered DMSD at 1,200 mg/kg-day and 3.0 ug/kg-day EE to test for antiestrogenic activity or were co-administered the estrogen receptor antagonist ICI 182,780 (3 mg/kg-day) and EE (3.0 ug/kg-day) as a positive control. The assay was conducted in two separate parts or experiments. Part 1 included: vehicle control, DMSD (600 and 1,000 mg/kg-day), EE (all doses), genistein (all doses), D4 + EE, and ICI + EE. Part 2 included: vehicle control, DMSD (1,000 mg/kg-day), EE (0.3 ug/kg-day).Animals were observed for mortality and clinical signs of toxicity twice daily. Body weights were measured daily and animals were sacrificed 24 hours after the last dose. Uteri were removed; wet and dry weights were recorded and the uterine weight change was calculated. No animals died. One animal in the 1,000 mg/kg-day group showed urogenital soiling and one in the 1,200 mg/kg-day group showed red soiling around the oral cavity, both occurring on day 3. 4/6 animals in the DMSD + EE group showed soiling around the nose, oral cavity, and urogenital regions, and one animal in this group showed decreased activity and an uncoordinated gait. No effects on terminal body weights were observed. The EE-positive controls tested valid. The Genistein control groups administered 10 or 25 mg/kg-day were also valid; however, animals administered 50 mg/kg-day genistein did not show the expected changes in uterine weight. The reason for the lack of change is unknown. DMSD treatment resulted in statistically significant increases in absolute and relative uterine weights (wet and blotted) and uterine weight changes (wet minus blotted) at $\geq$1,000 mg/kg-day, relative to controls. No uterine weight changes were observed in animals dosed with DMSD alone at 600 mg/kg-day. In the co-administered groups, DMSD failed to decrease the uterine weight changes caused by EE alone, indicating no antiestrogenic effects. The control animals (co-administered ICI 182,780 and EE) showed the expected response. Overall, the data indicate that the test material was positive for a uterotrophic response. The results were consistent between both experimental parts described.

[2] 9651848: In a uterotrophic assay, groups of ovariectomized Crl:CD(SD)IGS BR (Sprague-Dawley) rats (6/group) were administered dimethylsilanediol (DMSD) (purity 99.3%) in corn oil at 0 (vehicle control), 60or 1,200 mg/kg-day (part 1) or 1,000 mg/kg-day (part 2), via gavage, for three consecutive days; these animals also received subcutaneous injections of corn oil plus 10% ethanol (the vehicle for the positive controls). Positive controls received oral doses of corn oil and were subcutaneously administered ethynyl estradiol (EE) at 0.3, 1.0, or 3.0 ug/kg-day or genistein at 10, 25, or 50 mg/kg-day. Other groups of animals were co-administered DMSD at 1,200 mg/kg-day and 3.0 ug/kg-day EE to test for antiestrogenic activity or were co-administered the estrogen receptor antagonist ICI 182,780 (3 mg/kg-day) and EE (3.0 ug/kg-day) as a positive control. The assay was conducted in two separate parts or experiments. Part 1 included: vehicle control, DMSD (600 and 1,000 mg/kg-day), EE (all doses), genistein (all doses), D4 + EE, and ICI + EE. Part 2 included: vehicle control, DMSD (1,000 mg/kg-day), EE (0.3 ug/kg-day).Animals were observed for mortality and clinical signs of toxicity twice daily. Body weights were measured daily and animals were sacrificed 24 hours after the last dose. Uteri were removed; wet and dry weights were recorded and the uterine weight change was calculated.No animals died. One animal in the 1,000 mg/kg-day group showed urogenital soiling and one in the 1,200 mg/kg-day group showed red soiling around the oral cavity, both occurring on day 3. 4/6 animals in the DMSD + EE group showed soiling around the nose, oral cavity, and urogenital regions, and one animal in this group showed decreased activity and an uncoordinated gait. No effects on terminal body weights were observed. The EE-positive controls tested valid. The Genistein control groups administered 10 or 25 mg/kg-day were also valid; however, animals administered 50 mg/kg-day genistein did not show the expected changes in uterine weight. The reason for the lack of change is unknown. DMSD treatment resulted in statistically significant increases in absolute and relative uterine weights (wet and blotted) and uterine weight changes (wet minus blotted) at $\geq$1,000 mg/kg-day, relative to controls. No uterine weight changes were observed in animals dosed with DMSD alone at 600 mg/kg-day. In the co-administered groups, DMSD failed to decrease the uterine weight changes caused by EE alone, indicating no antiestrogenic effects. The control animals (co-administered ICI 182,780 and EE) showed the expected response. Overall, the data indicate that the test material was positive for a uterotrophic response. The results were consistent between both experimental parts described.

