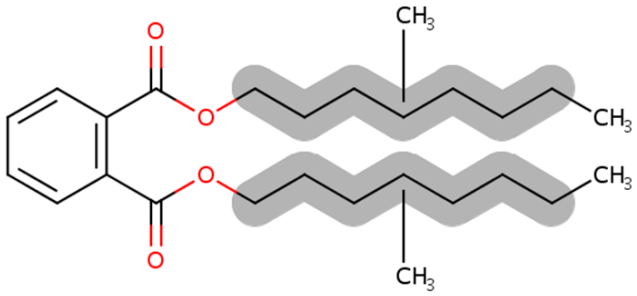
United States
Environmental Protection Agency

January 2025
Office of Chemical Safety and
Pollution Prevention

Data Extraction Information for Environmental Hazard and Human Health Hazard Animal Toxicology and Epidemiology for Diisononyl Phthalate (DINP)

Systematic Review Support Document for the Risk Evaluation

CASRNs: 28553-12-0 and 68515-48-0



January 2025

This supplemental file contains information regarding the data extraction results relevant to the *Environmental Hazard Assessment for Diisononyl Phthalate (DINP)* and the *Human Health Hazard Assessment for Diisononyl Phthalate (DINP)*. 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 *Risk Evaluation for Diisononyl Phthalate (DINP) - 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 for DINP 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 DINP, toxicity data gaps were identified for mammalian wildlife relevant to the terrestrial compartment of the environmental hazard assessment. This table includes rodent data for DINP, 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 *Risk Evaluation for Diisononyl Phthalate (DINP) - Systematic Review Protocol*. Data from references that were within an order of magnitude of the existing assessment HED were extracted and detailed data were extracted from each individual health outcome within each organ/system. Any co-critical effects were reported along with OQD for the health outcome. A detailed summary statement of each study is reported along with the major limitations as identified by the reviewer and any guidelines used.

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

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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
28553-12-0	96 Hour(s), (96 Hour(s))	*Americamysis bahia* (Opossum Shrimp), <=24 Hour(s), Not Reported, Not reported (NR)	Fresh water, Aqueous (aquatic habitat), Static, Not Reported	Measured	NR / NR	Mortality (Mortality-Mortality, Response Site: Not reported)	LC50 (>0.39 mg/L)	Mortality	High	1321996
28553-12-0	96 Hour(s), (96 Hour(s))	*Americamysis bahia* (Opossum Shrimp), Not reported, Not Reported, Laboratory (BIONOMICS MARINE RESEARCH LABORATORY, PENSACOLA, FL)	Salt water, Aqueous (aquatic habitat), Static, Not Reported	Measured	0 mg/L / 0.39 (0-0.77) mg/L	Mortality (Mortality-Mortality, Response Site: Not reported)	LC50 (>0.77 mg/L)	Mortality	High	1316220
28553-12-0	10 Day(s), (10 Day(s))	*Chironomus tentans* (Midge), 2-3 Instar, Not Reported, Laboratory (NR)	Fresh water, Aqueous (aquatic habitat), Leaching , Not Reported	Measured	<0.043 mg/L / 0.869 (0.356-1.55) mg/L	Growth (Growth-Weight, Response Site: Whole organism)	NR (0.869 (0.356-1.55) mg/L)	Development/Growth	High	679311
28553-12-0	10 Day(s), (10 Day(s))	*Chironomus tentans* (Midge), 2-3 Instar, Not Reported, Laboratory (NR)	Fresh water, Aqueous (aquatic habitat), Leaching , Not Reported	Measured	<0.043 mg/L / 0.869 (0.356-1.55) mg/L	Mortality (Mortality-Survival, Response Site: Not reported)	NR (0.869 (0.356-1.55) mg/L)	Mortality	High	679311
28553-12-0	10 Day(s), (10 Day(s))	*Chironomus tentans* (Midge), 2-3 Instar, Not Reported, Laboratory (NR)	Fresh water, Aqueous (aquatic habitat), Sediment, Not Reported	Measured	<2.58 mg/kg dw sediment / 2680 (2280-3020) mg/kg dw sediment	Growth (Growth-Weight, Response Site: Whole organism)	NR (2680 (2280-3020) mg/kg dw sediment)	Development/Growth	High	679311
28553-12-0	10 Day(s), (10 Day(s))	*Chironomus tentans* (Midge), 2-3 Instar, Not Reported, Laboratory (NR)	Fresh water, Aqueous (aquatic habitat), Sediment, Not Reported	Measured	<2.58 mg/kg dw sediment / 2680 (2280-3020) mg/kg dw sediment	Mortality (Mortality-Survival, Response Site: Not reported)	NR (2680 (2280-3020) mg/kg dw sediment)	Mortality	High	679311

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28553-12-0	10 Day(s), (10 Day(s))	*Chironomus tentans* (Midge), 2-3 Instar, Not Reported, Laboratory (NR)	Fresh water, Aqueous (aquatic habitat), Sediment, Not Reported	Measured	<2.58 mg/kg dw sediment / 2680 (2280-3020) mg/kg dw sediment	Mortality (Mortality-Survival, Response Site: Not reported)	NR (2680 (2280-3020) mg/kg dw sediment)	Mortality	High	679311
28553-12-0	10 Day(s), (10 Day(s))	*Chironomus tentans* (Midge), 2-3 Instar, Not Reported, Laboratory (NR)	Fresh water, Aqueous (aquatic habitat), Leaching , Not Reported	Measured	<0.043 mg/L / 0.869 (0.356-1.55) mg/L	Growth (Growth-Weight, Response Site: Whole organism)	NR (0.869 (0.356-1.55) mg/L)	Development/Growth	High	679311
28553-12-0	10 Day(s), (10 Day(s))	*Chironomus tentans* (Midge), 2-3 Instar, Not Reported, Laboratory (NR)	Fresh water, Aqueous (aquatic habitat), Leaching , Not Reported	Measured	<0.043 mg/L / 0.869 (0.356-1.55) mg/L	Mortality (Mortality-Survival, Response Site: Not reported)	NR (0.869 (0.356-1.55) mg/L)	Mortality	High	679311
28553-12-0	10 Day(s), (10 Day(s))	*Chironomus tentans* (Midge), 2-3 Instar, Not Reported, Laboratory (NR)	Fresh water, Aqueous (aquatic habitat), Sediment, Not Reported	Measured	<2.58 mg/kg dw sediment / 2680 (2280-3020) mg/kg dw sediment	Growth (Growth-Weight, Response Site: Whole organism)	NR (2680 (2280-3020) mg/kg dw sediment)	Development/Growth	High	679311
28553-12-0	48 Hour(s), (48 Hour(s))	*Daphnia magna* (Water Flea), <=24 Hour(s), Not Reported, Not reported (NR)	Fresh water, Aqueous (aquatic habitat), Static, Not Reported	Measured	NR / NR	Physiology (Intoxication-Immobile, Response Site: Not reported)	EC50 (>0.06 mg/L)	Immobilization	High	1321996
28553-12-0	7 Day(s), (21 Day(s))	*Daphnia magna* (Water Flea), Adult, <=24 Hour(s), Not Reported, Laboratory (OBTAINED FROM LABORATORY STOCKS CULTURED AT SPRINGBORN BIONOMICS, INC.)	Fresh water, Aqueous (aquatic habitat), Flow-through, Not Reported	Measured	<0.0040 (<0.0030-<0.0040) mg/L / 0.010 (<0.0037-0.014) mg/L / 0.018 (0.010-0.030) mg/L / 0.034 (0.020-0.052) mg/L / 0.089 (0.057-0.16) mg/L / 0.17 (0.11-0.28) mg/L	Mortality (Mortality-Survival, Response Site: Not reported)	NOEC (0.17 (0.11-0.28) mg/L)	Mortality	High	1316195

