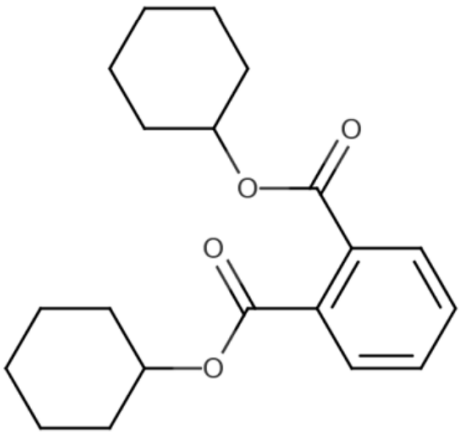
United States
Environmental Protection Agency

December 2024
Office of Chemical Safety and
Pollution Prevention

Draft Data Extraction Information for Environmental Hazard and Human Health Hazard Animal Toxicology and Epidemiology for Dicyclohexyl Phthalate (DCHP) (1,2- Benzenedicarboxylic acid, 1,2-dicyclohexyl ester)

Systematic Review Support Document for the Draft Risk Evaluation

CASRN: 84-61-7



December 2024

This supplemental file contains information regarding the data extraction results relevant to the *Draft Environmental Hazard Assessment for Dicyclohexyl Phthalate (DCHP)* and the *Draft Human Health Hazard Assessment for Dicyclohexyl Phthalate (DCHP)*. 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 Dicyclohexyl Phthalate (DCHP) – 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 DCHP, toxicity data gaps were identified for mammalian wildlife relevant to the terrestrial compartment of the environmental hazard assessment. This table includes rodent data for DCHP, 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 Dicyclohexyl Phthalate (DCHP) – 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: The criteria for extracting data from epidemiology references were that the reference met PECO screening criteria and further filtering criteria, and had an overall quality determination of High, Medium, or Low, and found statistically significant results. No epidemiology references met all of these criteria. Therefore, epidemiology data are not included in these tables.

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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
84-61-7	8-11 Day(s), (21 Day(s))	*Daphnia magna* (Water Flea), Young, <24 Hour(s), Not Reported, Laboratory (NATIONAL INSTITUTE FOR ENVIRONMENTAL STUDIES)	Fresh water, Aqueous (aquatic habitat), Renewal, Not Reported	Measured	<0.007-<0.008 mg/L / <0.007-<0.008 mg/L / 0.018 (0.015-0.020) mg/L / 0.058 (0.055-0.062) mg/L / 0.181 (0.141-0.211) mg/L / 0.572 (0.504-0.609) mg/L / 1.90 (1.58-2.02) mg/L	Reproduction (Reproduction-Time to first progeny, Response Site: Not reported)	NR (0.015-2.02 mg/L)	Reproductive/Teratogenic	High	11803962
84-61-7	21 Day(s), (21 Day(s))	*Daphnia magna* (Water Flea), Young, <24 Hour(s), Not Reported, Laboratory (NATIONAL INSTITUTE FOR ENVIRONMENTAL STUDIES)	Fresh water, Aqueous (aquatic habitat), Renewal, Not Reported	Measured	<0.007-<0.008 mg/L / <0.007-<0.008 mg/L / 0.018 (0.015-0.020) mg/L / 0.058 (0.055-0.062) mg/L / 0.181 (0.141-0.211) mg/L / 0.572 (0.504-0.609) mg/L / 1.90 (1.58-2.02) mg/L	Mortality (Mortality-Mortality, Response Site: Not reported)	NR-LETH (1.90 (1.58-2.02) mg/L)	Mortality	Medium	11803962
84-61-7	21 Day(s), (21 Day(s))	*Daphnia magna* (Water Flea), Young, <24 Hour(s), Not Reported, Laboratory (NATIONAL INSTITUTE FOR ENVIRONMENTAL STUDIES)	Fresh water, Aqueous (aquatic habitat), Renewal, Not Reported	Measured	<0.007-<0.008 mg/L / <0.007-<0.008 mg/L / 0.018 (0.015-0.020) mg/L / 0.058 (0.055-0.062) mg/L / 0.181 (0.141-0.211) mg/L / 0.572 (0.504-0.609) mg/L / 1.90 (1.58-2.02) mg/L	Reproduction (Reproduction-Progeny counts/numbers, Response Site: Not reported)	NOEC (0.181 (0.141-0.211) mg/L)	Reproductive/Teratogenic	High	11803962

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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
84-61-7	21 Day(s), (21 Day(s))	*Daphnia magna* (Water Flea), Young, <24 Hour(s), Not Reported, Laboratory (NATIONAL INSTITUTE FOR ENVIRONMENTAL STUDIES)	Fresh water, Aqueous (aquatic habitat), Renewal, Not Reported	Measured	<0.007-<0.008 mg/L / <0.007-<0.008 mg/L / 0.018 (0.015-0.020) mg/L / 0.058 (0.055-0.062) mg/L / 0.181 (0.141-0.211) mg/L / 0.572 (0.504-0.609) mg/L / 1.90 (1.58-2.02) mg/L	Reproduction (Reproduction-Progeny counts/numbers, Response Site: Not reported)	LOEC (0.572 (0.504-0.609) mg/L)	Reproductive/Teratogenic	High	11803962
84-61-7	21 Day(s), (21 Day(s))	*Daphnia magna* (Water Flea), Young, <24 Hour(s), Not Reported, Laboratory (NATIONAL INSTITUTE FOR ENVIRONMENTAL STUDIES)	Fresh water, Aqueous (aquatic habitat), Renewal, Not Reported	Measured	<0.007-<0.008 mg/L / <0.007-<0.008 mg/L / 0.018 (0.015-0.020) mg/L / 0.058 (0.055-0.062) mg/L / 0.181 (0.141-0.211) mg/L / 0.572 (0.504-0.609) mg/L / 1.90 (1.58-2.02) mg/L	Mortality (Mortality-Mortality, Response Site: Not reported)	LC50 (1.04 (0.572-1.90) mg/L)	Mortality	Medium	11803962
84-61-7	21 Day(s), (21 Day(s))	*Daphnia magna* (Water Flea), Young, <24 Hour(s), Not Reported, Laboratory (NATIONAL INSTITUTE FOR ENVIRONMENTAL STUDIES)	Fresh water, Aqueous (aquatic habitat), Renewal, Not Reported	Measured	<0.007-<0.008 mg/L / <0.007-<0.008 mg/L / 0.018 (0.015-0.020) mg/L / 0.058 (0.055-0.062) mg/L / 0.181 (0.141-0.211) mg/L / 0.572 (0.504-0.609) mg/L / 1.90 (1.58-2.02) mg/L	Reproduction (Reproduction-Progeny counts/numbers, Response Site: Not reported)	EC50 (0.679 mg/L)	Reproductive/Teratogenic	High	11803962

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84-61-7	24 Hour(s), (48 Hour(s))	*Daphnia magna* (Water Flea), Young, <24 Hour(s), Not Reported, Laboratory (NATIONAL INSTITUTE FOR ENVIRONMENTAL STUDIES)	Fresh water, Aqueous (aquatic habitat), Static, Not Reported	Measured	<0.007 mg/L / <0.007 mg/L / 2.02 (1.99-2.05) mg/L	Physiology (Intoxication-Immobile, Response Site: Not reported)	LOEC (>2.02 (1.99-2.05) mg/L)	Immobilization	Medium	11803964
84-61-7	24 Hour(s), (48 Hour(s))	*Daphnia magna* (Water Flea), Young, <24 Hour(s), Not Reported, Laboratory (NATIONAL INSTITUTE FOR ENVIRONMENTAL STUDIES)	Fresh water, Aqueous (aquatic habitat), Static, Not Reported	Measured	<0.007 mg/L / <0.007 mg/L / 2.02 (1.99-2.05) mg/L	Physiology (Intoxication-Immobile, Response Site: Not reported)	EC50 (>2.02 (1.99-2.05) mg/L)	Immobilization	Medium	11803964
84-61-7	24 Hour(s), (48 Hour(s))	*Daphnia magna* (Water Flea), Young, <24 Hour(s), Not Reported, Laboratory (NATIONAL INSTITUTE FOR ENVIRONMENTAL STUDIES)	Fresh water, Aqueous (aquatic habitat), Static, Not Reported	Measured	<0.007 mg/L / <0.007 mg/L / 2.02 (1.99-2.05) mg/L	Physiology (Intoxication-Immobile, Response Site: Not reported)	NOEC (>=2.02 (1.99-2.05) mg/L)	Immobilization	Medium	11803964
84-61-7	48 Hour(s), (48 Hour(s))	*Daphnia magna* (Water Flea), Young, <24 Hour(s), Not Reported, Laboratory (NATIONAL INSTITUTE FOR ENVIRONMENTAL STUDIES)	Fresh water, Aqueous (aquatic habitat), Static, Not Reported	Measured	<0.007 mg/L / <0.007 mg/L / 2.02 (1.99-2.05) mg/L	Physiology (Intoxication-Immobile, Response Site: Not reported)	NOEC (>=2.02 (1.99-2.05) mg/L)	Immobilization	Medium	11803964

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84-61-7	48 Hour(s), (48 Hour(s))	*Daphnia magna* (Water Flea), Young, <24 Hour(s), Not Reported, Laboratory (NATIONAL INSTITUTE FOR ENVIRONMENTAL STUDIES)	Fresh water, Aqueous (aquatic habitat), Static, Not Reported	Measured	<0.007 mg/L / <0.007 mg/L / 2.02 (1.99-2.05) mg/L	Physiology (Intoxication-Immobile, Response Site: Not reported)	LOEC (>2.02 (1.99-2.05) mg/L)	Immobilization	Medium	11803964
84-61-7	48 Hour(s), (48 Hour(s))	*Daphnia magna* (Water Flea), Young, <24 Hour(s), Not Reported, Laboratory (NATIONAL INSTITUTE FOR ENVIRONMENTAL STUDIES)	Fresh water, Aqueous (aquatic habitat), Static, Not Reported	Measured	<0.007 mg/L / <0.007 mg/L / 2.02 (1.99-2.05) mg/L	Physiology (Intoxication-Immobile, Response Site: Not reported)	EC50 (>2.02 (1.99-2.05) mg/L)	Immobilization	Medium	11803964
84-61-7	24-48 Hour(s), (48 Hour(s))	*Daphnia magna* (Water Flea), Not reported, Not Reported, Not reported (NR)	Fresh water, Aqueous (aquatic habitat), Not reported, Not Reported	Unmeasured	0 mg/L / 0 mg/L / 0.200 mg/L / 0.600 mg/L / 2.00 mg/L	Physiology (Intoxication-Immobile, Response Site: Not reported)	NR (0.200-2.00 mg/L)	Immobilization	Medium	11803964
84-61-7	40 Minute(s), (40 Minute(s))	*Macrobrachium rosenbergii* (Giant River Prawn), Not intact, Not Reported, Laboratory (LOCAL PRAWN FARM)	Culture, In Vitro, In Vitro, Not Reported	Unmeasured	0 ug/ml / 100 ug/ml	Cellular (Genetics-Apoptosis, Response Site: Hemocyte)	NOEC (100 ug/ml)	Mechanistic: Cell signaling/function	Medium	789598
84-61-7	40 Minute(s), (40 Minute(s))	*Macrobrachium rosenbergii* (Giant River Prawn), Not intact, Not Reported, Laboratory (LOCAL PRAWN FARM)	Culture, In Vitro, In Vitro, Not Reported	Unmeasured	0 ug/ml / 100 ug/ml	Cellular (Histology-Necrosis, Response Site: Hemocyte)	LOEC (100 ug/ml)	Mechanistic: Cell signaling/function	Medium	789598
84-61-7	10 Minute(s), (40 Minute(s))	*Macrobrachium rosenbergii* (Giant River Prawn), Not intact, Not Reported, Laboratory (LOCAL PRAWN FARM)	Culture, In Vitro, In Vitro, Not Reported	Unmeasured	0 ug/ml / 100 ug/ml	Cellular (Histology-Necrosis, Response Site: Hemocyte)	NOEC (100 ug/ml)	Mechanistic: Cell signaling/function	Medium	789598