Octamethylcyclotetrasiloxane (D4)- Metabolite: Dimethylsilanediol (DMSD) - Reproductive/Developmental

Guideline and Animal Species, Strain, Sex	Exposure Route and Exposure Duration	Study-wide POD and Dose/ Concentration(s)	Summary	Major Limitations	Principal Target Organs/Systems and OQD*	HERO ID
The study was conducted according to OECD TG 422 and EPA OPPTS 870.6200. The study was GLP compliant. Rat-Other (CRl:CD (SD) IGS BR VAF/Plus)-Both	Oral-Gavage-Duration: Reproductive/Developmental-1-F0- premating (2-weeks)-F0- mating (up to 2-weeks)-F0 - gestation (21 days)-F0- lactation (3 days)-F0- premating (2-weeks)-F0- mating (up to 2-weeks) Animals in the reproductive group were dosed from 2 weeks prior to mating, through mating for a total of 29 days (males) or through gestation to post-partum day 3 (females)	**POD: 250 mg/kg-bw/day (NOAEL) -Liver protoporphyrinosis in males** n= 20 Dose= 0, n= 20 Dose= 50, n= 20 Dose= 250, n= 20 Dose= 500, mg/kg-bw/dayTotal # of generations: 1 Male Exposure: F0- premating, 2-weeks, F0- mating, up to 2-weeks Female Exposure: F0- premating, 2-weeks, F0- mating, up to 2-weeks, F0 - gestation, 21 days, F0- lactation, 3 days	See footnotes for full summary [1]	No major limitations were identified. There were slight deviations from the OECD TG 422 guideline: The study did not assess thyroid hormones in males or in pups and an unmated satellite group of males was not included.	Reproductive/Developmental; Systemic: organ weights (testes, seminal vesicles, prostate, epididymides, ovaries, uterus), gross necropsy, histopathology. Reproductive: mating and fertility indices, duration of gestation, number of corpora lutea and implantation sites. Developmental: number and sex of pups, number of live and dead pups, number of runts, presence of gross abnormalities at birth, litter weights on PND 1 and 4, observations for abnormal behaviors, external gross abnormalities-Immune/Hematological-hematology, organ weights (spleen, thymus), gross pathology, histopathology (spleen, thymus, lymph nodes)-Hepatic/Liver-serum chemistry (glucose, albumin, ALT, ALP, AST, cholesterol, total bilirubin, total protein), gross necropsy; histopathology-Thyroid-Histopathology (thyroid); High	Dow Corning, 2009 9652986

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Octamethylcyclotetrasiloxane (D4)- Metabolite: Dimethylsilanediol (DMSD) - Reproductive/Developmental

Guideline and Animal Species, Strain, Sex	Exposure Route and Exposure Duration	Study-wide POD and Dose/ Concentration(s)	Summary	Major Limitations	Principal Target Organs/Systems and OQD*	HERO ID
The study was conducted according to OECD TG 422 and EPA OPPTS 870.6200. The study was GLP compliant. Rat-Other (CRl:CD (SD) IGS BR VAF/Plus)-Both	Oral-Gavage-Duration: Short-term (>1-30 days)-7-29-day(s) Animals in the reproductive group were dosed from 2 weeks prior to mating, through mating for a total of 29 days (males) or through gestation to post-partum day 3 (females)	**POD: 250 mg/kg-bw/day (NOAEL) -Hepatocellular vacuolation in females** n= 10 Dose= 0, n= 10 Dose= 50, n= 10 Dose= 250, n= 10 Dose= 500, mg/kg-bw/dayTotal # of generations: 1 Male Exposure: F0- premating, 2-weeks, F0- mating, up to 2-weeks Female Exposure: F0- premating, 2-weeks, F0- mating, up to 2-weeks, F0 - gestation, 21 days, F0- lactation, 3 days	See footnotes for full summary [2]	No major limitations were identified. There were slight deviations from the OECD TG 422 guideline: The study did not include an unmated satellite group of males.	Hepatic/Liver-serum chemistry (glucose, albumin, ALT, ALP, AST, cholesterol, total bilirubin, total protein), gross necropsy; histopathology; High	Dow Corning, 2009 9652986