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CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
28553-12-0	7 Day(s), (21 Day(s))	*Daphnia magna* (Water Flea), Adult, <=24 Hour(s), Not Reported, Laboratory (OBTAINED FROM LABORATORY STOCKS CULTURED AT SPRINGBORN BIONOMICS, INC.)	Fresh water, Aqueous (aquatic habitat), Flow-through, Not Reported	Measured	<0.0040 (<0.0030-<0.0040) mg/L / 0.010 (<0.0037-0.014) mg/L / 0.018 (0.010-0.030) mg/L / 0.034 (0.020-0.052) mg/L / 0.089 (0.057-0.16) mg/L / 0.17 (0.11-0.28) mg/L	Reproduction (Reproduction-Progeny counts/numbers, Response Site: Not reported)	LOEC (0.17 (0.11-0.28) mg/L)	Reproductive/Teratogenic	High	1316195
28553-12-0	7 Day(s), (21 Day(s))	*Daphnia magna* (Water Flea), Adult, <=24 Hour(s), Not Reported, Laboratory (OBTAINED FROM LABORATORY STOCKS CULTURED AT SPRINGBORN BIONOMICS, INC.)	Fresh water, Aqueous (aquatic habitat), Flow-through, Not Reported	Measured	<0.0040 (<0.0030-<0.0040) mg/L / 0.010 (<0.0037-0.014) mg/L / 0.018 (0.010-0.030) mg/L / 0.034 (0.020-0.052) mg/L / 0.089 (0.057-0.16) mg/L / 0.17 (0.11-0.28) mg/L	Reproduction (Reproduction-Progeny counts/numbers, Response Site: Not reported)	NOEC (0.089 (0.057-0.16) mg/L)	Reproductive/Teratogenic	High	1316195
28553-12-0	8 Day(s), (21 Day(s))	*Daphnia magna* (Water Flea), Adult, <=24 Hour(s), Not Reported, Laboratory (OBTAINED FROM LABORATORY STOCKS CULTURED AT SPRINGBORN BIONOMICS, INC.)	Fresh water, Aqueous (aquatic habitat), Flow-through, Not Reported	Measured	<0.0040 (<0.0030-<0.0040) mg/L / 0.010 (<0.0037-0.014) mg/L / 0.018 (0.010-0.030) mg/L / 0.034 (0.020-0.052) mg/L / 0.089 (0.057-0.16) mg/L / 0.17 (0.11-0.28) mg/L	Reproduction (Reproduction-Progeny counts/numbers, Response Site: Not reported)	LOEC (0.089 (0.057-0.16) mg/L)	Reproductive/Teratogenic	High	1316195

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28553-12-0	8 Day(s), (21 Day(s))	*Daphnia magna* (Water Flea), Adult, <=24 Hour(s), Not Reported, Laboratory (OBTAINED FROM LABORATORY STOCKS CULTURED AT SPRINGBORN BIONOMICS, INC.)	Fresh water, Aqueous (aquatic habitat), Flow-through, Not Reported	Measured	<0.0040 (<0.0030-<0.0040) mg/L / 0.010 (<0.0037-0.014) mg/L / 0.018 (0.010-0.030) mg/L / 0.034 (0.020-0.052) mg/L / 0.089 (0.057-0.16) mg/L / 0.17 (0.11-0.28) mg/L	Reproduction (Reproduction-Progeny counts/numbers, Response Site: Not reported)	NOEC (0.034 (0.020-0.052) mg/L)	Reproductive/Teratogenic	High	1316195
28553-12-0	11 Day(s), (21 Day(s))	*Daphnia magna* (Water Flea), Adult, <=24 Hour(s), Not Reported, Laboratory (OBTAINED FROM LABORATORY STOCKS CULTURED AT SPRINGBORN BIONOMICS, INC.)	Fresh water, Aqueous (aquatic habitat), Flow-through, Not Reported	Measured	<0.0040 (<0.0030-<0.0040) mg/L / 0.010 (<0.0037-0.014) mg/L / 0.018 (0.010-0.030) mg/L / 0.034 (0.020-0.052) mg/L / 0.089 (0.057-0.16) mg/L / 0.17 (0.11-0.28) mg/L	Reproduction (Reproduction-Progeny counts/numbers, Response Site: Not reported)	NOEC (0.17 (0.11-0.28) mg/L)	Reproductive/Teratogenic	High	1316195
28553-12-0	12 Day(s), (21 Day(s))	*Daphnia magna* (Water Flea), Adult, <=24 Hour(s), Not Reported, Laboratory (OBTAINED FROM LABORATORY STOCKS CULTURED AT SPRINGBORN BIONOMICS, INC.)	Fresh water, Aqueous (aquatic habitat), Flow-through, Not Reported	Measured	<0.0040 (<0.0030-<0.0040) mg/L / 0.010 (<0.0037-0.014) mg/L / 0.018 (0.010-0.030) mg/L / 0.034 (0.020-0.052) mg/L / 0.089 (0.057-0.16) mg/L / 0.17 (0.11-0.28) mg/L	Reproduction (Reproduction-Progeny counts/numbers, Response Site: Not reported)	NOEC (0.17 (0.11-0.28) mg/L)	Reproductive/Teratogenic	High	1316195

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28553-12-0	13 Day(s), (21 Day(s))	*Daphnia magna* (Water Flea), Adult, <=24 Hour(s), Not Reported, Laboratory (OBTAINED FROM LABORATORY STOCKS CULTURED AT SPRINGBORN BIONOMICS, INC.)	Fresh water, Aqueous (aquatic habitat), Flow-through, Not Reported	Measured	<0.0040 (<0.0030-<0.0040) mg/L / 0.010 (<0.0037-0.014) mg/L / 0.018 (0.010-0.030) mg/L / 0.034 (0.020-0.052) mg/L / 0.089 (0.057-0.16) mg/L / 0.17 (0.11-0.28) mg/L	Reproduction (Reproduction-Progeny counts/numbers, Response Site: Not reported)	NOEC (0.17 (0.11-0.28) mg/L)	Reproductive/Teratogenic	High	1316195
28553-12-0	14 Day(s), (21 Day(s))	*Daphnia magna* (Water Flea), Adult, <=24 Hour(s), Not Reported, Laboratory (OBTAINED FROM LABORATORY STOCKS CULTURED AT SPRINGBORN BIONOMICS, INC.)	Fresh water, Aqueous (aquatic habitat), Flow-through, Not Reported	Measured	<0.0040 (<0.0030-<0.0040) mg/L / 0.010 (<0.0037-0.014) mg/L / 0.018 (0.010-0.030) mg/L / 0.034 (0.020-0.052) mg/L / 0.089 (0.057-0.16) mg/L / 0.17 (0.11-0.28) mg/L	Reproduction (Reproduction-Progeny counts/numbers, Response Site: Not reported)	NOEC (0.17 (0.11-0.28) mg/L)	Reproductive/Teratogenic	High	1316195
28553-12-0	14 Day(s), (21 Day(s))	*Daphnia magna* (Water Flea), Adult, <=24 Hour(s), Not Reported, Laboratory (OBTAINED FROM LABORATORY STOCKS CULTURED AT SPRINGBORN BIONOMICS, INC.)	Fresh water, Aqueous (aquatic habitat), Flow-through, Not Reported	Measured	<0.0040 (<0.0030-<0.0040) mg/L / 0.010 (<0.0037-0.014) mg/L / 0.018 (0.010-0.030) mg/L / 0.034 (0.020-0.052) mg/L / 0.089 (0.057-0.16) mg/L / 0.17 (0.11-0.28) mg/L	Mortality (Mortality-Survival, Response Site: Not reported)	NOEC (0.034 (0.020-0.052) mg/L)	Mortality	High	1316195