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84-61-7	10 Minute(s), (40 Minute(s))	*Macrobrachium rosenbergii* (Giant River Prawn), Not intact, Not Reported, Laboratory (LOCAL PRAWN FARM)	Culture, In Vitro, In Vitro, Not Reported	Unmeasured	0 ug/ml / 100 ug/ml	Cellular (Genetics-Apoptosis, Response Site: Hemocyte)	NOEC (100 ug/ml)	Mechanistic: Cell signaling/function	Medium	789598
84-61-7	10 Minute(s), (10 Minute(s))	*Macrobrachium rosenbergii* (Giant River Prawn), Not intact, Not Reported, Laboratory (LOCAL PRAWN FARM)	Culture, In Vitro, In Vitro, Not Reported	Unmeasured	0 ug/ml / 100 ug/ml	Cellular (Cell(s)-Aggregation/adhesion, Response Site: Hemocyte)	NOEC (100 ug/ml)	Mechanistic: Cell signaling/function	Medium	789598
84-61-7	10 Minute(s), (10 Minute(s))	*Macrobrachium rosenbergii* (Giant River Prawn), Not intact, Not Reported, Laboratory (LOCAL PRAWN FARM)	Culture, In Vitro, In Vitro, Not Reported	Unmeasured	0 ug/ml / 100 ug/ml	Biochemical (Enzyme(s)-Phenoloxidase, Response Site: Hemocyte)	NOEC (100 ug/ml)	Mechanistic: Cell signaling/function	Medium	789598
84-61-7	40 Minute(s), (40 Minute(s))	*Macrobrachium rosenbergii* (Giant River Prawn), Not intact, Not Reported, Laboratory (LOCAL PRAWN FARM)	Culture, In Vitro, In Vitro, Not Reported	Unmeasured	0 ug/ml / 100 ug/ml	Cellular (Histology-Necrosis, Response Site: Hemocyte)	LOEC (100 ug/ml)	Mechanistic: Cell signaling/function	Medium	789598
84-61-7	40 Minute(s), (40 Minute(s))	*Macrobrachium rosenbergii* (Giant River Prawn), Not intact, Not Reported, Laboratory (LOCAL PRAWN FARM)	Culture, In Vitro, In Vitro, Not Reported	Unmeasured	0 ug/ml / 100 ug/ml	Cellular (Genetics-Apoptosis, Response Site: Hemocyte)	NOEC (100 ug/ml)	Mechanistic: Cell signaling/function	Medium	789598
84-61-7	10 Minute(s), (10 Minute(s))	*Macrobrachium rosenbergii* (Giant River Prawn), Not intact, Not Reported, Laboratory (LOCAL PRAWN FARM)	Culture, In Vitro, In Vitro, Not Reported	Unmeasured	0 ug/ml / 100 ug/ml	Physiology (Physiology-Superoxide generation, Response Site: Hemocyte)	NOEC (100 ug/ml)	Mechanistic: Cell signaling/function	Medium	789598

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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
84-61-7	10 Minute(s), (10 Minute(s))	*Macrobrachium rosenbergii* (Giant River Prawn), Not intact, Not Reported, Laboratory (LOCAL PRAWN FARM)	Culture, In Vitro, In Vitro, Not Reported	Unmeasured	0 ug/ml / 100 ug/ml	Physiology (Immunological-Pseudopodia formation, Response Site: Hemocyte)	NOEC (100 ug/ml)	Mechanistic: Cell signaling/function	Medium	789598
84-61-7	10 Minute(s), (40 Minute(s))	*Macrobrachium rosenbergii* (Giant River Prawn), Not intact, Not Reported, Laboratory (LOCAL PRAWN FARM)	Culture, In Vitro, In Vitro, Not Reported	Unmeasured	0 ug/ml / 100 ug/ml	Cellular (Histology-Necrosis, Response Site: Hemocyte)	NOEC (100 ug/ml)	Mechanistic: Cell signaling/function	Medium	789598
84-61-7	10 Minute(s), (40 Minute(s))	*Macrobrachium rosenbergii* (Giant River Prawn), Not intact, Not Reported, Laboratory (LOCAL PRAWN FARM)	Culture, In Vitro, In Vitro, Not Reported	Unmeasured	0 ug/ml / 100 ug/ml	Cellular (Genetics-Apoptosis, Response Site: Hemocyte)	NOEC (100 ug/ml)	Mechanistic: Cell signaling/function	Medium	789598
84-61-7	10 Minute(s), (10 Minute(s))	*Macrobrachium rosenbergii* (Giant River Prawn), Not intact, Not Reported, Laboratory (LOCAL PRAWN FARM)	Culture, In Vitro, In Vitro, Not Reported	Unmeasured	0 ug/ml / 100 ug/ml	Cellular (Cell(s)-Aggregation/adhesion, Response Site: Hemocyte)	NOEC (100 ug/ml)	Mechanistic: Cell signaling/function	Medium	789598
84-61-7	10 Minute(s), (10 Minute(s))	*Macrobrachium rosenbergii* (Giant River Prawn), Not intact, Not Reported, Laboratory (LOCAL PRAWN FARM)	Culture, In Vitro, In Vitro, Not Reported	Unmeasured	0 ug/ml / 100 ug/ml	Biochemical (Enzyme(s)-Phenoloxidase, Response Site: Hemocyte)	NOEC (100 ug/ml)	Mechanistic: Cell signaling/function	Medium	789598
84-61-7	10 Minute(s), (10 Minute(s))	*Macrobrachium rosenbergii* (Giant River Prawn), Not intact, Not Reported, Laboratory (LOCAL PRAWN FARM)	Culture, In Vitro, In Vitro, Not Reported	Unmeasured	0 ug/ml / 100 ug/ml	Physiology (Immunological-Pseudopodia formation, Response Site: Hemocyte)	NOEC (100 ug/ml)	Mechanistic: Cell signaling/function	Medium	789598

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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
84-61-7	10 Minute(s), (10 Minute(s))	*Macrobrachium rosenbergii* (Giant River Prawn), Not intact, Not Reported, Laboratory (LOCAL PRAWN FARM)	Culture, In Vitro, In Vitro, Not Reported	Unmeasured	0 ug/ml / 100 ug/ml	Physiology (Physiology-Superoxide generation, Response Site: Hemocyte)	NOEC (100 ug/ml)	Mechanistic: Cell signaling/function	Medium	789598

* 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: Amphibian 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
84-61-7	72 Hour(s), (72 Hour(s))	*Xenopus tropicalis* (Clawed Frog), Larva, 11-12 Nieuwkoop-faber-stage, Not Reported, Laboratory	Culture, Aqueous (aquatic habitat), Renewal, Not Reported	Measured	0 mg/L / 0 mg/L / 0.3 mg/L / 1.5 mg/L / 4.1 mg/L / 19.0 mg/L / 99.3 mg/L	Cellular (Genetics-Steroidogenic Acute Regulatory protein mRNA, Response Site: Whole organism)	LOEC (1.5 mg/L)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function	High	3230411
84-61-7	72 Hour(s), (72 Hour(s))	*Xenopus tropicalis* (Clawed Frog), Larva, 11-12 Nieuwkoop-faber-stage, Not Reported, Laboratory	Culture, Aqueous (aquatic habitat), Renewal, Not Reported	Measured	0 mg/L / 0 mg/L / 0.3 mg/L / 1.5 mg/L / 4.1 mg/L / 19.0 mg/L / 99.3 mg/L	Cellular (Genetics-Type I iodothyronine deiodinase mRNA, Response Site: Whole organism)	LOEC (1.5 mg/L)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function	High	3230411
84-61-7	72 Hour(s), (72 Hour(s))	*Xenopus tropicalis* (Clawed Frog), Larva, 11-12 Nieuwkoop-faber-stage, Not Reported, Laboratory	Culture, Aqueous (aquatic habitat), Renewal, 150 Organism	Measured	0 mg/L / 0 mg/L / 0.3 mg/L / 1.5 mg/L / 4.1 mg/L / 19.0 mg/L / 99.3 mg/L	Cellular (Histology-Edema, Response Site: Whole organism)	LOEC (1.5 mg/L)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function	High	3230411
84-61-7	72 Hour(s), (72 Hour(s))	*Xenopus tropicalis* (Clawed Frog), Larva, 11-12 Nieuwkoop-faber-stage, Not Reported, Laboratory	Culture, Aqueous (aquatic habitat), Renewal, 150 Organism	Measured	0 mg/L / 0 mg/L / 0.3 mg/L / 1.5 mg/L / 4.1 mg/L / 19.0 mg/L / 99.3 mg/L	Growth (Morphology-Abnormal, Response Site: Tail)	LOEC (1.5 mg/L)	Development/Growth	High	3230411
84-61-7	72 Hour(s), (72 Hour(s))	*Xenopus tropicalis* (Clawed Frog), Larva, 11-12 Nieuwkoop-faber-stage, Not Reported, Laboratory	Culture, Aqueous (aquatic habitat), Renewal, 17 Organism	Measured	0 mg/L / 0 mg/L / 0.3 mg/L / 1.5 mg/L / 4.1 mg/L / 19.0 mg/L / 99.3 mg/L	Growth (Morphology-Abnormal, Response Site: Gill(s))	LOEC (19.0 mg/L)	Development/Growth	High	3230411
84-61-7	72 Hour(s), (72 Hour(s))	*Xenopus tropicalis* (Clawed Frog), Larva, 11-12 Nieuwkoop-faber-stage, Not Reported, Laboratory	Culture, Aqueous (aquatic habitat), Renewal, 216 Organism	Measured	0 mg/L / 0 mg/L / 0.3 mg/L / 1.5 mg/L / 4.1 mg/L / 19.0 mg/L / 99.3 mg/L	Growth (Morphology-Abnormal, Response Site: Gut)	LOEC (19.0 mg/L)	Development/Growth	High	3230411

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Aquatic: Amphibian 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
84-61-7	72 Hour(s), (72 Hour(s))	*Xenopus tropicalis* (Clawed Frog), Larva, 11-12 Nieuwkoop-faber-stage, Not Reported, Laboratory	Culture, Aqueous (aquatic habitat), Renewal, 17 Organism	Measured	0 mg/L / 0 mg/L / 0.3 mg/L / 1.5 mg/L / 4.1 mg/L / 19.0 mg/L / 99.3 mg/L	Growth (Morphology-Abnormal, Response Site: Heart)	LOEC (19.0 mg/L)	Development/Growth	High	3230411
84-61-7	72 Hour(s), (72 Hour(s))	*Xenopus tropicalis* (Clawed Frog), Larva, 11-12 Nieuwkoop-faber-stage, Not Reported, Laboratory	Culture, Aqueous (aquatic habitat), Renewal, Not Reported	Measured	0 mg/L / 0 mg/L / 0.3 mg/L / 1.5 mg/L / 4.1 mg/L / 19.0 mg/L / 99.3 mg/L	Cellular (Genetics-HSP70 mRNA, Response Site: Whole organism)	LOEC (4.1 mg/L)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function	High	3230411
84-61-7	72 Hour(s), (72 Hour(s))	*Xenopus tropicalis* (Clawed Frog), Larva, 11-12 Nieuwkoop-faber-stage, Not Reported, Laboratory	Culture, Aqueous (aquatic habitat), Renewal, 216 Organism	Measured	0 mg/L / 0 mg/L / 0.3 mg/L / 1.5 mg/L / 4.1 mg/L / 19.0 mg/L / 99.3 mg/L	Growth (Development-Slowed, Retarded, Delayed or Non-development, Response Site: Not reported)	LOEC (4.1 mg/L)	Development/Growth	High	3230411
84-61-7	72 Hour(s), (72 Hour(s))	*Xenopus tropicalis* (Clawed Frog), Larva, 11-12 Nieuwkoop-faber-stage, Not Reported, Laboratory	Culture, Aqueous (aquatic habitat), Renewal, Not Reported	Measured	0 mg/L / 0 mg/L / 0.3 mg/L / 1.5 mg/L / 4.1 mg/L / 19.0 mg/L / 99.3 mg/L	Growth (Growth-Length, Response Site: Whole organism)	LOEC (4.1 mg/L)	Development/Growth	High	3230411
84-61-7	72 Hour(s), (72 Hour(s))	*Xenopus tropicalis* (Clawed Frog), Larva, 11-12 Nieuwkoop-faber-stage, Not Reported, Laboratory	Culture, Aqueous (aquatic habitat), Renewal, 216 Organism	Measured	0 mg/L / 0 mg/L / 0.3 mg/L / 1.5 mg/L / 4.1 mg/L / 19.0 mg/L / 99.3 mg/L	Growth (Morphology-Abnormal, Response Site: Cement gland)	LOEC (4.1 mg/L)	Development/Growth	High	3230411
84-61-7	72 Hour(s), (72 Hour(s))	*Xenopus tropicalis* (Clawed Frog), Larva, 11-12 Nieuwkoop-faber-stage, Not Reported, Laboratory	Culture, Aqueous (aquatic habitat), Renewal, 400 Organism	Measured	0 mg/L / 0 mg/L / 0.3 mg/L / 1.5 mg/L / 4.1 mg/L / 19.0 mg/L / 99.3 mg/L	Mortality (Mortality-Mortality, Response Site: Not reported)	LOEC (4.1 mg/L)	Mortality	High	3230411