* Overall Quality Determination

[1] 9652986: In a combined repeated dose toxicity study with a reproductive/developmental screening text, groups of CRl:CD (SD) IGS BR VAF/Plus rats (10 male and 10 females/group) were administered dimethyldilanediol (DMSD) (purity 97.8%) daily, via gavage, at 0, 50, 250, and 500 mg/kg-day from two weeks prior to mating, through mating for 28 days (males) or through gestation to post-partum day 3 (females). An additional 10 females were included that were left unmated; these females were dosed for 29 days and used to assess systemic toxicity endpoints. The complete study is summarized here; however, this form is focused on the reproductive groups (mated males and females).All animals were monitored for mortality, morbidity, and moribundity. General clinical observations were conducted daily and detailed physical examinations were conducted weekly. Body weights were recorded weekly and at termination, during GDs 0, 7, 14, and 20, and post-partum day 4. Other systemic endpoints evaluated in males and in the10 toxicity group females included hematology and clinical chemistry, select organ weights (including reproductive organs), gross necropsy, and histopathology. Baseline FOB and motor activity evaluations were conducted prior to dosing and again during the 4th week of dosing. Reproductive endpoints included mating and fertility indices, gestation length, and numbers of corpora lutea and implantations. Developmental endpoints included litter size, litter weights, ratio of live births/litter size, sex ratio, post-implantation loss, post-natal loss, and pup body weights on PND 1 and 4. Offspring were examined externally for gross abnormalities. No adult animals were found dead during the study. One animal was euthanized due to a gavage error. Significant clinical signs included incidences of soiling in the muzzle region at 500 mg/kg-day and in the abdominal and urogenital region at $\geq$250 mg/kg-day in males. In the toxicity group females, soiling of the muzzle was significant at 500 mg/kg-day, and in mated females, incidences of both abdominal and urogenital soiling were significant at 500 mg/kg-day. No effects on body weights were observed; however, body weight gain was significantly reduced in males during week 4 and overall (days 1-29) and in the toxicity group females during week 3. These changes occurred in the absence of any differences in food consumption. No treatment-related FOB or motor activity effects were observed. Hematological changes included decreased hemoglobin, MCH, and hematocrit levels in high-dose males; the MCH and hematocrit values fell below the historical range. High-dose females also showed significant decreases in MCH and hemoglobin, but the values were within historical control ranges. No changes in RBC levels were observed. Significant changes in prothrombin time were observed in mid- and high-dose males and females, but the change was directionally inconsistent (increased in males and decreased in females). Male rats showed increases in serum ALT, total protein, and BUN at 500 mg/kg-day. ALT was also increased in high-dose females along with total cholesterol. Other observed serum chemistry changes (e.g., decreased AST, ALP, and bilirubin) were not considered to be toxicologically significant. The study authors noted that most changes fell within historical control ranges and did not correlate with a pathological outcome. Notable organ weight changes included dose-related increases in absolute and relative liver weights in both males and females that were significant at $\geq$250 mg/kg-day. Absolute liver weights were increased 19-31% in males and 24-61% in females, and relative liver weights were increased 22-41% in males and 25-65% in females, compared with controls. Males also showed significant dose-related decreases in absolute and relative thymus and adrenal weights, and in absolute testes weights, all significant at 500 mg/kg-day. The liver weight changes correlated with mottled discoloration and liver enlargement in both sexes at necropsy. Microscopic analysis showed increased incidences of hypertrophy at $\geq$250 mg/kg-day in both sexes, and increased incidences of inflammation, hyperplasia in the bile duct, and protoporphyrinosis in males, and in hepatocellular vacuolation in females at 500 mg/kg-day. These incidences also increased in severity with dose. Mid-and high-dose male rats also showed small, discolored thymuses and a tendency towards lung discoloration at necropsy. There was an increasing trend in incidences of lung histiocytosis in males, but no histopathology was observed in the thymus. Follicular hypertrophy of the thyroid increased in incidence and severity with dose in males and was significant at $\geq$250 mg/kg-day. There was also evidence of chronic inflammation in the prostates of high-dose males. Three females, one each in the control, 50, and 250 mg/kg-day groups, did not become pregnant. The authors reported no significant treatment-related effects for any of the reproductive or developmental endpoints using pair-wise comparisons or after adjusting for litter size. Author reported toxicity values included a systemic NOAEL of 250 mg/kg-day and a LOAEL of 500 mg/kg-day for liver protoporphyrinosis in males (this form) and vacuolation in females (separate form). The authors considered the effects observed at 250 mg/kg-day (e.g., organ weight changes, and liver, thyroid, and thymus hypertrophy,) to be adaptive in nature and not adverse, or not applicable to other species (thyroid). However, a more conservative NOAEL of 50 mg/kg-day should be considered based on clearly significant and biologically relevant dose-related changes, and increasing severity of histopathological lesions.A reproductive and developmental NOAEL of 500 mg/kg-day, the highest dose, was determined based on the lack of adverse reproductive or developmental effects.