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28553-12-0	14 Day(s), (21 Day(s))	*Daphnia magna* (Water Flea), Adult, <=24 Hour(s), Not Reported, Laboratory (OBTAINED FROM LABORATORY STOCKS CULTURED AT SPRINGBORN BIONOMICS, INC.)	Fresh water, Aqueous (aquatic habitat), Flow-through, Not Reported	Measured	<0.0040 (<0.0030-<0.0040) mg/L / 0.010 (<0.0037-0.014) mg/L / 0.018 (0.010-0.030) mg/L / 0.034 (0.020-0.052) mg/L / 0.089 (0.057-0.16) mg/L / 0.17 (0.11-0.28) mg/L	Mortality (Mortality-Survival, Response Site: Not reported)	LOEC (0.089 (0.057-0.16) mg/L)	Mortality	High	1316195
28553-12-0	15 Day(s), (21 Day(s))	*Daphnia magna* (Water Flea), Adult, <=24 Hour(s), Not Reported, Laboratory (OBTAINED FROM LABORATORY STOCKS CULTURED AT SPRINGBORN BIONOMICS, INC.)	Fresh water, Aqueous (aquatic habitat), Flow-through, Not Reported	Measured	<0.0040 (<0.0030-<0.0040) mg/L / 0.010 (<0.0037-0.014) mg/L / 0.018 (0.010-0.030) mg/L / 0.034 (0.020-0.052) mg/L / 0.089 (0.057-0.16) mg/L / 0.17 (0.11-0.28) mg/L	Reproduction (Reproduction-Progeny counts/numbers, Response Site: Not reported)	NOEC (0.17 (0.11-0.28) mg/L)	Reproductive/Teratogenic	High	1316195
28553-12-0	19 Day(s), (21 Day(s))	*Daphnia magna* (Water Flea), Adult, <=24 Hour(s), Not Reported, Laboratory (OBTAINED FROM LABORATORY STOCKS CULTURED AT SPRINGBORN BIONOMICS, INC.)	Fresh water, Aqueous (aquatic habitat), Flow-through, Not Reported	Measured	<0.0040 (<0.0030-<0.0040) mg/L / 0.010 (<0.0037-0.014) mg/L / 0.018 (0.010-0.030) mg/L / 0.034 (0.020-0.052) mg/L / 0.089 (0.057-0.16) mg/L / 0.17 (0.11-0.28) mg/L	Reproduction (Reproduction-Progeny counts/numbers, Response Site: Not reported)	NOEC (0.17 (0.11-0.28) mg/L)	Reproductive/Teratogenic	High	1316195

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CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
28553-12-0	20 Day(s), (21 Day(s))	*Daphnia magna* (Water Flea), Adult, <=24 Hour(s), Not Reported, Laboratory (OBTAINED FROM LABORATORY STOCKS CULTURED AT SPRINGBORN BIONOMICS, INC.)	Fresh water, Aqueous (aquatic habitat), Flow-through, Not Reported	Measured	<0.0040 (<0.0030-<0.0040) mg/L / 0.010 (<0.0037-0.014) mg/L / 0.018 (0.010-0.030) mg/L / 0.034 (0.020-0.052) mg/L / 0.089 (0.057-0.16) mg/L / 0.17 (0.11-0.28) mg/L	Reproduction (Reproduction-Progeny counts/numbers, Response Site: Not reported)	NOEC (0.17 (0.11-0.28) mg/L)	Reproductive/Teratogenic	High	1316195
28553-12-0	24 Hour(s), (48 Hour(s))	*Daphnia magna* (Water Flea), <24 Hour(s), Not Reported, Laboratory (EG&G BIONOMICS)	Fresh water, Aqueous (aquatic habitat), Static, Not Reported	Measured	<0.014 mg/L / 0.035-0.088 mg/L	Mortality (Mortality-Mortality, Response Site: Not reported)	LC50 (>0.086 mg/L)	Mortality	Medium	1316223
28553-12-0	48 Hour(s), (48 Hour(s))	*Daphnia magna* (Water Flea), <24 Hour(s), Not Reported, Laboratory (EG&G BIONOMICS)	Fresh water, Aqueous (aquatic habitat), Static, Not Reported	Measured	<0.014 mg/L / 0.035-0.088 mg/L	Mortality (Mortality-Mortality, Response Site: Not reported)	NR-ZERO (0.036-0.086 mg/L)	Mortality	Medium	1316223
28553-12-0	48 Hour(s), (48 Hour(s))	*Daphnia magna* (Water Flea), <24 Hour(s), Not Reported, Laboratory (EG&G BIONOMICS)	Fresh water, Aqueous (aquatic habitat), Static, Not Reported	Measured	<0.014 mg/L / 0.035-0.088 mg/L	Multiple (Multiple-Multiple effects reported as one result, Response Site: Not reported)	NOEC (<0.086 mg/L)	Mortality	Medium	1316223
28553-12-0	48 Hour(s), (48 Hour(s))	*Daphnia magna* (Water Flea), <24 Hour(s), Not Reported, Laboratory (EG&G BIONOMICS)	Fresh water, Aqueous (aquatic habitat), Static, Not Reported	Measured	<0.014 mg/L / 0.035-0.088 mg/L	Mortality (Mortality-Mortality, Response Site: Not reported)	NOEC (0.086 mg/L)	Mortality	Medium	1316223

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28553-12-0	48 Hour(s), (48 Hour(s))	*Daphnia magna* (Water Flea), <24 Hour(s), Not Reported, Laboratory (EG&G BIONOMICS)	Fresh water, Aqueous (aquatic habitat), Static, Not Reported	Measured	<0.014 mg/L / 0.035-0.088 mg/L	Mortality (Mortality-Mortality, Response Site: Not reported)	LC50 (>0.086 mg/L)	Mortality	Medium	1316223
28553-12-0	48 Hour(s), (48 Hour(s))	*Daphnia magna* (Water Flea), <24 Hour(s), Not Reported, Laboratory (CONTINUOUS LABORATORY CULTURES)	Fresh water, Aqueous (aquatic habitat), Not reported, Not Reported	Unmeasured	0 mg/L / 0 mg/L / 1 mg/L	Physiology (Intoxication-Immobile, Response Site: Not reported)	NR (1 mg/L)	Mortality	Uninformative	679904
28553-12-0	21 Day(s), (21 Day(s))	*Daphnia magna* (Water Flea), <24 Hour(s) (Measured in: F0 generation), Not Reported, Laboratory (CONTINUOUS LABORATORY CULTURES)	Fresh water, Aqueous (aquatic habitat), Renewal, NA F0 generation	Measured	0 mg/L / 0 mg/L / 1.0-1.1 mg/L	Reproduction (Reproduction-Progeny counts/numbers, Response Site: Not reported)	NOEC (1.0-1.1 mg/L)	Reproductive/Teratogenic	High	679904
28553-12-0	21 Day(s), (21 Day(s))	*Daphnia magna* (Water Flea), <24 Hour(s) (Measured in: F0 generation), Not Reported, Laboratory (CONTINUOUS LABORATORY CULTURES)	Fresh water, Aqueous (aquatic habitat), Renewal, NA F0 generation	Measured	0 mg/L / 0 mg/L / 0.77-1.1 mg/L	Mortality (Mortality-Mortality, Response Site: Not reported)	NR (0.77-1.1 mg/L)	Mortality	High	679904
28553-12-0	21 Day(s), (21 Day(s))	*Daphnia magna* (Water Flea), <24 Hour(s) (Measured in: F0 generation), Not Reported, Laboratory (CONTINUOUS LABORATORY CULTURES)	Fresh water, Aqueous (aquatic habitat), Renewal, NA F0 generation	Measured	0 mg/L / 0 mg/L / 0.77-1.1 mg/L	Reproduction (Reproduction-Progeny counts/numbers, Response Site: Not reported)	NOEC (0.77-1.1 mg/L)	Reproductive/Teratogenic	High	679904