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Aquatic: Amphibian 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
84-61-7	72 Hour(s), (72 Hour(s))	*Xenopus tropicalis* (Clawed Frog), Larva, 11-12 Nieuwkoop-faber-stage, Not Reported, Laboratory	Culture, Aqueous (aquatic habitat), Renewal, Not Reported	Measured	0 mg/L / 0 mg/L / 0.3 mg/L / 1.5 mg/L / 4.1 mg/L / 19.0 mg/L / 99.3 mg/L	Accumulation (Accumulation-Residue, Response Site: Whole organism)	LOEC (99.3 mg/L)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function	High	3230411
84-61-7	72 Hour(s), (72 Hour(s))	*Xenopus tropicalis* (Clawed Frog), Larva, 11-12 Nieuwkoop-faber-stage, Not Reported, Laboratory	Culture, Aqueous (aquatic habitat), Renewal, Not Reported	Measured	0 mg/L / 0 mg/L / 0.3 mg/L / 1.5 mg/L / 4.1 mg/L / 19.0 mg/L / 99.3 mg/L	Cellular (Genetics-Steroidogenic Acute Regulatory protein mRNA, Response Site: Whole organism)	NOEC (0.3 mg/L)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function	High	3230411
84-61-7	72 Hour(s), (72 Hour(s))	*Xenopus tropicalis* (Clawed Frog), Larva, 11-12 Nieuwkoop-faber-stage, Not Reported, Laboratory	Culture, Aqueous (aquatic habitat), Renewal, Not Reported	Measured	0 mg/L / 0 mg/L / 0.3 mg/L / 1.5 mg/L / 4.1 mg/L / 19.0 mg/L / 99.3 mg/L	Cellular (Genetics-Type I iodothyronine deiodinase mRNA, Response Site: Whole organism)	NOEC (0.3 mg/L)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function	High	3230411
84-61-7	72 Hour(s), (72 Hour(s))	*Xenopus tropicalis* (Clawed Frog), Larva, 11-12 Nieuwkoop-faber-stage, Not Reported, Laboratory	Culture, Aqueous (aquatic habitat), Renewal, 147 Organism	Measured	0 mg/L / 0 mg/L / 0.3 mg/L / 1.5 mg/L / 4.1 mg/L / 19.0 mg/L / 99.3 mg/L	Cellular (Histology-Edema, Response Site: Whole organism)	NOEC (0.3 mg/L)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function	High	3230411
84-61-7	72 Hour(s), (72 Hour(s))	*Xenopus tropicalis* (Clawed Frog), Larva, 11-12 Nieuwkoop-faber-stage, Not Reported, Laboratory	Culture, Aqueous (aquatic habitat), Renewal, 147 Organism	Measured	0 mg/L / 0 mg/L / 0.3 mg/L / 1.5 mg/L / 4.1 mg/L / 19.0 mg/L / 99.3 mg/L	Growth (Morphology-Abnormal, Response Site: Tail)	NOEC (0.3 mg/L)	Development/Growth	High	3230411
84-61-7	72 Hour(s), (72 Hour(s))	*Xenopus tropicalis* (Clawed Frog), Larva, 11-12 Nieuwkoop-faber-stage, Not Reported, Laboratory	Culture, Aqueous (aquatic habitat), Renewal, Not Reported	Measured	0 mg/L / 0 mg/L / 0.3 mg/L / 1.5 mg/L / 4.1 mg/L / 19.0 mg/L / 99.3 mg/L	Cellular (Genetics-HSP70 mRNA, Response Site: Whole organism)	NOEC (1.5 mg/L)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function	High	3230411

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Aquatic: Amphibian 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
84-61-7	72 Hour(s), (72 Hour(s))	*Xenopus tropicalis* (Clawed Frog), Larva, 11-12 Nieuwkoop-faber-stage, Not Reported, Laboratory	Culture, Aqueous (aquatic habitat), Renewal, 150 Organism	Measured	0 mg/L / 0 mg/L / 0.3 mg/L / 1.5 mg/L / 4.1 mg/L / 19.0 mg/L / 99.3 mg/L	Growth (Development-Slowed, Retarded, Delayed or Non-development, Response Site: Not reported)	NOEC (1.5 mg/L)	Development/Growth	High	3230411
84-61-7	72 Hour(s), (72 Hour(s))	*Xenopus tropicalis* (Clawed Frog), Larva, 11-12 Nieuwkoop-faber-stage, Not Reported, Laboratory	Culture, Aqueous (aquatic habitat), Renewal, Not Reported	Measured	0 mg/L / 0 mg/L / 0.3 mg/L / 1.5 mg/L / 4.1 mg/L / 19.0 mg/L / 99.3 mg/L	Growth (Growth-Length, Response Site: Whole organism)	NOEC (1.5 mg/L)	Development/Growth	High	3230411
84-61-7	72 Hour(s), (72 Hour(s))	*Xenopus tropicalis* (Clawed Frog), Larva, 11-12 Nieuwkoop-faber-stage, Not Reported, Laboratory	Culture, Aqueous (aquatic habitat), Renewal, 150 Organism	Measured	0 mg/L / 0 mg/L / 0.3 mg/L / 1.5 mg/L / 4.1 mg/L / 19.0 mg/L / 99.3 mg/L	Growth (Morphology-Abnormal, Response Site: Cement gland)	NOEC (1.5 mg/L)	Development/Growth	High	3230411
84-61-7	72 Hour(s), (72 Hour(s))	*Xenopus tropicalis* (Clawed Frog), Larva, 11-12 Nieuwkoop-faber-stage, Not Reported, Laboratory	Culture, Aqueous (aquatic habitat), Renewal, 320 Organism	Measured	0 mg/L / 0 mg/L / 0.3 mg/L / 1.5 mg/L / 4.1 mg/L / 19.0 mg/L / 99.3 mg/L	Mortality (Mortality-Mortality, Response Site: Not reported)	NOEC (1.5 mg/L)	Mortality	High	3230411
84-61-7	72 Hour(s), (72 Hour(s))	*Xenopus tropicalis* (Clawed Frog), Larva, 11-12 Nieuwkoop-faber-stage, Not Reported, Laboratory	Culture, Aqueous (aquatic habitat), Renewal, Not Reported	Measured	0 mg/L / 0 mg/L / 0.3 mg/L / 1.5 mg/L / 4.1 mg/L / 19.0 mg/L / 99.3 mg/L	Accumulation (Accumulation-Residue, Response Site: Whole organism)	NOEC (19.0 mg/L)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function	High	3230411
84-61-7	72 Hour(s), (72 Hour(s))	*Xenopus tropicalis* (Clawed Frog), Larva, 11-12 Nieuwkoop-faber-stage, Not Reported, Laboratory	Culture, Aqueous (aquatic habitat), Renewal, 17 Organism	Measured	0 mg/L / 0 mg/L / 0.3 mg/L / 1.5 mg/L / 4.1 mg/L / 19.0 mg/L / 99.3 mg/L	Growth (Morphology-Abnormal, Response Site: Head)	NOEC (19.0 mg/L)	Development/Growth	High	3230411

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Aquatic: Amphibian 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
84-61-7	72 Hour(s), (72 Hour(s))	*Xenopus tropicalis* (Clawed Frog), Larva, 11-12 Nieuwkoop-faber-stage, Not Reported, Laboratory	Culture, Aqueous (aquatic habitat), Renewal, 216 Organism	Measured	0 mg/L / 0 mg/L / 0.3 mg/L / 1.5 mg/L / 4.1 mg/L / 19.0 mg/L / 99.3 mg/L	Growth (Morphology-Abnormal, Response Site: Gill(s))	NOEC (4.1 mg/L)	Development/Growth	High	3230411
84-61-7	72 Hour(s), (72 Hour(s))	*Xenopus tropicalis* (Clawed Frog), Larva, 11-12 Nieuwkoop-faber-stage, Not Reported, Laboratory	Culture, Aqueous (aquatic habitat), Renewal, 216 Organism	Measured	0 mg/L / 0 mg/L / 0.3 mg/L / 1.5 mg/L / 4.1 mg/L / 19.0 mg/L / 99.3 mg/L	Growth (Morphology-Abnormal, Response Site: Gut)	NOEC (4.1 mg/L)	Development/Growth	High	3230411
84-61-7	72 Hour(s), (72 Hour(s))	*Xenopus tropicalis* (Clawed Frog), Larva, 11-12 Nieuwkoop-faber-stage, Not Reported, Laboratory	Culture, Aqueous (aquatic habitat), Renewal, 216 Organism	Measured	0 mg/L / 0 mg/L / 0.3 mg/L / 1.5 mg/L / 4.1 mg/L / 19.0 mg/L / 99.3 mg/L	Growth (Morphology-Abnormal, Response Site: Heart)	NOEC (4.1 mg/L)	Development/Growth	High	3230411
84-61-7	72 Hour(s), (72 Hour(s))	*Xenopus tropicalis* (Clawed Frog), Larva, 11-12 Nieuwkoop-faber-stage, Not Reported, Laboratory	Culture, Aqueous (aquatic habitat), Renewal, Not Reported	Measured	0 mg/L / 0 mg/L / 0.3 mg/L / 1.5 mg/L / 4.1 mg/L / 19.0 mg/L / 99.3 mg/L	Growth (Morphology-Abnormal, Response Site: Eye)	NR (0.3-19.0 mg/L)	Development/Growth	High	3230411
84-61-7	72 Hour(s), (72 Hour(s))	*Xenopus tropicalis* (Clawed Frog), Larva, 11-12 Nieuwkoop-faber-stage, Not Reported, Laboratory	Culture, Aqueous (aquatic habitat), Renewal, Not Reported	Measured	0 mg/L / 0 mg/L / 0.3 mg/L / 1.5 mg/L / 4.1 mg/L / 19.0 mg/L / 99.3 mg/L	Cellular (Genetics-CYP19 mRNA, Response Site: Whole organism)	NR (0.3-4.1 mg/L)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function	High	3230411
84-61-7	72 Hour(s), (72 Hour(s))	*Xenopus tropicalis* (Clawed Frog), Larva, 11-12 Nieuwkoop-faber-stage, Not Reported, Laboratory	Culture, Aqueous (aquatic habitat), Renewal, Not Reported	Measured	0 mg/L / 0 mg/L / 0.3 mg/L / 1.5 mg/L / 4.1 mg/L / 19.0 mg/L / 99.3 mg/L	Cellular (Genetics-Peroxisome proliferator-activated receptor gamma mRNA, Response Site: Whole organism)	NR (0.3-4.1 mg/L)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function	High	3230411

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Aquatic: Amphibian 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
84-61-7	72 Hour(s), (72 Hour(s))	*Xenopus tropicalis* (Clawed Frog), Larva, 11-12 Nieuwkoop-faber-stage, Not Reported, Laboratory	Culture, Aqueous (aquatic habitat), Renewal, 51 Organism	Measured	0 mg/L / 0 mg/L / 0.3 mg/L / 1.5 mg/L / 4.1 mg/L / 19.0 mg/L / 99.3 mg/L	Growth (Morphology-Abnormal, Response Site: Eye)	NR (0.3-99.3 mg/L)	Development/Growth	High	3230411
84-61-7	72 Hour(s), (72 Hour(s))	*Xenopus tropicalis* (Clawed Frog), Larva, 11-12 Nieuwkoop-faber-stage, Not Reported, Laboratory	Culture, Aqueous (aquatic habitat), Renewal, Not Reported	Measured	0 mg/L / 0 mg/L / 0.3 mg/L / 1.5 mg/L / 4.1 mg/L / 19.0 mg/L / 99.3 mg/L	Growth (Morphology-Abnormal, Response Site: Gut)	NR (0.3-99.3 mg/L)	Development/Growth	High	3230411
84-61-7	72 Hour(s), (72 Hour(s))	*Xenopus tropicalis* (Clawed Frog), Larva, 11-12 Nieuwkoop-faber-stage, Not Reported, Laboratory	Culture, Aqueous (aquatic habitat), Renewal, NA Organism	Measured	0 mg/L / 0 mg/L / 0.3 mg/L / 1.5 mg/L / 4.1 mg/L / 19.0 mg/L / 99.3 mg/L	Growth (Morphology-Abnormal, Response Site: Whole organism)	NR (0.3-99.3 mg/L)	Development/Growth	High	3230411