[2] 9652986: In a combined repeated dose toxicity study with a reproductive/developmental screening text, groups of CRl:CD (SD) IGS BR VAF/Plus rats (10 male and 10 females/group) were administered dimethyldilanediol (DMSD) (purity 97.8%) daily, via gavage, at 0, 50, 250, and 500 mg/kg-day from two weeks prior to mating, through mating for 28 days (males) or through gestation to post-partum day 3 (females). An additional 10 females were included that were left unmated; these females were dosed for 29 days and used to assess systemic toxicity endpoints (this form). The complete study is described below, but this form is focused on unmated females. All animals were monitored for mortality, morbidity, and moribundity. General clinical observations were conducted daily and detailed physical examinations were conducted weekly. Body weights were recorded weekly and at termination. Other systemic endpoints evaluated in males and the 10 toxicity group females included hematology and clinical chemistry, selected organ weights (including reproductive organs), gross necropsy, and histopathology. Baseline FOB and motor activity evaluations were conducted prior to dosing and again during the 4th week of dosing. No adult animals were found dead during the study. One animal was euthanized due to a gavage error. Significant clinical signs included incidences of soiling in the muzzle region at 500 mg/kg-day and in the abdominal and urogenital region at ≥250 mg/kg-day in males. In the toxicity group females, soiling of the muzzle was significant at 500 mg/kg-day. In mated females, incidences of both abdominal and urogenital soiling were significant at 500 mg/kg-day. No effects on body weights were observed; however, body weight gain was significantly reduced in males during week 4 and overall (days 1-29) and in the toxicity group females during week 3. These changes occurred in the absence of any differences in food consumption. No treatment-related FOB or motor activity effects were observed. Hematological changes included decreased hemoglobin, MCH, and hematocrit levels in high-dose males; the MCH and hematocrit values fell below the historical range. High-dose toxicity group females also showed significant decreases in MCH and hemoglobin, but the values were within historical control ranges. No changes in RBC levels were observed. Significant changes in prothrombin time were observed in mid- and high-dose males and females, but the change was directionally inconsistent (increased in males and decreased in females). Male rats showed increases in serum ALT, total protein, and BUN at 500 mg/kg-day. ALT was also increased in high-dose females along with total cholesterol. Other observed serum chemistry changes (e.g., decreased AST, ALP, and bilirubin) were not considered to be toxicologically significant. The study authors noted that most changes fell within historical control ranges and did not correlate with a pathological outcome. Notable organ weight changes included dose-related increases in absolute and relative liver weights in both males and toxicity group females that were significant at ≥250 mg/kg-day. Absolute liver weights were increased 19-31% in males and 24-61% in females, and relative liver weights were increased 22-41% in males and 25-65% in females, compared with controls. Males also showed significant dose-related decreases in absolute and relative thymus and adrenal weights, and in absolute testes weights, all significant at 500 mg/kg-day. The liver weight changes correlated with mottled discoloration and liver enlargement in both sexes at necropsy. Microscopic analysis showed increased incidences of hypertrophy at ≥250 mg/kg-day in both sexes, and increased incidences of inflammation, hyperplasia in the bile duct, and protoporphyrinosis in males, and in hepatocellular vacuolation in females at 500 mg/kg-day. These incidences also increased in severity with dose. Mid-and high-dose male rats also showed small, discolored thymuses and a tendency towards lung discoloration at necropsy. There was an increasing trend in incidences of lung histiocytosis in males, but no histopathology was observed in the thymus. Follicular hypertrophy of the thyroid increased in incidence and severity with dose in males and was significant at ≥250 mg/kg-day. There was also evidence of chronic inflammation in the prostates of high-dose males. The author reported systemic NOAEL was 250 mg/kg-day and LOAEL was 500 mg/kg-day for liver protoporphyrinosis in males (other form) and vacuolation in females (this form). The authors considered the effects observed at 250 mg/kg-day (e.g., organ weight changes, and liver, thyroid, and thymus hypertrophy,) to be adaptive in nature and not adverse, or not applicable to other species (thyroid). However, a more conservative NOAEL of 50 mg/kg-day should be considered based on clearly significant and biologically relevant dose-related changes, and increasing severity of histopathological lesions.

Human Health Hazard Epidemiology Extraction Table:

Author Reported Outcome	Measured Effect/ Endpoints	Study Population	Exposure	Method	Results	Citation, HERO ID, and OQD*
AST	Health Effect: Hepatic/Liver-ALT, AST-Non-cancer. Outcome measure: Laboratory blood test	General public. Adults (18+). United States; Rochester, NY. Female, Male. Randomized Controlled Trial. PESS: . 12 non-smoking adult participants (n=8 males, n=4 females). NR.	Direct administration Exposure Route: Inhalation Acute (less than 24 hours) Exposure measured prior to the outcome.	Not specified. Confounders adjusted for: NR.	Lowest exposure concentration for a significant adverse health outcome response: 10 ppm. NR. ”AST was slightly higher with air exposure than with D4 exposure. Statistical analysis indicated that the difference between the two exposures may have been unrelated to the exposure itself.”.	University of Rochester, 1997 5887568 Medium