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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
28553-12-0	21 Day(s), (21 Day(s))	*Daphnia magna* (Water Flea), <24 Hour(s) (Measured in: F0 generation), Not Reported, Laboratory (CONTINUOUS LABORATORY CULTURES)	Fresh water, Aqueous (aquatic habitat), Renewal, NA F0 generation	Measured	0 mg/L / 0 mg/L / 0.77-1.1 mg/L	Growth (Growth-Length, Response Site: Whole organism)	NOEC (0.77-1.1 mg/L)	Development/Growth	High	679904
28553-12-0	21 Day(s), (21 Day(s))	*Daphnia magna* (Water Flea), <24 Hour(s) (Measured in: F0 generation), Not Reported, Laboratory (CONTINUOUS LABORATORY CULTURES)	Fresh water, Aqueous (aquatic habitat), Renewal, NA F0 generation	Measured	0 mg/L / 0 mg/L / 1.0-1.1 mg/L	Growth (Growth-Length, Response Site: Whole organism)	NOEC (1.0-1.1 mg/L)	Development/Growth	High	679904
28553-12-0	21 Day(s), (21 Day(s))	*Daphnia magna* (Water Flea), <24 Hour(s) (Measured in: F0 generation), Not Reported, Laboratory (CONTINUOUS LABORATORY CULTURES)	Fresh water, Aqueous (aquatic habitat), Renewal, NA F0 generation	Measured	0 mg/L / 0 mg/L / 1.0-1.1 mg/L	Mortality (Mortality-Mortality, Response Site: Not reported)	NR (1.0-1.1 mg/L)	Mortality	High	679904
28553-12-0	21 Day(s), (21 Day(s))	*Daphnia magna* (Water Flea), <=24 Hour(s), Not Reported, Laboratory (SPRINGBORN LABORATORIES)	Fresh water, Aqueous (aquatic habitat), Flow-through, Not Reported	Measured	0 mg/L / 0.010 mg/L / 0.018 mg/L / 0.034 mg/L / 0.089 mg/L / 0.17 mg/L	Mortality (Mortality-Survival, Response Site: Not reported)	NOEC (0.034 mg/L)	Mortality	High	680120

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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
28553-12-0	21 Day(s), (21 Day(s))	*Daphnia magna* (Water Flea), <=24 Hour(s), Not Reported, Laboratory (SPRINGBORN LABORATO-RIES)	Fresh water, Aque-ous (aquatic habi-tat), Flow-through, Not Reported	Measured	0 mg/L / 0.010 mg/L / 0.018 mg/L / 0.034 mg/L / 0.089 mg/L / 0.17 mg/L	Reproduction (Reproduction-Progeny counts/numbers, Response Site: Not reported)	MATC (0.055 mg/L)	Reproduc-tive/Teratogenic	High	680120
28553-12-0	21 Day(s), (21 Day(s))	*Daphnia magna* (Water Flea), <=24 Hour(s), Not Reported, Laboratory (SPRINGBORN LABORATO-RIES)	Fresh water, Aque-ous (aquatic habi-tat), Flow-through, Not Reported	Measured	0 mg/L / 0.010 mg/L / 0.018 mg/L / 0.034 mg/L / 0.089 mg/L / 0.17 mg/L	Mortality (Mortality-Survival, Re-sponse Site: Not reported)	MATC (0.055 mg/L)	Mortality	High	680120
28553-12-0	21 Day(s), (21 Day(s))	*Daphnia magna* (Water Flea), <=24 Hour(s), Not Reported, Laboratory (SPRINGBORN LABORATO-RIES)	Fresh water, Aque-ous (aquatic habi-tat), Flow-through, Not Reported	Measured	0 mg/L / 0.010 mg/L / 0.018 mg/L / 0.034 mg/L / 0.089 mg/L / 0.17 mg/L	Reproduction (Reproduction-Progeny counts/numbers, Response Site: Not reported)	LOEC (0.089 mg/L)	Reproduc-tive/Teratogenic	High	680120
28553-12-0	21 Day(s), (21 Day(s))	*Daphnia magna* (Water Flea), <=24 Hour(s), Not Reported, Laboratory (SPRINGBORN LABORATO-RIES)	Fresh water, Aque-ous (aquatic habi-tat), Flow-through, Not Reported	Measured	0 mg/L / 0.010 mg/L / 0.018 mg/L / 0.034 mg/L / 0.089 mg/L / 0.17 mg/L	Mortality (Mortality-Survival, Re-sponse Site: Not reported)	LOEC (0.089 mg/L)	Mortality	High	680120
28553-12-0	21 Day(s), (21 Day(s))	*Daphnia magna* (Water Flea), <=24 Hour(s), Not Reported, Laboratory (SPRINGBORN LABORATO-RIES)	Fresh water, Aque-ous (aquatic habi-tat), Flow-through, Not Reported	Measured	0 mg/L / 0.010 mg/L / 0.018 mg/L / 0.034 mg/L / 0.089 mg/L / 0.17 mg/L	Reproduction (Reproduction-Progeny counts/numbers, Response Site: Not reported)	NOEC (0.034 mg/L)	Reproduc-tive/Teratogenic	High	680120

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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
28553-12-0	21 Day(s), (21 Day(s))	*Daphnia magna* (Water Flea), <=24 Hour(s), Not Reported, Laboratory (SPRINGBORN LABORATORIES)	Fresh water, Aqueous (aquatic habitat), Flow-through, Not Reported	Measured	0 mg/L / 0.010 mg/L / 0.018 mg/L / 0.034 mg/L / 0.089 mg/L / 0.17 mg/L	Mortality (Mortality-Mortality, Response Site: Not reported)	NR-LETH (0.17 mg/L)	Mortality	High	680120
28553-12-0	48 Hour(s), (48 Hour(s))	*Daphnia magna* (Water Flea), Instar, <20 Hour(s), Not Reported, Laboratory (UNION CARBIDE ENVIRONMENTAL SERVICES STOCK CULTURE)	Fresh water, Aqueous (aquatic habitat), Static, Not Reported	Unmeasured	0 mg/L / 0.32 mg/L / 0.56 mg/L / 1.00 mg/L / 1.80 mg/L / 3.20 mg/L / 5.60 mg/L	Mortality (Mortality-Mortality, Response Site: Not reported)	NOEC (<0.32 mg/L)	Mortality	Uninformative	1325557
28553-12-0	48 Hour(s), (48 Hour(s))	*Daphnia magna* (Water Flea), Instar, <20 Hour(s), Not Reported, Laboratory (UNION CARBIDE ENVIRONMENTAL SERVICES STOCK CULTURE)	Fresh water, Aqueous (aquatic habitat), Static, Not Reported	Unmeasured	0 mg/L / 0.32 mg/L / 0.56 mg/L / 1.00 mg/L / 1.80 mg/L / 3.20 mg/L / 5.60 mg/L	Mortality (Mortality-Mortality, Response Site: Not reported)	LOEC (0.32 mg/L)	Mortality	Uninformative	1325557
28553-12-0	10 Day(s), (10 Day(s))	*Hyalella azteca* (Scud), 7-14 Day(s), Not Reported, Laboratory (NR)	Fresh water, Aqueous (aquatic habitat), Sediment, Not Reported	Measured	<2.58 mg/kg dw sediment / 2900 (2670-3170) mg/kg dw sediment	Mortality (Mortality-Survival, Response Site: Not reported)	NR (2900 (2670-3170) mg/kg dw sediment)	Mortality	High	679311
28553-12-0	10 Day(s), (10 Day(s))	*Hyalella azteca* (Scud), 7-14 Day(s), Not Reported, Laboratory (NR)	Fresh water, Aqueous (aquatic habitat), Leaching , Not Reported	Measured	<0.043 mg/L / 0.442 (0.289-0.560) mg/L	Mortality (Mortality-Survival, Response Site: Not reported)	NR (0.442 (0.289-0.560) mg/L)	Mortality	High	679311
28553-12-0	10 Day(s), (10 Day(s))	*Hyalella azteca* (Scud), 7-14 Day(s), Not Reported, Laboratory (NR)	Fresh water, Aqueous (aquatic habitat), Sediment, Not Reported	Measured	<2.58 mg/kg dw sediment / 2900 (2670-3170) mg/kg dw sediment	Growth (Growth-Weight, Response Site: Whole organism)	NR (2900 (2670-3170) mg/kg dw sediment)	Development/Growth	High	679311