* 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
84-61-7	24 Hour(s), (96 Hour(s))	*Oryzias latipes* (Japanese Medaka), Not reported, Not Reported, Laboratory (SANKYO SUISAN CO., LTD (1 BANCHI, 1 CHOME, ICHIGAYATA-MACHI, SHINJUKU-KU))	Fresh water, Aqueous (aquatic habitat), Renewal, Not Reported	Measured	<0.007 mg/L / <0.007 mg/L / 1.91 (1.83-2.00) mg/L	Mortality (Mortality-Mortality, Response Site: Not reported)	LC50 (>1.91 (1.83-2.00) mg/L)	Mortality	High	11803931
84-61-7	48 Hour(s), (96 Hour(s))	*Oryzias latipes* (Japanese Medaka), Not reported, Not Reported, Laboratory (SANKYO SUISAN CO., LTD (1 BANCHI, 1 CHOME, ICHIGAYATA-MACHI, SHINJUKU-KU))	Fresh water, Aqueous (aquatic habitat), Renewal, Not Reported	Measured	<0.007 mg/L / <0.007 mg/L / 1.91 (1.83-2.00) mg/L	Mortality (Mortality-Mortality, Response Site: Not reported)	LC50 (>1.91 (1.83-2.00) mg/L)	Mortality	High	11803931
84-61-7	72 Hour(s), (96 Hour(s))	*Oryzias latipes* (Japanese Medaka), Not reported, Not Reported, Laboratory (SANKYO SUISAN CO., LTD (1 BANCHI, 1 CHOME, ICHIGAYATA-MACHI, SHINJUKU-KU))	Fresh water, Aqueous (aquatic habitat), Renewal, Not Reported	Measured	<0.007 mg/L / <0.007 mg/L / 1.91 (1.83-2.00) mg/L	Mortality (Mortality-Mortality, Response Site: Not reported)	LC50 (>1.91 (1.83-2.00) mg/L)	Mortality	High	11803931

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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
84-61-7	96 Hour(s), (96 Hour(s))	*Oryzias latipes* (Japanese Medaka), Not reported, Not Reported, Laboratory (SANKYO SUISAN CO., LTD (1 BANCHI, 1 CHOME, ICHIGAYATA-MACHI, SHINJUKU-KU))	Fresh water, Aqueous (aquatic habitat), Renewal, Not Reported	Measured	<0.007 mg/L / <0.007 mg/L / 1.91 (1.83-2.00) mg/L	Mortality (Mortality-Mortality, Response Site: Not reported)	LC50 (>1.91 (1.83-2.00) mg/L)	Mortality	High	11803931
84-61-7	96 Hour(s), (96 Hour(s))	*Oryzias latipes* (Japanese Medaka), Not reported, Not Reported, Laboratory (SANKYO SUISAN CO., LTD (1 BANCHI, 1 CHOME, ICHIGAYATA-MACHI, SHINJUKU-KU))	Fresh water, Aqueous (aquatic habitat), Renewal, Not Reported	Measured	<0.007 mg/L / <0.007 mg/L / 1.91 (1.83-2.00) mg/L	Mortality (Mortality-Mortality, Response Site: Not reported)	NR-ZERO (1.91 (1.83-2.00) mg/L)	Mortality	High	11803931

* 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
84-61-7	24-48 Hour(s), (72 Hour(s))	*Raphidocelis subcapitata* (Green Algae), Not reported, Not Reported, Not Reported, Laboratory (NR)	Culture, Aqueous (aquatic habitat), Static, Not Reported	Measured	<0.007 mg/L / <0.007 mg/L / 1.68-1.93 mg/L	Population (Population-Population growth rate, Response Site: Not reported)	EC50 (1.68-1.93 mg/L)	Development/Growth	Medium	11803966
84-61-7	24-48 Hour(s), (72 Hour(s))	*Raphidocelis subcapitata* (Green Algae), Not reported, Not Reported, Not Reported, Laboratory (NR)	Culture, Aqueous (aquatic habitat), Static, Not Reported	Measured	<0.007 mg/L / <0.007 mg/L / 1.68-1.93 mg/L	Population (Population-Population growth rate, Response Site: Not reported)	LOEC (>1.68-1.93 mg/L)	Development/Growth	Medium	11803966
84-61-7	24-48 Hour(s), (72 Hour(s))	*Raphidocelis subcapitata* (Green Algae), Not reported, Not Reported, Not Reported, Laboratory (NR)	Culture, Aqueous (aquatic habitat), Static, Not Reported	Measured	<0.007 mg/L / <0.007 mg/L / 1.68-1.93 mg/L	Population (Population-Population growth rate, Response Site: Not reported)	NOEC (>=1.68-1.93 mg/L)	Development/Growth	Medium	11803966
84-61-7	0-72 Hour(s), (72 Hour(s))	*Raphidocelis subcapitata* (Green Algae), Not reported, Not Reported, Not Reported, Laboratory (NR)	Culture, Aqueous (aquatic habitat), Static, Not Reported	Measured	<0.007 mg/L / <0.007 mg/L / 1.68-1.93 mg/L	Population (Population-Population growth rate, Response Site: Not reported)	EC50 (1.68-1.93 mg/L)	Development/Growth	Medium	11803966
84-61-7	24-72 Hour(s), (72 Hour(s))	*Raphidocelis subcapitata* (Green Algae), Not reported, Not Reported, Not Reported, Laboratory (NR)	Culture, Aqueous (aquatic habitat), Static, Not Reported	Measured	<0.007 mg/L / <0.007 mg/L / 1.68-1.93 mg/L	Population (Population-Population growth rate, Response Site: Not reported)	EC50 (1.68-1.93 mg/L)	Development/Growth	Medium	11803966
84-61-7	0-72 Hour(s), (72 Hour(s))	*Raphidocelis subcapitata* (Green Algae), Not reported, Not Reported, Not Reported, Laboratory (NR)	Culture, Aqueous (aquatic habitat), Static, Not Reported	Measured	<0.007 mg/L / <0.007 mg/L / 1.68-1.93 mg/L	Population (Population-Population growth rate, Response Site: Not reported)	LOEC (>1.68-1.93 mg/L)	Development/Growth	Medium	11803966
84-61-7	24-72 Hour(s), (72 Hour(s))	*Raphidocelis subcapitata* (Green Algae), Not reported, Not Reported, Not Reported, Laboratory (NR)	Culture, Aqueous (aquatic habitat), Static, Not Reported	Measured	<0.007 mg/L / <0.007 mg/L / 1.68-1.93 mg/L	Population (Population-Population growth rate, Response Site: Not reported)	LOEC (>1.68-1.93 mg/L)	Development/Growth	Medium	11803966

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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
84-61-7	0-72 Hour(s), (72 Hour(s))	*Raphidocelis subcapitata* (Green Algae), Not reported, Not Reported, Not Reported, Laboratory (NR)	Culture, Aqueous (aquatic habitat), Static, Not Reported	Measured	<0.007 mg/L / <0.007 mg/L / 1.68-1.93 mg/L	Population (Population-Population growth rate, Response Site: Not reported)	NOEC (>=1.68-1.93 mg/L)	Development/Growth	Medium	11803966
84-61-7	24-72 Hour(s), (72 Hour(s))	*Raphidocelis subcapitata* (Green Algae), Not reported, Not Reported, Not Reported, Laboratory (NR)	Culture, Aqueous (aquatic habitat), Static, Not Reported	Measured	<0.007 mg/L / <0.007 mg/L / 1.68-1.93 mg/L	Population (Population-Population growth rate, Response Site: Not reported)	NOEC (>=1.68-1.93 mg/L)	Development/Growth	Medium	11803966
84-61-7	0-72 Hour(s), (72 Hour(s))	*Raphidocelis subcapitata* (Green Algae), Not reported, Not Reported, Not Reported, Laboratory (NR)	Culture, Aqueous (aquatic habitat), Static, Not Reported	Measured	<0.007 mg/L / <0.007 mg/L / 1.68-1.93 mg/L	Population (Population-Abundance, Response Site: Not reported)	NR (1.68-1.93 mg/L)	Development/Growth	Medium	11803966
84-61-7	0-72 Hour(s), (72 Hour(s))	*Raphidocelis subcapitata* (Green Algae), Not reported, Not Reported, Not Reported, Laboratory (NR)	Culture, Aqueous (aquatic habitat), Static, Not Reported	Measured	<0.007 mg/L / <0.007 mg/L / 1.68-1.93 mg/L	Population (Population-Population growth rate, Response Site: Not reported)	NR (1.68-1.93 mg/L)	Development/Growth	Medium	11803966

* 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
84-61-7	2 weeks, (2 weeks)	Rat (Rattus norvegicus), Sampling Age:Juvenile Exposure Age: AdultF, Sprague-Dawley	Gavage	Unmeasured	0/20/100/501	20	LOAEL	Reproduction	High	2914645
84-61-7	10 weeks, (10 weeks)	Rat (Rattus norvegicus), Sampling Age:Adult Exposure Age: AdultM, Sprague-Dawley	Diet	Unmeasured	0/16/80/402	80	NOAEL	Reproduction	Medium	1414996
84-61-7	10 weeks, (11 weeks)	Rat (Rattus norvegicus), Sampling Age:Adult Exposure Age: AdultM, Sprague-Dawley	Diet	Unmeasured	0/16/80/402	402	LOAEL	Reproduction	Medium	1414996
84-61-7	16 weeks, (16 weeks)	Rat (Rattus norvegicus), Sampling Age:Adult Exposure Age: AdultF, Sprague-Dawley	Diet	Unmeasured	0/16/80/402	80	NOAEL	Reproduction	Medium	1414996
84-61-7	16 weeks, (17 weeks)	Rat (Rattus norvegicus), Sampling Age:Adult Exposure Age: AdultF, Sprague-Dawley	Diet	Unmeasured	0/16/80/402	402	LOAEL	Reproduction	Medium	1414996

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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
84-61-7	9 days, (9 days)	Rat (Rattus norvegicus), Sampling Age:Fetus Exposure Age: AdultF, Sprague-Dawley	Gavage	Unmeasured	0/10/100/500	10	NOAEL	Reproduction	Medium	3350245
84-61-7	9 days, (9 days)	Rat (Rattus norvegicus), Sampling Age:Fetus Exposure Age: AdultF, Sprague-Dawley	Gavage	Unmeasured	0/10/100/500	100	LOAEL	Reproduction	Medium	3350245

Dicyclohexyl Phthalate- 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 do not report adherence to any guidelines, but the study design is similar to what is recommended in OECD TG 414. Rat-Other (Wistar albino)-Female	Oral-Gavage-Duration: Short-term (>1-30 days)-1-F0 - gestation (GD6-19) Animals exposed from GD6 to 19	**POD: 20 mg/kg-bw/day (LOAEL) -Increased litters with resorption and percentage of resorption, decreased AGD, AGD/body weight and AGD/cubic foot of body weight, decreased testosterone, MIS and FSH/inhibin B ratio, incidence of atrophic and small seminiferous tubules, reduced germ cells in tubules, Sertoli cell only tubules, detached cells from tubular wall and MNG, decreased number of LEydig cell clusters, and decreased relative integrated immunodensity of 3beta-HSD, MIS/AMH and AR.** n= 10 Dose= 0, n= 10 Dose= 20, n= 10 Dose= 100, n= 10 Dose= 500, mg/kg-bw/dayTotal # of generations: 1 Female Exposure: F0 - gestation, GD6-19	See footnotes for full summary [1]	Limitations of this study include lower sample size than what is recommended for similar studies, and lacking detail on randomization and analytical verification of the test substance.	Reproductive/Developmental- Litters with resorptions, percentage resorption, offspring length (from head to tail), weight of male offspring, anogenital distance (AGD), GD20 fetal hormones including: testosterone, follicle stimulating hormone, inhibin B, Mullerian inhibiting substance/antimullarian hormone (MIS/AMH) and testes histopathology including: H and E staining, immunohistochemistry for 3-beta-hydroxysteroid dehydrogenase, and MIS/AMH, androgen receptor and proliferating cell nuclear antigen, determination of Leydig cell number and clusters.; High	2914645

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Dicyclohexyl Phthalate- 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

* Overall Quality Determination

[1] 2914645: Pregnant Wistar albino rats (10/group) were exposed to 0, 20, 100 or 500 mg/kg/day of dicylcohexyl phtalate (DCHP) via oral gavage in corn oil vehicle for 13 days from GD 6 to 19. Maternal body weights, food and water consumption and clinical signs of toxicity were recorded daily. On GD20, dams were euthanized and litters with resorptions, percentage resorption and weight and length (from rump to crown) of male pups were recorded. Anogenital distance (AGD) was measured in male pups at the time of necropsy. Fetal blood from males was collected and used to measure testosterone, follicle stimulating hormone (FSH), inhibin B and mullerian inhibiting substance/antimullarian hormone (MIS/AMH). The testes from offspring were taken and processed for histopathology, including H and E staining, immunohistochemistry for 3-beta-hydroxysteroid dehydrogenase (3beta-HSD), and MIS/AMH, androgen receptor (AR) and proliferating cell nuclear antigen (PNCA), determination of Leydig cell number and clusters.There were no significant differences in maternal body weight gain, food or water consumption in animals exposed to DCHP. There were no significant differences in length of pregnancy, the numbers of implantation sites, live pups, male pups and male/female ratio in DCHP-exposed groups. Significantly increased litters with resorptions and percentage of resorption were observed at doses of 20 mg/kg/day and higher. Increased pup body weight was also observed at all doses of DCHP exposure, but this increase did not exhibit linear dose-response. Significantly decreased AGD, AGD/body weight and AGD/cubic foot of body weight were observed at doses of 20 mg/kg/day and higher. Significantly decreased testosterone (by 12%), MIS (by 16%) and FSH/inhibin B ratio were observed at doses of 20 mg/kg/day and higher. Significantly increased FSH (by 50%) and inhibin B (by 176%) were observed at doses of 20 mg/kg/day and higher. Significantly increased incidence of atrophic and small seminiferous tubules, reduced germ cells in tubules, Sertoli cell only tubules, detached cells from tubular wall and multinucelated gonocytes (MNG) were observed via histopathology at doses of 20 mg/kg/day and higher. Significantly decreased number of Leydig cell clusters/testicular cross section area was observed at doses of 20 mg/kg/day and higher, although the overall number of Leydig cells/testicular cross section area was not significantly altered. Significantly decreased relative integrated immunodensity of 3beta-HSD, MIS/AMH and AR were observed at doses of 20 mg/kg/day and higher, whereas decreased relative integrated immunodensity of PCNA was only observed at 500 mg/kg/day. A LOAEL of 20 mg/kg/day for reproductive/developmental effects was determined. A NOAEL was not determined.

Dicyclohexyl Phthalate- 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 or GLP were specified. Rat-Wistar - [rat]-Female	Oral-Gavage-Duration: Reproductive/Developmental-1-F0 - gestation (GD 6-19)	**POD: 20 mg/kg-bw/day (LOAEL) -Decreased fetal bone ossification and skeletal retardation.** n= 10 Dose= 0, n= 10 Dose= 20, n= 10 Dose= 100, n= 10 Dose= 500, mg/kg-bw/dayTotal # of generations: 1 Female Exposure: F0 - gestation, GD 6-19	See footnotes for full summary [1]	Purity of test substance not reported.	Reproductive/Developmental-skeletal retardation, delayed ossification in offspring, and placental histopathology.; Medium	4729046

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Dicyclohexyl Phthalate- 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
"Data were presented for most outcomes of interest and statistical analysis was appropriate. Not all data were reported for F1 adults (organ wt and histology), but lack of reporting this information is not likely to substantially impact interpretation of results." Rat-Sprague-Dawley - [rat]-Both	Oral-Diet-Duration: Reproductive/Developmental-2-F0- premating (10 weeks)-F0- mating (10 weeks)-F0 - gestation (3 weeks)-F0- lactation (3 weeks)-F1- premating (10 weeks)-F1- mating (10 weeks)-F1 - gestation (10 weeks)-F1- lactation (10 weeks)-F0- premating (10 weeks)-F0- mating (10 weeks)-F1- premating (10 week)-F1- mating (10 weeks) Doses of DCHP administered to (F0) males was continued until necropsy through 10 weeks or more of the premating and mating periods, while (Fo) females lasted through 10 weeks of premating, mating, gestation and lactation period, however in their result table gestation and lactation shows 3 wks. Administration to(F1) male parental animals started at about 3 weeks old and continued through 10 weeks or more of premating, mating and similarly for (F1) females through the 10 weeks of premating, mating , gestation and lactation period.	**POD: 15.88 mg/kg-bw/day (Other) -Reproductive toxicology** n= 24 Dose= 0, n= 24 Dose= 15.88, n= 24 Dose= 79.57, n= 24 Dose= 401.8, mg/kg-bw/dayTotal # of generations: 2 Male Exposure: F0- premating, 10 weeks, F0- mating, 10 weeks, F1- premating, 10 week, F1- mating, 10 weeks Female Exposure: F0- premating, 10 weeks, F0- mating, 10 weeks, F0 - gestation, 3 weeks, F0- lactation, 3 weeks, F1- premating, 10 weeks, F1- mating, 10 weeks, F1 - gestation, 10 weeks, F1- lactation, 10 weeks	See footnotes for full summary [2]	Analytical measurements were not performed to verify concentrations in diet.	Nutritional/Metabolic-Body weight and food intake-Hepatic/Liver-Liver weight and histology-Thyroid-Thyroid weight and histology (including parathyroid)-Mortality-Lethality-Renal/Kidney-Kidney weight and histology-Reproductive/Developmental-Parental animals: Weights and histology of: testes, epididymis, prostate, seminal vesicles, ovaries and uterus. Histology on vagina and mammary glands. Estrous cycle, sperm motility, numbers of homogenization-resistan spermatids in testes, number of sperm in cauda epididymal, sperm morphology. Serum levels of testosterone, LH, FSH, estradiol. Reproductive parameters and developmental parameters in offspring.; Medium	1414996

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Dicyclohexyl Phthalate- 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 compliance is not reported Rat-Sprague-Dawley - [rat]-Female	Oral-Gavage-Duration: Reproductive/Developmental-1-F0 - gestation (GD 12-21) Dams were dosed daily from GD 12 to GD 21	**POD: 10 mg/kg-bw/day (LOAEL) -Decreased pup body weights, abnormal Leydig cell clustering in fetal testes, reduced fetal testicular mRNA levels for steroidogenic genes (e.g., Star).** n= 6 Dose= 0, n= 6 Dose= 10, n= 6 Dose= 100, n= 6 Dose= 500, mg/kg-bw/dayTotal # of generations: 1 Female Exposure: F0 - gestation, GD 12-21	See footnotes for full summary [3]	The dose selections did not allow for the determination of a NOAEL. There is some ambiguity surrounding the use of a 1,000 mg/kg-day group. Some study details (e.g., gavage volume, preparation of test solutions, test substance purity etc.,) were not provided in the study report. It is unclear whether the study authors took measures to reduce exposure to other plasticizers in an endocrine disruption study.	Reproductive/Developmental- Pup body weights, length, AGD, analysis of cell distribution in the testes, testicular testosterone, Leydig cell counts and cell size and nuclear size, testes immunohistochemistry and histopathology, gene expression.; Medium	3350245
No guidelines or GLP compliance were specified. Rat-Sprague-Dawley - [rat]-Female	Oral-Gavage-Duration: Reproductive/Developmental-1-F0 - gestation (GD 6-20) Pregnant dams were dosed from GD 6-20 and sacrificed on GD 21	**POD: 250 mg/kg-bw/day (LOAEL) - Decreased AGD and AGD/body weight in male fetuses at GD 21** n= 25 Dose= 0, n= 25 Dose= 250, n= 24 Dose= 500, n= 24 Dose= 750, mg/kg-bw/dayTotal # of generations: 1 Female Exposure: F0 - gestation, GD 6-20	See footnotes for full summary [4]	The study did not control for potential co-exposure to plasticizers.	Reproductive/Developmental- Uterine weight, number of implantation sites, resorption, dead and live fetuses, and corpora lutea. Live fetuses weight, sex, anogenital distance, external, visceral and skeletal abnormalities, and the degree of trans-abdominal testicular migration.; High	1465017

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Dicyclohexyl Phthalate- 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 guidelines or GLP compliance were specified. Rat-Sprague-Dawley - [rat]-Female	Oral-Gavage-Duration: Reproductive/Developmental-1-F0 - gestation (GD 6-20) Pregnant dams were dosed from GD 6-20 and sacrificed on GD 21	**POD: 250 mg/kg-bw/day (LOAEL) - Decreased AGD and AGD/body weight in male fetuses at GD 21** n= 25 Dose= 0, n= 25 Dose= 250, n= 24 Dose= 500, n= 24 Dose= 750, mg/kg-bw/dayTotal # of generations: 1 Female Exposure: F0 - gestation, GD 6-20	See footnotes for full summary [5]	The study did not control for potential co-exposure to plasticizers.	Reproductive/Developmental-Uterine weight, number of implantation sites, resorption, dead and live fetuses, and corpora lutea. Live fetuses weight, sex, anogenital distance, external, visceral and skeletal abnormalities, and the degree of trans-abdominal testicular migration.; High	1465017
No guidelines or GLP compliance were specified. Rat-Sprague-Dawley - [rat]-Female	Oral-Gavage-Duration: Reproductive/Developmental-1-F0 - gestation (GD 6-20) Pregnant dams were dosed from GD 6-20 and sacrificed on GD 21	**POD: 250 mg/kg-bw/day (LOAEL) - Decreased AGD and AGD/body weight in male fetuses at GD 21** n= 25 Dose= 0, n= 25 Dose= 250, n= 24 Dose= 500, n= 24 Dose= 750, mg/kg-bw/dayTotal # of generations: 1 Female Exposure: F0 - gestation, GD 6-20	See footnotes for full summary [6]	The study did not control for potential co-exposure to plasticizers.	Reproductive/Developmental-Uterine weight, number of implantation sites, resorption, dead and live fetuses, and corpora lutea. Live fetuses weight, sex, anogenital distance, external, visceral and skeletal abnormalities, and the degree of trans-abdominal testicular migration.; Medium	1465017

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Dicyclohexyl Phthalate- 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 guidelines or GLP compliance were specified. Rat-Sprague-Dawley - [rat]-Female	Oral-Gavage-Duration: Reproductive/Developmental-1-F0 - gestation (GD 6-20) Satellite group- hepatic effects. Pregnant dams were dosed from GD 6-20 and sacrificed on GD 21	**POD: 250 mg/kg-bw/day (Other) -Increased hepatic enzymatic activity of peroxisomal β-oxidation** n= 6 Dose= 0, n= 6 Dose= 250, n= 6 Dose= 500, n= 6 Dose= 750, mg/kg-bw/dayTotal # of generations: 1 Female Exposure: F0 - gestation, GD 6-20	Female Sprague-Dawley rats were housed with males until the presence of vaginal sperm was detected (gestational day 0). Mated females (6-9/group) were administered 0, 250, 500, or 750 mg/kg/day of dicyclohexyl phthalate (DCHP) in olive oil via gavage from GD 6-20. On GD 21, dams were sacrificed. Endpoints evaluated body weight, serum AST, ALT, cholesterol, and triglycerides, liver and uterine weight, liver histopathology, and liver enzyme activity (cyanide-insensitive palmitoyl CoA oxidase and peroxisomal β-oxidation).Terminal body weight of the dams (minus uterine weight) was significantly decreased in the 750 mg/kg/day group (12%) compared with control (uterine weight not reported). Significant increases in serum AST (49%) and ALT (120%) were seen at 750 mg/kg/day compared with control. Serum cholesterol and triglycerides were not significantly different across groups. Absolute liver weights were not significantly different from control. At 500 and 750 mg/kg/day, respectively, relative liver weights were significantly increased (17% and 28%), and absolute liver weights were increased (10% and 13%), though not statistically significant, compared with control. No treatment related histopathological changes were seen (data not shown). Mild, yet significant increases in hepatic peroxisomal β-oxidation activity was seen (1.7-2.1-fold) at $\geq$250 mg/kg/day compared with control. No author-reported toxicity values were provided. A LOEL of 250 mg/kg/day was determined based on a significant increase in hepatic enzymatic activity of peroxisomal β-oxidation. An apical NOAEL of 250 mg/kg/day and LOAEL of 500 mg/kg/day was identified based on a significant increase in relative liver weights.	The study does not control for potential co-exposure to plasticizers.	Hepatic/Liver-Serum AST, ALT, cholesterol, and triglycerides, liver weight, liver histopathology, and liver enzyme activity (cyanide-insensitive palmitoyl CoA oxidase and peroxisomal β-oxidation).; Uninformative	1465017