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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
28553-12-0	10 Day(s), (10 Day(s))	*Hyalella azteca* (Scud), 7-14 Day(s), Not Reported, Laboratory (NR)	Fresh water, Aqueous (aquatic habitat), Leaching , Not Reported	Measured	<0.043 mg/L / 0.442 (0.289-0.560) mg/L	Growth (Growth-Weight, Response Site: Whole organism)	NR (0.442 (0.289-0.560) mg/L)	Development/Growth	High	679311
28553-12-0	10 Day(s), (10 Day(s))	*Hyalella azteca* (Scud), 7-14 Day(s), Not Reported, Laboratory (NR)	Fresh water, Aqueous (aquatic habitat), Leaching , Not Reported	Measured	<0.043 mg/L / 0.442 (0.289-0.560) mg/L	Growth (Growth-Weight, Response Site: Whole organism)	NR (0.442 (0.289-0.560) mg/L)	Development/Growth	High	679311
28553-12-0	10 Day(s), (10 Day(s))	*Hyalella azteca* (Scud), 7-14 Day(s), Not Reported, Laboratory (NR)	Fresh water, Aqueous (aquatic habitat), Sediment, Not Reported	Measured	<2.58 mg/kg dw sediment / 2900 (2670-3170) mg/kg dw sediment	Growth (Growth-Weight, Response Site: Whole organism)	NR (2900 (2670-3170) mg/kg dw sediment)	Development/Growth	High	679311
28553-12-0	10 Day(s), (10 Day(s))	*Hyalella azteca* (Scud), 7-14 Day(s), Not Reported, Laboratory (NR)	Fresh water, Aqueous (aquatic habitat), Sediment, Not Reported	Measured	<2.58 mg/kg dw sediment / 2900 (2670-3170) mg/kg dw sediment	Mortality (Mortality-Survival, Response Site: Not reported)	NR (2900 (2670-3170) mg/kg dw sediment)	Mortality	High	679311
28553-12-0	10 Day(s), (10 Day(s))	*Hyalella azteca* (Scud), 7-14 Day(s), Not Reported, Laboratory (NR)	Fresh water, Aqueous (aquatic habitat), Leaching , Not Reported	Measured	<0.043 mg/L / 0.442 (0.289-0.560) mg/L	Mortality (Mortality-Survival, Response Site: Not reported)	NR (0.442 (0.289-0.560) mg/L)	Mortality	High	679311
28553-12-0	96 Hour(s), (96 Hour(s))	*Paratanytarsus parthenogeneticus* (Midge), 2-3 Instar, Not Reported, Not reported (NR)	Fresh water, Aqueous (aquatic habitat), Static, Not Reported	Measured	NR / NR	Mortality (Mortality-Mortality, Response Site: Not reported)	LC50 (>0.08 mg/L)	Mortality	High	1321996
28553-12-0	24 Hour(s), (48 Hour(s))	*Paratanytarsus parthenogeneticus* (Midge), Larva, Not Reported, Laboratory (EG&G BIONOMICS)	Fresh water, Aqueous (aquatic habitat), Static, Not Reported	Measured	<0.014 AI mg/L / 0.12-0.36 AI mg/L	Mortality (Mortality-Mortality, Response Site: Not reported)	LC50 (>0.12 AI mg/L)	Mortality	High	1316219

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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
28553-12-0	48 Hour(s), (48 Hour(s))	*Paratanytarsus parthenogeneticus* (Midge), Larva, Not Reported, Laboratory (EG&G BIONOMICS)	Fresh water, Aqueous (aquatic habitat), Static, Not Reported	Measured	<0.014 AI mg/L / 0.12-0.36 AI mg/L	Mortality (Mortality-Mortality, Response Site: Not reported)	NR-ZERO (0.12-0.36 AI mg/L)	Mortality	High	1316219
28553-12-0	48 Hour(s), (48 Hour(s))	*Paratanytarsus parthenogeneticus* (Midge), Larva, Not Reported, Laboratory (EG&G BIONOMICS)	Fresh water, Aqueous (aquatic habitat), Static, Not Reported	Measured	<0.014 AI mg/L / 0.12-0.36 AI mg/L	Mortality (Mortality-Mortality, Response Site: Not reported)	LC50 (>0.12 AI mg/L)	Mortality	High	1316219

* 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
28553-12-0	96 Hour(s), (96 Hour(s))	*Cyprinodon variegatus* (Sheepshead Minnow), Juvenile, Not Reported, Not reported (NR)	Fresh water, Aqueous (aquatic habitat), Flow-through, Not Reported	Measured	NR / NR	Mortality (Mortality-Mortality, Response Site: Not reported)	LC50 (>0.52 mg/L)	Mortality	High	1321996
28553-12-0	24 Hour(s), (96 Hour(s))	*Cyprinodon variegatus* (Sheepshead Minnow), Juvenile, <=10 Week(s), Not Reported, Laboratory (EITHER CULTURED AT LAB OR PURCHASED FROM A PROVEN HATCHERY IN MASSACHUSETTS)	Salt water, Aqueous (aquatic habitat), Flow-through, Not Reported	Measured	<0.0005 ppm / 0.21 (0.08-0.40) ppm / 0.52 (0.32-0.69) ppm	Mortality (Mortality-Mortality, Response Site: Not reported)	LC50 (>0.52 ppm)	Mortality	High	1316224
28553-12-0	48 Hour(s), (96 Hour(s))	*Cyprinodon variegatus* (Sheepshead Minnow), Juvenile, <=10 Week(s), Not Reported, Laboratory (EITHER CULTURED AT LAB OR PURCHASED FROM A PROVEN HATCHERY IN MASSACHUSETTS)	Salt water, Aqueous (aquatic habitat), Flow-through, Not Reported	Measured	<0.0005 ppm / 0.21 (0.08-0.40) ppm / 0.52 (0.32-0.69) ppm	Mortality (Mortality-Mortality, Response Site: Not reported)	LC50 (>0.52 ppm)	Mortality	High	1316224

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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
28553-12-0	72 Hour(s), (96 Hour(s))	*Cyprinodon variegatus* (Sheepshead Minnow), Juvenile, <=10 Week(s), Not Reported, Laboratory (EITHER CULTURED AT LAB OR PURCHASED FROM A PROVEN HATCHERY IN MASSACHUSETTS)	Salt water, Aqueous (aquatic habitat), Flow-through, Not Reported	Measured	<0.0005 ppm / 0.21 (0.08-0.40) ppm / 0.52 (0.32-0.69) ppm	Mortality (Mortality-Mortality, Response Site: Not reported)	LC50 (>0.52 ppm)	Mortality	High	1316224
28553-12-0	96 Hour(s), (96 Hour(s))	*Cyprinodon variegatus* (Sheepshead Minnow), Juvenile, <=10 Week(s), Not Reported, Laboratory (EITHER CULTURED AT LAB OR PURCHASED FROM A PROVEN HATCHERY IN MASSACHUSETTS)	Salt water, Aqueous (aquatic habitat), Flow-through, Not Reported	Measured	<0.0005 ppm / 0.21 (0.08-0.40) ppm / 0.52 (0.32-0.69) ppm	Mortality (Mortality-Mortality, Response Site: Not reported)	NOEC (0.52 ppm)	Mortality	High	1316224
28553-12-0	96 Hour(s), (96 Hour(s))	*Cyprinodon variegatus* (Sheepshead Minnow), Juvenile, <=10 Week(s), Not Reported, Laboratory (EITHER CULTURED AT LAB OR PURCHASED FROM A PROVEN HATCHERY IN MASSACHUSETTS)	Salt water, Aqueous (aquatic habitat), Flow-through, Not Reported	Measured	<0.0005 ppm / 0.21 (0.08-0.40) ppm / 0.52 (0.32-0.69) ppm	Mortality (Mortality-Mortality, Response Site: Not reported)	NR-ZERO (0.52 (0.37-0.69) ppm)	Mortality	High	1316224