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Dicyclohexyl Phthalate- 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 guidelines or GLP compliance were specified. Rat-Sprague-Dawley - [rat]-Female	Oral-Gavage-Duration: Reproductive/Developmental-1-F0 - gestation (GD 6-20) Satellite group- hepatic effects. Pregnant dams were dosed from GD 6-20 and sacrificed on GD 21	**POD: 250 mg/kg-bw/day (Other) -Increased hepatic enzymatic activity of peroxisomal β-oxidation** n= 6 Dose= 0, n= 6 Dose= 250, n= 6 Dose= 500, n= 6 Dose= 750, mg/kg-bw/dayTotal # of generations: 1 Female Exposure: F0 - gestation, GD 6-20	Female Sprague-Dawley rats were housed with males until the presence of vaginal sperm was detected (gestational day 0). Mated females (6-9/group) were administered 0, 250, 500, or 750 mg/kg/day of dicyclohexyl phthalate (DCHP) in olive oil via gavage from GD 6-20. On GD 21, dams were sacrificed. Endpoints evaluated body weight, serum AST, ALT, cholesterol, and triglycerides, liver and uterine weight, liver histopathology, and liver enzyme activity (cyanide-insensitive palmitoyl CoA oxidase and peroxisomal β-oxidation).Terminal body weight of the dams (minus uterine weight) was significantly decreased in the 750 mg/kg/day group (12%) compared with control (uterine weight not reported). Significant increases in serum AST (49%) and ALT (120%) were seen at 750 mg/kg/day compared with control. Serum cholesterol and triglycerides were not significantly different across groups. Absolute liver weights were not significantly different from control. At 500 and 750 mg/kg/day, respectively, relative liver weights were significantly increased (17% and 28%), and absolute liver weights were increased (10% and 13%), though not statistically significant, compared with control. No treatment related histopathological changes were seen (data not shown). Mild, yet significant increases in hepatic peroxisomal β-oxidation activity was seen (1.7-2.1-fold) at $\geq$250 mg/kg/day compared with control. No author-reported toxicity values were provided. A LOEL of 250 mg/kg/day was determined based on a significant increase in hepatic enzymatic activity of peroxisomal β-oxidation. An apical NOAEL of 250 mg/kg/day and LOAEL of 500 mg/kg/day was identified based on a significant increase in relative liver weights.	The study does not control for potential co-exposure to plasticizers.	Hepatic/Liver-Serum AST, ALT, cholesterol, and triglycerides, liver weight, liver histopathology, and liver enzyme activity (cyanide-insensitive palmitoyl CoA oxidase and peroxisomal β-oxidation).; Medium	1465017

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Dicyclohexyl Phthalate- 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 describe adherence to any guidelines of compliance documents. Rat-Other (Crl:CD (SD))-Female	Oral-Gavage-Duration: Reproductive/Developmental-1-F0 - gestation (GD 6-GD 20)-F0- lactation (PND 0-PND 20) Dams exposed from GD 6-PND 20	**POD: 100 mg/kg-bw/day (NOAEL) - Endocrine-mediated changes in offspring.** n= 10 Dose= 0, n= 10 Dose= 20, n= 10 Dose= 100, n= 10 Dose= 500, mg/kg-bw/dayTotal # of generations: 1 Female Exposure: F0 - gestation, GD 6-GD 20, F0- lactation, PND 0-PND 20	See footnotes for full summary [7]	The study is generally well designed, though some endpoints (such as ovary, thyroid and kidney weights in F0 dams or quantitative incidence data for F1 offspring) are not discussed in the results, and data are not shown for several endpoints. There may be unmeasured confounding from animal bedding or water dispensing materials., and there is a lack of reporting on gavage volume and test substance storage and preparation conditions.	Reproductive/Developmental; Hepatic/Liver; Uninformative	1061309
The authors do not describe adherence to any guidelines of compliance documents. Rat-Other (Crl:CD (SD))-Female	Oral-Gavage-Duration: Reproductive/Developmental-1-F0 - gestation (GD 6-GD 20)-F0- lactation (PND 0-PND 20) Dams exposed from GD 6-PND 20	**POD: 100 mg/kg-bw/day (NOAEL) - Endocrine-mediated changes in offspring.** n= 10 Dose= 0, n= 10 Dose= 20, n= 10 Dose= 100, n= 10 Dose= 500, mg/kg-bw/dayTotal # of generations: 1 Female Exposure: F0 - gestation, GD 6-GD 20, F0- lactation, PND 0-PND 20	See footnotes for full summary [8]	The study is generally well designed, though some endpoints (such as ovary, thyroid and kidney weights in F0 dams or quantitative incidence data for F1 offspring) are not discussed in the results, and data are not shown for several endpoints. There may be unmeasured confounding from animal bedding or water dispensing materials., and there is a lack of reporting on gavage volume and test substance storage and preparation conditions.	Reproductive/Developmental; Hepatic/Liver.; Medium	1061309
The authors do not describe adherence to any guidelines of compliance documents. Rat-Other (Crl:CD (SD))-Female	Oral-Gavage-Duration: Reproductive/Developmental-1-F0 - gestation (GD 6-GD 20)-F0- lactation (PND 0-PND 20) Dams exposed from GD 6-PND 20	**POD: 100 mg/kg-bw/day (NOAEL) - Endocrine-mediated changes in offspring.** n= 10 Dose= 0, n= 10 Dose= 20, n= 10 Dose= 100, n= 10 Dose= 500, mg/kg-bw/dayTotal # of generations: 1 Female Exposure: F0 - gestation, GD 6-GD 20, F0- lactation, PND 0-PND 20	See footnotes for full summary [9]	The study is generally well designed, though some endpoints (such as ovary, thyroid and kidney weights in F0 dams or quantitative incidence data for F1 offspring) are not discussed in the results, and data are not shown for several endpoints. There may be unmeasured confounding from animal bedding or water dispensing materials., and there is a lack of reporting on gavage volume and test substance storage and preparation conditions.	Reproductive/Developmental; Hepatic/Liver.; Medium	1061309

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Dicyclohexyl Phthalate- 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 describe adherence to any guidelines of compliance documents. Rat-Other (Crl:CD (SD))-Female	Oral-Gavage-Duration: Reproductive/Developmental-1-F0 - gestation (GD 6-GD 20)-F0- lactation (PND 0-PND 20) Dams exposed from GD 6-PND 20	**POD: 100 mg/kg-bw/day (NOAEL) - Endocrine-mediated changes in offspring.** n= 10 Dose= 0, n= 10 Dose= 20, n= 10 Dose= 100, n= 10 Dose= 500, mg/kg-bw/dayTotal # of generations: 1 Female Exposure: F0 - gestation, GD 6-GD 20, F0- lactation, PND 0-PND 20	See footnotes for full summary [10]	The study is generally well designed, though some endpoints (such as ovary, thyroid and kidney weights in F0 dams or quantitative incidence data for F1 offspring) are not discussed in the results, and data are not shown for several endpoints. There may be unmeasured confounding from animal bedding or water dispensing materials., and there is a lack of reporting on gavage volume and test substance storage and preparation conditions.	Reproductive/Developmental; Hepatic/Liver.; Medium	1061309

* Overall Quality Determination

[1] 4729046: Groups of pregnant Wistar rats (10/group) were administered dicyclohexyl phthalate (purity not reported) via gavage in corn oil at doses of 0, 20, 100, or 500mg/kg/day during gestation days (GD) 6-19. Maternal body weights, food consumption, clinical signs of toxicity were recorded daily. Animals were sacrificed on GD 20, after exposure and organs were collected and weighed (liver and kidney) and fetuses were excised. One placenta per litter was collected and weighed and examined for histopathology. The uterus was examined for implantation sites. Resorptions, rate of resorptions were measured.Fetuses were weighed, sexed, and examined for gross abnormalities. Skeletal examination was performed on randomly selected surviving fetuses; one per sex per litter. Fetal hematology was examined in a random selection. Anogenital distance was recorded at necropsy.The endpoints specifically evaluated herein are skeletal retardation, delayed ossification, and placental histopathology.ResultsSkeletal retardation and delayed ossificationImpaired fetal skeletal development was observed. The intensity of alizarin red stain (bone) was significantly reduced in all treated groups compared to controls indicating delayed ossification. There was, however, no dose related effect.Skeletal retardation was also observed in male and female fetuses. Most absolute and relative (to body length) bone ossification centers were decreased in fetuses of both sexes. Bone biometrics indicate that in male fetuses the following absolute values were altered: body length was increased at all doses; skull diameter (x and y axes) were significantly reduced at all doses; the left and right scapula were decreased at doses $\geq$ 100 mg/kg/day; and the left ulna was decreased at 500 mg/kg/day. Changes in bone biometrics in male fetuses relative to length of body include decreased skull diameter (x and y axes), both (left and right) scapula, humerus, and ulna at all doses as well as decreased left and right radius, decreased right ilium and left femur at 500 mg/kg/day. Decreases in left tibia and fibula were noted at $\geq$ 100 mg/kg/day and decreases in the right fibula were noted at 500 mg/kg/day. Female fetuses exhibited the following bone biometric data: decreased absolute body length, skull diameter (x and y axes), and right scapula at all doses. Decreases in both humeri, right ulna, and fibula, and left scapula, ilium, and tibia were noted at $\geq$ 100 mg/kg/d. All absolute bone parameters were decreased in female fetuses at 500 mg/kg/day. There was a noted significant increase in the absolute R radius at 20 mg/kg/day that decreased with increasing doses. Relative (to body length) bone biometrics on female fetuses included decreases on skull diameter (x and y axes), and both (left and right) scapula, humeri, ulna, ilium, tibia, and fibula, as well as left femur at all doses. R radius was decreased at $\geq$ 100 mg/kg/day; and right femur was decreased at 500 mg/kg/day. The left radius was decreased but only at 20 and 500 mg/kg/day. The significant reduction of bone staining and many fetal bone biometrics indicates adverse skeletal development. Placental histopathology:Adverse effects on the placenta were observed and include hemorrhage in labyrinth, degeneration of spongiotrophoblast, hemorrhage, decreased/irregular vessel formation, and edema in the basal zone. Placental histopathology showed increased incidences of trophoblastic giant cells with polymorphism in the nucleus (9/10 compared with 0/10 in controls) and degeneration in the cytoplasm (5/10 compared to 0/10 in controls) at 500 mg/kg/day. The following histopathological effects are reported in order of 0, 20, 100 and 500 mg/kg/day, respectively. Effects on spongiotrophoblasts include degeneration (0/10, 3/10, 7/10* and 9/10*); labyrinth hemorrhage (0/10,5/10*, 4/10, 10/10*); decreased and irregular vessel formation (0/10, 8/10*, 9/10*, and 10/10*); as well as basal zone hemorrhage (2/10, 5/10, 10/10*, 10/10*) and edema (0/10, 5/10, 10/10*, 10/10*). The study author did not determine a LOAEL or NOAEL. The LOAEL is 20 mg/kg/day based on decreased bone ossification and retardation. No NOAEL was derived.

[2] 1414996: In a two-generation reproductive toxicity study, male and female Sprague-Dawley rats (24/sex/group) were provided a diet containing 0, 240, 1200 or 6000 ppm of dicyclohexyl phthalate (DCHP) beginning at 5 weeks of age for 10 weeks (premating) and through the mating period. Males were sacrificed after mating, females continued to be fed dosed diets through gestation (21-23 days) and lactation (21 days) and were sacrificed on PND 21. Study authors calculated the mean daily intake for F0 males as 0, 15.88, 79.57 and 401.8 mg/kg/day; and for F0 females as 0, 20.8, 104.19, and 510.7 mg/kg/day. F1 parental animals were fed dosed diets from PND 21 for 10 weeks (premating) and through the mating period. F1 parental males were sacrificed after mating, parental F1 females were maintained on the diet through weaning of F2 generation (PND 21). Study authors calculated the mean daily intake for F1 males as 0, 17.84, 89.89, and 457.4; and for F1 females as 0, 20.95, 107.15, and 534.2 mg/kg/day. Rats were mated in a 1:1 ratio at 15 weeks of age (F0) or 14-15 weeks of age (F1) until presence of vaginal plug or sperm was detected by vaginal smear (gestion day [GD]0). Parental F1 rats were chosen randomly from each litter (1 male and 1 female) on PND 21. All other F1 offspring were sacrificed on PND 21. Endpoints evaluated in F0 and F1 adult rats included clinical signs of toxicity, body weights, food intake, organ weights (brain, pituitary gland, thyroid including parathyroid, liver, kidneys, adrenal glands, spleen, testes, epididymis [whole and caudal parts], prostate [ventral lobe], seminal vesicles [including the coagulating glands, ovaries, and uterus [including the cervical region]), histopathology (control and high dose group: brain, pituitary gland, thyroid including parathyroid, liver, kidneys, adrenal glands, spleen, testes, epididymis, seminal vesicles [including coagulating glands], prostate [ventral love], ovaries, uterus [including the cervical region], vagina, and mammary glands; in low and mid dose groups liver and thyroid in males and females, kidney in males, testes in F1 males, and adrenals in F1 males and F1 females). Estrous cycle was evaluated via vaginal smears two weeks before mating (week 13 for F0 females and week 11 for F1 females). Sperm motility, spermatid head counts, and numbers of sperm in the cauda epididymal (all dose groups), and number morphologically abnormal sperm (control and high dose group). Serum levels of testosterone, FSH and LH in males and estradiol, FSH, and LH in females were measured; females were in pro-estrous stage at time of sacrifice (n=6). Pups were culled to 8 pups (4 of each sex when possible) on PND 4. Endpoints examined in pups included clinical signs, body weights (PND 0, 4, 7, 14 and 21), anogenital distance (AGD) on PND 4, appearance of areolae (or nipples) on PND 12 (F2 pups) or PND 14 (F1 pups), pinna unfolding (PND 2-4), day of upper incisor eruption, eye opening, preputial separation (and body weight) and vaginal opening (and body weight) were recorded. On PND 19, all pups were evaluated for pain response, negative geotaxis, air righting reflex, and pinna reflex. On PND 21, one male and one female from each litter was sacrificed to evaluated brain, thymus and organ weight. All sacrificed or pups found dead were necropsied.No deaths occurred during the study period of F0 parents. Two F1 parental females died (in the 240 ppm and 6000 ppm groups), however these deaths were not considered by study authors to be related to treatment. No clinical signs of toxicity were seen in F0 or F1 parents. No significant difference in body weight was seen in the F0 males throughout dosing, compared to control. Body weight were significantly decreased in F0 females and F1 males at $\geq$ 1200 ppm and F1 females at 6000 ppm compared to control. Terminal body weights of F0 females were significantly decreased (5% and 8%) and in F1 males (10% and 12%) at 1200 and 6000 ppm, respectively. Food intake was significantly decreased in F0 females at some time points evaluated at 1200 ppm (GD 14, LD 4, LD 21) and 6000 ppm (Day 49, GD 7, GD14); and in F1 males at 1200 ppm (PND 91) and 6000 ppm (PND 28, 56 and 91) compared to control; decreased in food consumption were $\leq$12% of control. Food consumption was not significantly different in F0 males or F2 females at any time points measured. Estrous cycle in F0 females was significantly longer in the 6000-ppm group (4.25 +/- 0.42 days compared to 4.04 +/- 0.14 days) compared to control. No difference in estrous cycle was seen in F1 females. In both F0 and F1 parental animals, no significant differences in number of days for copulation, number of estrous stages missed until completion of copulation, mating index, fertility index, gestation length, gestation index, birth index, number of implantations, total number of offspring at birth number offspring born alive or sex ratio. In F0 and F1 males, no treatment related changes in sperm motility rate, number of sperm in caudal epididymis, or incidence or morphologically abnormal sperm were seen. The number of homogenization-resistant spermatids was not significantly different in F0 males but was significantly decreased in F1 males (15% and 24%) at 1200 and 6000 ppm, respectively. Soft and small sized testes, with no sperm was observed in one F1 parental male at 6000 ppm. No treatment related changes in serum levels of testosterone, FSH or LSH or estradiol was seen in F0 and F1 parental males and females. In F0 males, significant increases in absolute and relative thyroid weight (27% and 30%, respectively) and absolute and relative liver weight (21% and 24%, respectively) were seen compared to control. In F0 females, absolute and relative liver weights were significantly increased (9% and 20%) at 1200 ppm and 6000 ppm, respectively compared to control; relative (but not absolute) thyroid weight was significantly increased in the 6000-ppm group (15% and 23% in left and right, respectively) although this may be a reflection of the decreased body weight and not necessarily a reflection on organ weight. In F1 parental males, significant decrease in absolute prostate weight were seen (19%, 16%, and 28%) at 240, 1200 and 6000 ppm, respectively and relative prostate weight at 6000 ppm (19%). Relative (but not absolute) liver weight was significantly increased (14%) at 6000 ppm, however this may be a reflection of the decreased body weight. In F1 parental females, relative liver weight was significantly increased 16% at 6000 ppm compared to control; absolute was increased 10%, albeit not statistically significant compared to control. No other organ weights were reported. Histological changes observe in F0 generation included increased incidence of hepatocyte hypertrophy in males (4/24 and 16/24) and females (3/24 and 12/24) at 1200 and 6000 ppm, respectively; and hypertrophy of follicular cells of the thyroid at in 3/24 males at 1200 ppm and at 6000 ppm (7/24 males; 6/24 females); these lesions were not seen in any control animal (0/24). In the F1 parental adults, hepatocyte hypertrophy was seen in 14/22 males and 9/22 females at 6000 ppm and hypertrophy of follicular cells of thyroid in 7/22 males and 6/22 females at 6000 ppm; these lesions were not observed in the control groups (0/20). In F1 parental males, severe atrophy of the seminiferous tubule with lack of sperm in the epididymis was seen in 3/22 rats at 6000 ppm (not seen in any other group) and slight atrophy in 1/20, 0/23, 2/20 and 6/22 males at 0, 240, 1200, and 6000 ppm, respectively. In F0 and F1 males, increased hyaline droplets in the renal proximal tubular epithelium were seen in all groups, however severity was increased (moderate grade) in the 6000-ppm group. Effects on offspring: No clinical signs of toxicity were seen in F1 and F2 offspring. At 6000 ppm, body weights were significantly decreased in males (4-12%) and females (6-11%) from PND 0-21 compared to control. In F2 pups, body weight was significantly decreased in the 6000-ppm group only on PND 21 (9% in males and 8% in females) compared to control. AGD and nipple development was not significantly different in F1 or F2 females from control. In F1 males at 6000 ppm, significant decreases in AGD (7%) and AGD/BW (8%) were seen, and increases in percentage of males with abnormal nipple development (16.1%) consisting of presence of areole mammae with no nipple; no abnormalities were seen in any other dose group. In F2 male pups, significant decreases in AGD (7% and 9%) and AGD/BW (7% and 9%) were seen at 1200 and 6000 ppm, respectively. Also in F2 males, the percentage or rats with abnormal nipple developments were (0%, 0%, 18.4% and 63.2%) at 0, 240, 1200, and 6000 ppm, respectively. Abnormal nipples had presence of areole mammae with no nipple. No significant differences in viability indices, parameters for physical development or sexual maturation were seen in F1 and F2 pups compared to control. No significant treatment related changes in thymus, spleen or brain weights were observed in F1 and F2 pups compared to control (changes seen at 6000 ppm were inconsistent and considered a reflection of body weight changes). No treatment related necropsy findings were observed in F1 or F2 offspring.Study authors determined a NOEL for effects on the parental animals as 240 ppm. NOEL for reproductive toxicological effects on parental animals was 240 for males and 1200 ppm for females; the NOEL for effects on offspring was 240 ppm for males and 1200 ppm for females.

[3] 3350245: Groups of pregnant Sprague-Dawley rats (6 dams/group) were administered DCHP daily at 0 (corn oil control), 10, 100, and 500 mg/kg-day from GD 12 to 21. After birth, birth rate, litter size, the percentage of male pups, number of pups, pup body weights and length and the anogenital distance (AGD) of male pups were recorded. Pups were then sacrificed on postnatal day (PND) 1. Testicular testosterone concentrations were measured. Other endpoints included Leydig cell counts, and immunohistochemical staining for desmin, to determine the frequency of testis dysgenesis, for 3β-HSD to label Leydig cells, and for Insulin-like 3 (INSL3). Histopathological analysis was conducted on testes tissues and the expression of seven testicular genes was analyzed using RT-qPCR. There were no effects of exposure on birth rates, litter size, or sex ratio. Male pup body weights were significantly decreased by 16%, 17%, and 16% at 10, 100, and 500 mg/kg-day, compared with controls. Absolute AGD was decreased (bodyweight normalized AGD not reported) and the occurrences of multinucleated gonocytes (MNG) increased in a dose-related manner in male pups, and the changes were significant at 100 and 500 mg/kg-day. Desmin staining showed testis dysgenesis, including irregular and disintegrated seminiferous tubules, in 1/6 and 3/6 treated animals in the 100 and 500 mg/kg-day groups, respectively, but none in controls or 10 mg/kg-day group. Testicular testosterone content was significantly decreased in a dose-dependent manner in the 100 and 500 mg/kg-day groups. No differences in the number of fetal Leydig cells were observed; however, the cytoplasmic size, nuclear size, and the ratio of cytoplasmic/nuclear sizes were significantly decreased in all treatment groups, albeit not in a dose-related manner. Although total fetal Leydig cell numbers did not change, there were significant dose-related increases in the Leydig cell numbers per cluster as well as increases in the percentage of large clusters in all treatment groups, compared with controls. There was some uncertainty in the gene expression data. Figure 4 shows data from a 1,000 mg/kg-day group; however, a 1,000 mg/kg-day dose group was not included in the study design or discussed anywhere in the paper. Gene expression analysis showed significant reductions in testes mRNA levels of Hsd17b3, Hsd3b1, and Star at $\geq$ 10

mg/kg-day, Insl3 at ≥ 100 mg/kg-day, Scarb1 at ≥ 500 mg/kg-day, and Lhcgr at 1,000 mg/kg-day. Semi-quantitative immunohistochemical staining showed significant reductions in INSL3 and HSD3B1 protein levels in all treatment groups. No author-reported toxicity values were provided. A LOAEL of 10 mg/kg-day (the lowest dose) was derived for this review, based on decreased pup body weights, abnormal Leydig cell clustering in fetal testes, and reductions in fetal testes mRNA levels for Hsd17b3, Hsd3b1 and Star.