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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
28553-12-0	72 Hour(s), (72 Hour(s))	*Danio rerio* (Zebra Danio), Embryo, 4-128 Cell stage, Not Reported, Laboratory (PURCHASED FROM THE ZEBRAFISH INTERNATIONAL RESOURCE CENTER (ZIRC) AT THE UNIVERSITY OF OREGON, EUGENE, OR)	Fresh water, Aqueous (aquatic habitat), Static, Not Reported	Unmeasured	0 ppm / 0 ppm / 0.01 ppm / 0.06 ppm / 0.30 ppm / 0.60 ppm / 1.50 ppm / 10.00 ppm / 50.00 ppm / 100.00 ppm / 500.00 ppm	Mortality (Mortality-Mortality, Response Site: Not reported)	NR (0.01-500.00 ppm)	Mortality	Medium	2298079
28553-12-0	21 Day(s), (21 Day(s))	*Danio rerio* (Zebra Danio), Adult, 1 Year(s), Both (Measured in: Female organisms), Laboratory	Fresh water, Aqueous (aquatic habitat), Renewal, NA Female organisms	Chemical analysis reported	0 ug/L / 0.42 ug/L / 4.2 ug/L / 42 ug/L	Cellular (Genetics-G-protein coupled receptor 55 mRNA, Response Site: Ovaries)	LOEC (42 ug/L)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Reproductive/Teratogenic	Medium	4829348
28553-12-0	21 Day(s), (21 Day(s))	*Danio rerio* (Zebra Danio), Adult, 1 Year(s), Both (Measured in: Female organisms), Laboratory	Fresh water, Aqueous (aquatic habitat), Renewal, NA Female organisms	Chemical analysis reported	0 ug/L / 0.42 ug/L / 4.2 ug/L / 42 ug/L	Biochemical (Biochemistry-Oleoylethanolamine, Response Site: Ovaries)	NOEC (4.2 ug/L)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Reproductive/Teratogenic	Medium	4829348
28553-12-0	21 Day(s), (21 Day(s))	*Danio rerio* (Zebra Danio), Adult, 1 Year(s), Both (Measured in: Male organisms), Laboratory	Fresh water, Aqueous (aquatic habitat), Renewal, NA Male organisms	Chemical analysis reported	0 ug/L / 0.42 ug/L / 4.2 ug/L / 42 ug/L	Cellular (Genetics-Endocannabinoid receptor type 2 mRNA, Response Site: Testes)	NOEC (4.2 ug/L)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Reproductive/Teratogenic	Medium	4829348
28553-12-0	21 Day(s), (21 Day(s))	*Danio rerio* (Zebra Danio), Adult, 1 Year(s), Both (Measured in: Female organisms), Laboratory	Fresh water, Aqueous (aquatic habitat), Renewal, NA Female organisms	Chemical analysis reported	0 ug/L / 0.42 ug/L / 4.2 ug/L / 42 ug/L	Cellular (Genetics-G-protein coupled receptor 55 mRNA, Response Site: Ovaries)	NOEC (4.2 ug/L)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Reproductive/Teratogenic	Medium	4829348

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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
28553-12-0	21 Day(s), (21 Day(s))	*Danio rerio* (Zebra Danio), Adult, 1 Year(s), Both (Measured in: Female organisms), Laboratory	Fresh water, Aqueous (aquatic habitat), Renewal, NA Female organisms	Chemical analysis reported	0 ug/L / 0.42 ug/L / 4.2 ug/L / 42 ug/L	Biochemical (Biochemistry-Anandamide, Response Site: Ovaries)	NOEC (42 ug/L)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Reproductive/Teratogenic	Medium	4829348
28553-12-0	21 Day(s), (21 Day(s))	*Danio rerio* (Zebra Danio), Adult, 1 Year(s), Both (Measured in: Female organisms), Laboratory	Fresh water, Aqueous (aquatic habitat), Renewal, NA Female organisms	Chemical analysis reported	0 ug/L / 0.42 ug/L / 4.2 ug/L / 42 ug/L	Biochemical (Biochemistry-Palmitoylethanolamide, Response Site: Ovaries)	NOEC (42 ug/L)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Reproductive/Teratogenic	Medium	4829348
28553-12-0	21 Day(s), (21 Day(s))	*Danio rerio* (Zebra Danio), Adult, 1 Year(s), Both (Measured in: Female organisms), Laboratory	Fresh water, Aqueous (aquatic habitat), Renewal, NA Female organisms	Chemical analysis reported	0 ug/L / 0.42 ug/L / 4.2 ug/L / 42 ug/L	Biochemical (Enzyme(s)-Fatty acid amide hydrolase, Response Site: Ovaries)	NOEC (42 ug/L)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Reproductive/Teratogenic	Medium	4829348
28553-12-0	21 Day(s), (21 Day(s))	*Danio rerio* (Zebra Danio), Adult, 1 Year(s), Both (Measured in: Male organisms), Laboratory	Fresh water, Aqueous (aquatic habitat), Renewal, NA Male organisms	Chemical analysis reported	0 ug/L / 0.42 ug/L / 4.2 ug/L / 42 ug/L	Cellular (Genetics-Transient receptor potential cation channel subfamily V member 1 mRNA, Response Site: Testes)	NR (0.42-42 ug/L)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Reproductive/Teratogenic	Medium	4829348
28553-12-0	21 Day(s), (21 Day(s))	*Danio rerio* (Zebra Danio), Adult, 1 Year(s), Both (Measured in: Male organisms), Laboratory	Fresh water, Aqueous (aquatic habitat), Renewal, NA Male organisms	Chemical analysis reported	0 ug/L / 0.42 ug/L / 4.2 ug/L / 42 ug/L	Cellular (Genetics-Abhydrolase domain containing 4 mRNA, Response Site: Testes)	NOEC (42 ug/L)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Reproductive/Teratogenic	Medium	4829348
28553-12-0	21 Day(s), (21 Day(s))	*Danio rerio* (Zebra Danio), Adult, 1 Year(s), Both (Measured in: Male organisms), Laboratory	Fresh water, Aqueous (aquatic habitat), Renewal, NA Male organisms	Chemical analysis reported	0 ug/L / 0.42 ug/L / 4.2 ug/L / 42 ug/L	Biochemical (Biochemistry-Anandamide, Response Site: Testes)	LOEC (4.2 ug/L)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Reproductive/Teratogenic	Medium	4829348

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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
28553-12-0	14-21 Day(s), (21 Day(s))	*Danio rerio* (Zebra Danio), Adult, 1 Year(s), Both (Measured in: Female organisms), Laboratory	Fresh water, Aqueous (aquatic habitat), Renewal, NA Female organisms	Chemical analysis reported	0 ug/L / 0.42 ug/L / 4.2 ug/L / 42 ug/L	Reproduction (Reproduction-Progeny counts/numbers, Response Site: Not reported)	NR (0.42-42 ug/L)	Reproductive/Teratogenic	Medium	4829348
28553-12-0	21 Day(s), (21 Day(s))	*Danio rerio* (Zebra Danio), Adult, 1 Year(s), Both (Measured in: Male organisms), Laboratory	Fresh water, Aqueous (aquatic habitat), Renewal, NA Male organisms	Chemical analysis reported	0 ug/L / 0.42 ug/L / 4.2 ug/L / 42 ug/L	Biochemical (Biochemistry-2-Arachidonoylglycerol, Response Site: Testes)	LOEC (0.42 ug/L)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Reproductive/Teratogenic	Medium	4829348
28553-12-0	21 Day(s), (21 Day(s))	*Danio rerio* (Zebra Danio), Adult, 1 Year(s), Both (Measured in: Male organisms), Laboratory	Fresh water, Aqueous (aquatic habitat), Renewal, NA Male organisms	Chemical analysis reported	0 ug/L / 0.42 ug/L / 4.2 ug/L / 42 ug/L	Cellular (Genetics-Androgen receptor mRNA, Response Site: Testes)	LOEC (0.42 ug/L)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Reproductive/Teratogenic	Medium	4829348
28553-12-0	21 Day(s), (21 Day(s))	*Danio rerio* (Zebra Danio), Adult, 1 Year(s), Both (Measured in: Male organisms), Laboratory	Fresh water, Aqueous (aquatic habitat), Renewal, NA Male organisms	Chemical analysis reported	0 ug/L / 0.42 ug/L / 4.2 ug/L / 42 ug/L	Cellular (Genetics-Diacylglycerol lipase, alpha mRNA, Response Site: Testes)	LOEC (0.42 ug/L)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Reproductive/Teratogenic	Medium	4829348
28553-12-0	21 Day(s), (21 Day(s))	*Danio rerio* (Zebra Danio), Adult, 1 Year(s), Both (Measured in: Male organisms), Laboratory	Fresh water, Aqueous (aquatic habitat), Renewal, NA Male organisms	Chemical analysis reported	0 ug/L / 0.42 ug/L / 4.2 ug/L / 42 ug/L	Cellular (Genetics-Endocannabinoid receptor type 1 mRNA, Response Site: Testes)	LOEC (0.42 ug/L)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Reproductive/Teratogenic	Medium	4829348
28553-12-0	21 Day(s), (21 Day(s))	*Danio rerio* (Zebra Danio), Adult, 1 Year(s), Both (Measured in: Male organisms), Laboratory	Fresh water, Aqueous (aquatic habitat), Renewal, NA Male organisms	Chemical analysis reported	0 ug/L / 0.42 ug/L / 4.2 ug/L / 42 ug/L	Cellular (Genetics-Estrogen receptor alpha mRNA, Response Site: Testes)	LOEC (0.42 ug/L)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Reproductive/Teratogenic	Medium	4829348

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CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
28553-12-0	21 Day(s), (21 Day(s))	*Danio rerio* (Zebra Danio), Adult, 1 Year(s), Both (Measured in: Male organisms), Laboratory	Fresh water, Aqueous (aquatic habitat), Renewal, NA Male organisms	Chemical analysis reported	0 ug/L / 0.42 ug/L / 4.2 ug/L / 42 ug/L	Cellular (Genetics-Estrogen receptor beta1 protein mRNA, Response Site: Testes)	LOEC (0.42 ug/L)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Reproductive/Teratogenic	Medium	4829348
28553-12-0	21 Day(s), (21 Day(s))	*Danio rerio* (Zebra Danio), Adult, 1 Year(s), Both (Measured in: Male organisms), Laboratory	Fresh water, Aqueous (aquatic habitat), Renewal, NA Male organisms	Chemical analysis reported	0 ug/L / 0.42 ug/L / 4.2 ug/L / 42 ug/L	Cellular (Genetics-Fatty acid amide hydrolase mRNA, Response Site: Testes)	LOEC (0.42 ug/L)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Reproductive/Teratogenic	Medium	4829348
28553-12-0	21 Day(s), (21 Day(s))	*Danio rerio* (Zebra Danio), Adult, 1 Year(s), Both (Measured in: Male organisms), Laboratory	Fresh water, Aqueous (aquatic habitat), Renewal, NA Male organisms	Chemical analysis reported	0 ug/L / 0.42 ug/L / 4.2 ug/L / 42 ug/L	Growth (Morphology-Organ weight in relationship to body weight, Response Site: Testes)	LOEC (0.42 ug/L)	Reproductive/Teratogenic	Medium	4829348
28553-12-0	21 Day(s), (21 Day(s))	*Danio rerio* (Zebra Danio), Adult, 1 Year(s), Both (Measured in: Female organisms), Laboratory	Fresh water, Aqueous (aquatic habitat), Renewal, NA Female organisms	Chemical analysis reported	0 ug/L / 0.42 ug/L / 4.2 ug/L / 42 ug/L	Cellular (Genetics-COX2 mRNA, Response Site: Ovaries)	NOEC (42 ug/L)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Reproductive/Teratogenic	Medium	4829348
28553-12-0	21 Day(s), (21 Day(s))	*Danio rerio* (Zebra Danio), Adult, 1 Year(s), Both (Measured in: Female organisms), Laboratory	Fresh water, Aqueous (aquatic habitat), Renewal, NA Female organisms	Chemical analysis reported	0 ug/L / 0.42 ug/L / 4.2 ug/L / 42 ug/L	Biochemical (Biochemistry-Oleoylethanolamine, Response Site: Ovaries)	LOEC (42 ug/L)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Reproductive/Teratogenic	Medium	4829348
28553-12-0	21 Day(s), (21 Day(s))	*Danio rerio* (Zebra Danio), Adult, 1 Year(s), Both (Measured in: Male organisms), Laboratory	Fresh water, Aqueous (aquatic habitat), Renewal, NA Male organisms	Chemical analysis reported	0 ug/L / 0.42 ug/L / 4.2 ug/L / 42 ug/L	Cellular (Genetics-Endocannabinoid receptor type 2 mRNA, Response Site: Testes)	LOEC (42 ug/L)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Reproductive/Teratogenic	Medium	4829348

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CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
28553-12-0	21 Day(s), (21 Day(s))	*Danio rerio* (Zebra Danio), Adult, 1 Year(s), Both (Measured in: Female organisms), Laboratory	Fresh water, Aqueous (aquatic habitat), Renewal, NA Female organisms	Chemical analysis reported	0 ug/L / 0.42 ug/L / 4.2 ug/L / 42 ug/L	Biochemical (Biochemistry-2-Arachidonoylglycerol, Response Site: Ovaries)	NR (0.42-42 ug/L)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Reproductive/Teratogenic	Medium	4829348
28553-12-0	21 Day(s), (21 Day(s))	*Danio rerio* (Zebra Danio), Adult, 1 Year(s), Both (Measured in: Male organisms), Laboratory	Fresh water, Aqueous (aquatic habitat), Renewal, NA Male organisms	Chemical analysis reported	0 ug/L / 0.42 ug/L / 4.2 ug/L / 42 ug/L	Biochemical (Biochemistry-Oleoylethanolamine, Response Site: Testes)	NR (0.42-42 ug/L)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Reproductive/Teratogenic	Medium	4829348
28553-12-0	21 Day(s), (21 Day(s))	*Danio rerio* (Zebra Danio), Adult, 1 Year(s), Both (Measured in: Male organisms), Laboratory	Fresh water, Aqueous (aquatic habitat), Renewal, NA Male organisms	Chemical analysis reported	0 ug/L / 0.42 ug/L / 4.2 ug/L / 42 ug/L	Biochemical (Biochemistry-Palmitoylethanolamide, Response Site: Testes)	NR (0.42-42 ug/L)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Reproductive/Teratogenic	Medium	4829348
28553-12-0	21 Day(s), (21 Day(s))	*Danio rerio* (Zebra Danio), Adult, 1 Year(s), Both (Measured in: Male organisms), Laboratory	Fresh water, Aqueous (aquatic habitat), Renewal, NA Male organisms	Chemical analysis reported	0 ug/L / 0.42 ug/L / 4.2 ug/L / 42 ug/L	Biochemical (Enzyme(s)-Fatty acid amide hydrolase, Response Site: Testes)	NR (0.42-42 ug/L)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Reproductive/Teratogenic	Medium	4829348
28553-12-0	21 Day(s), (21 Day(s))	*Danio rerio* (Zebra Danio), Adult, 1 Year(s), Both (Measured in: Female organisms), Laboratory	Fresh water, Aqueous (aquatic habitat), Renewal, NA Female organisms	Chemical analysis reported	0 ug/L / 0.42 ug/L / 4.2 ug/L / 42 ug/L	Cellular (Genetics-Abhydrolase domain containing 4 mRNA, Response Site: Ovaries)	NR (0.42-42 ug/L)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Reproductive/Teratogenic	Medium	4829348
28553-12-0	21 Day(s), (21 Day(s))	*Danio rerio* (Zebra Danio), Adult, 1 Year(s), Both (Measured in: Male organisms), Laboratory	Fresh water, Aqueous (aquatic habitat), Renewal, NA Male organisms	Chemical analysis reported	0 ug/L / 0.42 ug/L / 4.2 ug/L / 42 ug/L	Cellular (Genetics-COX2 mRNA, Response Site: Testes)	NR (0.42-42 ug/L)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Reproductive/Teratogenic	Medium	4829348