[4] 1465017: Female Sprague-Dawley rats were housed with males until the presence of vaginal sperm was detected (gestational day 0). Mated females (24-25/group) were administered 0, 250, 500, or 750 mg/kg/day of dicyclohexyl phthalate (DCHP) in olive oil via gavage from GD 6-20. Animals were observed daily for mortality and clinical signs of toxicity. Body weights were measured on GD 0, 6, 9, 12, 15, 18, and 21. Food consumption was measured at 3-day intervals beginning on GD 6. Dams were sacrificed on GD21. Endpoints evaluated included uterine weight, number of implantation sites, resorption, dead and live fetuses, and corpora lutea. Live fetuses were weighed, sexed, examined for external anomalies (including oral cavity), and anogenital distance was measured. Half of the live fetuses were examined for internal soft tissue changes (Bouin's solution), the other half were examined for skeletal changes (alizarin red S). The degree of trans-abdominal testicular migration (TTM) was determined in all fetuses by measuring the distance from the bladder neck to the lower pole of the testes; measurements were standardized to the distance from the bladder neck to the lower pole of the kidney (as 100 U). No dams died during the experiment. No treatment-related clinical signs were observed (data not shown). In the 750 mg/kg/day group significant decreases in body weight gains were seen for the entire dosing period, GD 6-21 (22%) compared with control. Body weight gains were significantly decreased during the first 3 days of exposure (GD 6-9) in the 500 mg/kg/day group (33%) and 750 mg/kg/day group (47%), and from GD 18-21 in the 750 mg/kg/day group (46%) compared with control. No significant difference in gravid uterine weights was seen compared to control. When body weight gain was corrected for gravid uterine weight (weight gain minus gravid uterine weight) the decrease remained significantly decreased in the 750 mg/kg/day group (50%) compared with control. Food intake during the exposure period (GD 6-21) was not significantly different. Food intake was significantly decreased from GD 6-9 in the 500 mg/kg/day (15%) and 750 mg/kg/day (20%) groups and from GD 18-21 in the 750 mg/kg/day group (18%), compared with control. No significant differences were seen in the number of implantation sites, percentage post-implantation loss per litter, number of litters with dead fetuses, percentage of dead fetuses per litter, number of litters with resorptions, percentage resorptions per litter, number of live fetuses per litter, or sex ratio per litter, compared with control. The number of corpora lutea were not reported. In the 750 mg/kg/day group, significant decreases in fetal body weights were seen in male (11%), female (11%), and combined sexes (11%), compared to control. In male fetuses, significant decreases in anogenital distance (AGD) (9, 12, and 17%) and AGD/body weight (8, 11, and 14%) were seen at 250, 500, and 750 mg/kg/day, respectively, compared with control. No significant difference in AGD or AGD/BW were seen in female fetuses. No treatment-related external, visceral or skeletal malformations were seen compared with control. No undescended testis was seen in male fetuses. The pattern of trans-abdominal testicular migration was similar between the groups. No author-reported toxicity values were reported. A LOAEL of 250 mg/kg/day was identified for developmental effects; significant decreases in AGD and AGD/body weight in male fetuses at GD 21.

[5] 1465017: Female Sprague-Dawley rats were housed with males until the presence of vaginal sperm was detected (gestational day 0). Mated females (24-25/group) were administered 0, 250, 500, or 750 mg/kg/day of dicyclohexyl phthalate (DCHP) in olive oil via gavage from GD 6-20. Animals were observed daily for mortality and clinical signs of toxicity. Body weights were measured on GD 0, 6, 9, 12, 15, 18, and 21. Food consumption was measured at 3-day intervals beginning on GD 6. Dams were sacrificed on GD21. Endpoints evaluated included uterine weight, number of implantation sites, resorption, dead and live fetuses, and corpora lutea. Live fetuses were weighed, sexed, examined for external anomalies (including oral cavity), and anogenital distance was measured. Half of the live fetuses were examined for internal soft tissue changes (Bouin's solution), the other half were examined for skeletal changes (alizarin red S). The degree of trans-abdominal testicular migration (TTM) was determined in all fetuses by measuring the distance from the bladder neck to the lower pole of the testes; measurements were standardized to the distance from the bladder neck to the lower pole of the kidney (as 100 U). No dams died during the experiment. No treatment-related clinical signs were observed (data not shown). In the 750 mg/kg/day group significant decreases in body weight gains were seen for the entire dosing period, GD 6-21 (22%) compared with control. Body weight gains were significantly decreased during the first 3 days of exposure (GD 6-9) in the 500 mg/kg/day group (33%) and 750 mg/kg/day group (47%), and from GD 18-21 in the 750 mg/kg/day group (46%) compared with control. No significant difference in gravid uterine weights was seen compared to control. When body weight gain was corrected for gravid uterine weight (weight gain minus gravid uterine weight) the decrease remained significantly decreased in the 750 mg/kg/day group (50%) compared with control. Food intake during the exposure period (GD 6-21) was not significantly different. Food intake was significantly decreased from GD 6-9 in the 500 mg/kg/day (15%) and 750 mg/kg/day (20%) groups and from GD 18-21 in the 750 mg/kg/day group (18%), compared with control. No significant differences were seen in the number of implantation sites, percentage post-implantation loss per litter, number of litters with dead fetuses, percentage of dead fetuses per litter, number of litters with resorptions, percentage resorptions per litter, number of live fetuses per litter, or sex ratio per litter, compared with control. The number of corpora lutea were not reported. In the 750 mg/kg/day group, significant decreases in fetal body weights were seen in male (11%), female (11%), and combined sexes (11%), compared to control. In male fetuses, significant decreases in anogenital distance (AGD) (9, 12, and 17%) and AGD/body weight (8, 11, and 14%) were seen at 250, 500, and 750 mg/kg/day, respectively, compared with control. No significant difference in AGD or AGD/BW were seen in female fetuses. No treatment-related external, visceral or skeletal malformations were seen compared with control. No undescended testis was seen in male fetuses. The pattern of trans-abdominal testicular migration was similar between the groups. No author-reported toxicity values were reported. A LOAEL of 250 mg/kg/day was identified for developmental effects; significant decreases in AGD and AGD/body weight in male fetuses at GD 21.

[6] 1465017: Female Sprague-Dawley rats were housed with males until the presence of vaginal sperm was detected (gestational day 0). Mated females (24-25/group) were administered 0, 250, 500, or 750 mg/kg/day of dicyclohexyl phthalate (DCHP) in olive oil via gavage from GD 6-20. Animals were observed daily for mortality and clinical signs of toxicity. Body weights were measured on GD 0, 6, 9, 12, 15, 18, and 21. Food consumption was measured at 3-day intervals beginning on GD 6. Dams were sacrificed on GD21. Endpoints evaluated included uterine weight, number of implantation sites, resorption, dead and live fetuses, and corpora lutea. Live fetuses were weighed, sexed, examined for external anomalies (including oral cavity), and anogenital distance was measured. Half of the live fetuses were examined for internal soft tissue changes (Bouin's solution), the other half were examined for skeletal changes (alizarin red S). The degree of trans-abdominal testicular migration (TTM) was determined in all fetuses by measuring the distance from the bladder neck to the lower pole of the testes; measurements were standardized to the distance from the bladder neck to the lower pole of the kidney (as 100 U). No dams died during the experiment. No treatment-related clinical signs were observed (data not shown). In the 750 mg/kg/day group significant decreases in body weight gains were seen for the entire dosing period, GD 6-21 (22%) compared with control. Body weight gains were significantly decreased during the first 3 days of exposure (GD 6-9) in the 500 mg/kg/day group (33%) and 750 mg/kg/day group (47%), and from GD 18-21 in the 750 mg/kg/day group (46%) compared with control. No significant difference in gravid uterine weights was seen compared to control. When body weight gain was corrected for gravid uterine weight (weight gain minus gravid uterine weight) the decrease remained significantly decreased in the 750 mg/kg/day group (50%) compared with control. Food intake during the exposure period (GD 6-21) was not significantly different. Food intake was significantly decreased from GD 6-9 in the 500 mg/kg/day (15%) and 750 mg/kg/day (20%) groups and from GD 18-21 in the 750 mg/kg/day group (18%), compared with control. No significant differences were seen in the number of implantation sites, percentage post-implantation loss per litter, number of litters with dead fetuses, percentage of dead fetuses per litter, number of litters with resorptions, percentage resorptions per litter, number of live fetuses per litter, or sex ratio per litter, compared with control. The number of corpora lutea were not reported. In the 750 mg/kg/day group, significant decreases in fetal body weights were seen in male (11%), female (11%), and combined sexes (11%), compared to control. In male fetuses, significant decreases in anogenital distance (AGD) (9, 12, and 17%) and AGD/body weight (8, 11, and 14%) were seen at 250, 500, and 750 mg/kg/day, respectively, compared with control. No significant difference in AGD or AGD/BW were seen in female fetuses. No treatment-related external, visceral or skeletal malformations were seen compared with control. No undescended testis was seen in male fetuses. The pattern of trans-abdominal testicular migration was similar between the groups. No author-reported toxicity values were reported. A LOAEL of 250 mg/kg/day was identified for developmental effects; significant decreases in AGD and AGD/body weight in male fetuses at GD 21.

[7] 1061309: Pregnant Crl:CD (SD) rats (10/group) were dosed nominally with 0 (vehicle controls), 20, 100 or 500 mg/kg/day of dicyclohexyl phthalate (purity 99.9%), via gavage, in an olive oil vehicle for 34 days, between gestational day (GD) 6 and postnatal day (PND) 20. Dams were monitored for mortality and clinical signs of toxicity. Body weights were recorded on GDs 0, 6, 13, and 20, and on PND 4, 7, 14, and 21. Other endpoints assessed in dams included absolute and relative liver, kidneys, ovaries, and thyroid weights, number of implantation sites, number of litters, gestation index (%), gestation length (days), number of pups born, delivery index (%), birth index (%) and live birth index (%). Litters were culled to 4/sex/group on PND4 and pups were separated into two groups. One group was sacrificed at 10 weeks of age; a second group (2/sex/dam) were used for further mating. Endpoints assessed in all offspring included sex ratio on PND 0, number of live pups and viability index and anogenital distance on PND 4, body weights on PND 0, 4, 7, 14, and 21, and examinations for nipple retention, vaginal opening, and preputial separation. A weaning index on PND 21 (%) was also determined. Pups in the 10-week sacrifice group were observed for clinical signs. The ventral surface was examined for abnormalities, body weights were recorded weekly, and estrous cycle was evaluated. At sacrifice, rats were necropsied and examined for ectopic/atrophic testes, agenesis of the gubernaculum, epididymides, sex accessory gland and epididymal granulomas. Absolute and relative organ weights (testis, epididymis, ventral prostate, seminal vesicle, levator ani-bulbocavernous muscle, ovary, uterus, brain, pituitary, thyroid, adrenal, kidney, liver) were recorded, and select organs (liver, kidneys, testes, epididymides, uterus, ovaries, vagina, pituitary, thyroid) were histologically examined. In the F1 mating group, at 12 weeks of age, male and female offspring from each group were mated. These offspring remained unexposed to the test substance. Caesarean sections were performed at GD 13, and males were necropsied on the same day. Endpoints assessed in this group included copulation index (%), fertility index (%), implantation index (%) and implantation loss (%) and the same organs were weighed and histologically examined as those in the 10-week sacrifice group. One dam died in the 500 mg/kg/day group from dystocia. No differences in maternal body weights nor other clinical signs were observed. Significantly increased absolute (data not shown; magnitude of change unknown) and relative liver weights in F0 dams were observed at ≥100 mg/kg/day; relative weights were increased by 7% and 24% at 100% at 100 and 500 mg/kg-day, respectively. Data for other organ weights and dam necropsies were not reported; however, the study discussion stated that renal dysfunction was observed in dams and offspring (no further details were provided). No significant differences were observed in gestation index (%), gestation length, number of pups born, deliver index (%), birth index (%) or live birth index (%).Early effects in F1 pups included a significantly different but small (<5%) decrease in the viability index (%) on PND4 at 500 mg/kg/day and significantly decreased body weights on PND 14 and 21 at 500 mg/kg/day (data not shown). Ventral observations indicated hypospadias and small testes in 2 males at 500 mg/kg/day. Significantly prolonged preputial separation, reduced anogenital distance and increased nipple retention were observed at 500 mg/kg/day in male offspring. Vaginal patency and timing of estrous cycle were not significantly altered. Most organ weights were not significantly altered in a dose-dependent manner, with the exception of the ventral prostate and levator ani-bulbocavernous muscle, which were both significantly decreased in males at 500 mg/kg/day. Observed histopathology was limited to decreased testicular germ cells and degenerated renal proximal tubules in males at 500 mg/kg/day (incidence and significance not reported).In the mated F1 groups, no changes in reproductive parameters were observed (data not shown). Results for organ weights and histopathological examinations were not reported for this subset. For endocrine-mediated changes, the study authors reported a NOAEL of 100 mg/kg-day, and a LOAEL of 500 mg/kg-day based on hypospadias accompanied with small testes, prolonged preputial separation, decreased anogenital distance, and areola/nipple retention. A non-biologically significant (7% magnitude) increase in relative liver weights was observed in dams treated with 100 mg/kg-day. Absolute liver weights were also increased at the same dose by an unknown magnitude, and histopathology results were not reported. Due to insufficient reporting, 100 mg/kg-day was not selected as a LOAEL.

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