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CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
28553-12-0	21 Day(s), (21 Day(s))	*Danio rerio* (Zebra Danio), Adult, 1 Year(s), Both (Measured in: Female organisms), Laboratory	Fresh water, Aqueous (aquatic habitat), Renewal, NA Female organisms	Chemical analysis reported	0 ug/L / 0.42 ug/L / 4.2 ug/L / 42 ug/L	Cellular (Genetics-Diacylglycerol lipase, alpha mRNA, Response Site: Ovaries)	NR (0.42-42 ug/L)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Reproductive/Teratogenic	Medium	4829348
28553-12-0	21 Day(s), (21 Day(s))	*Danio rerio* (Zebra Danio), Adult, 1 Year(s), Both (Measured in: Female organisms), Laboratory	Fresh water, Aqueous (aquatic habitat), Renewal, NA Female organisms	Chemical analysis reported	0 ug/L / 0.42 ug/L / 4.2 ug/L / 42 ug/L	Cellular (Genetics-Endocannabinoid receptor type 1 mRNA, Response Site: Ovaries)	NR (0.42-42 ug/L)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Reproductive/Teratogenic	Medium	4829348
28553-12-0	21 Day(s), (21 Day(s))	*Danio rerio* (Zebra Danio), Adult, 1 Year(s), Both (Measured in: Female organisms), Laboratory	Fresh water, Aqueous (aquatic habitat), Renewal, NA Female organisms	Chemical analysis reported	0 ug/L / 0.42 ug/L / 4.2 ug/L / 42 ug/L	Cellular (Genetics-Fatty acid amide hydrolase mRNA, Response Site: Ovaries)	NR (0.42-42 ug/L)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Reproductive/Teratogenic	Medium	4829348
28553-12-0	21 Day(s), (21 Day(s))	*Danio rerio* (Zebra Danio), Adult, 1 Year(s), Both (Measured in: Male organisms), Laboratory	Fresh water, Aqueous (aquatic habitat), Renewal, NA Male organisms	Chemical analysis reported	0 ug/L / 0.42 ug/L / 4.2 ug/L / 42 ug/L	Cellular (Genetics-G-protein coupled receptor 55 mRNA, Response Site: Testes)	NR (0.42-42 ug/L)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Reproductive/Teratogenic	Medium	4829348
28553-12-0	21 Day(s), (21 Day(s))	*Danio rerio* (Zebra Danio), Adult, 1 Year(s), Both (Measured in: Male organisms), Laboratory	Fresh water, Aqueous (aquatic habitat), Renewal, NA Male organisms	Chemical analysis reported	0 ug/L / 0.42 ug/L / 4.2 ug/L / 42 ug/L	Cellular (Genetics-Monoacylglycerol hydrolyzate mRNA, Response Site: Testes)	NR (0.42-42 ug/L)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Reproductive/Teratogenic	Medium	4829348
28553-12-0	21 Day(s), (21 Day(s))	*Danio rerio* (Zebra Danio), Adult, 1 Year(s), Both (Measured in: Female organisms), Laboratory	Fresh water, Aqueous (aquatic habitat), Renewal, NA Female organisms	Chemical analysis reported	0 ug/L / 0.42 ug/L / 4.2 ug/L / 42 ug/L	Cellular (Genetics-N-acyl phosphatidylethanolamine phospholipase D mRNA, Response Site: Ovaries)	NR (0.42-42 ug/L)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Reproductive/Teratogenic	Medium	4829348

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CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
28553-12-0	21 Day(s), (21 Day(s))	*Danio rerio* (Zebra Danio), Adult, 1 Year(s), Both (Measured in: Male organisms), Laboratory	Fresh water, Aqueous (aquatic habitat), Renewal, NA Male organisms	Chemical analysis reported	0 ug/L / 0.42 ug/L / 4.2 ug/L / 42 ug/L	Cellular (Genetics-N-acyl phosphatidylethanolamine phospholipase D mRNA, Response Site: Testes)	NR (0.42-42 ug/L)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Reproductive/Teratogenic	Medium	4829348
28553-12-0	21 Day(s), (21 Day(s))	*Danio rerio* (Zebra Danio), Adult, 1 Year(s), Both (Measured in: Female organisms), Laboratory	Fresh water, Aqueous (aquatic habitat), Renewal, NA Female organisms	Chemical analysis reported	0 ug/L / 0.42 ug/L / 4.2 ug/L / 42 ug/L	Cellular (Genetics-Transient receptor potential cation channel subfamily V member 1 mRNA, Response Site: Ovaries)	NR (0.42-42 ug/L)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Reproductive/Teratogenic	Medium	4829348
28553-12-0	21 Day(s), (21 Day(s))	*Danio rerio* (Zebra Danio), Adult, 1 Year(s), Both (Measured in: Female organisms), Laboratory	Fresh water, Aqueous (aquatic habitat), Renewal, NA Female organisms	Chemical analysis reported	0 ug/L / 0.42 ug/L / 4.2 ug/L / 42 ug/L	Cellular (Histology-Histological changes, general, Response Site: Ovaries)	NR (0.42-42 ug/L)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Reproductive/Teratogenic	Medium	4829348
28553-12-0	21 Day(s), (21 Day(s))	*Danio rerio* (Zebra Danio), Adult, 1 Year(s), Both (Measured in: Male organisms), Laboratory	Fresh water, Aqueous (aquatic habitat), Renewal, NA Male organisms	Chemical analysis reported	0 ug/L / 0.42 ug/L / 4.2 ug/L / 42 ug/L	Cellular (Histology-Histological changes, general, Response Site: Testes)	NR (0.42-42 ug/L)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Reproductive/Teratogenic	Medium	4829348
28553-12-0	21 Day(s), (21 Day(s))	*Danio rerio* (Zebra Danio), Adult, 1 Year(s), Both (Measured in: Female organisms), Laboratory	Fresh water, Aqueous (aquatic habitat), Renewal, NA Female organisms	Chemical analysis reported	0 ug/L / 0.42 ug/L / 4.2 ug/L / 42 ug/L	Growth (Morphology-Organ weight in relationship to body weight, Response Site: Ovaries)	NR (0.42-42 ug/L)	Reproductive/Teratogenic	Medium	4829348
28553-12-0	21 Day(s), (21 Day(s))	*Danio rerio* (Zebra Danio), Adult, 1 Year(s), Both (Measured in: Male organisms), Laboratory	Fresh water, Aqueous (aquatic habitat), Renewal, NA Male organisms	Chemical analysis reported	0 ug/L / 0.42 ug/L / 4.2 ug/L / 42 ug/L	Biochemical (Biochemistry-Anandamide, Response Site: Testes)	NOEC (0.42 ug/L)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Reproductive/Teratogenic	Medium	4829348

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CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
28553-12-0	21 Day(s), (21 Day(s))	*Danio rerio* (Zebra Danio), Adult, 1 Year(s), Both (Measured in: Female organisms), Laboratory	Fresh water, Aqueous (aquatic habitat), Renewal, NA Female organisms	Chemical analysis reported	0 ug/L / 0.42 ug/L / 4.2 ug/L / 42 ug/L	Cellular (Genetics-Monoacylglycerol hydrolyzate mRNA, Response Site: Ovaries)	NR (0.42-42 ug/L)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Reproductive/Teratogenic	Medium	4829348
28553-12-0	21 Day(s), (21 Day(s))	*Danio rerio* (Zebra Danio), Adult, 1 Year(s), Both (Measured in: Female organisms), Laboratory	Fresh water, Aqueous (aquatic habitat), Renewal, NA Female organisms	Chemical analysis reported	0 ug/L / 0.42 ug/L / 4.2 ug/L / 42 ug/L	Cellular (Genetics-Endocannabinoid receptor type 2 mRNA, Response Site: Ovaries)	NOEC (42 ug/L)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Reproductive/Teratogenic	Medium	4829348
28553-12-0	21 Day(s), (21 Day(s))	*Danio rerio* (Zebra Danio), Adult, 1 Year(s), Female, Not reported (NR)	Fresh water, Aqueous (aquatic habitat), Static, Not Reported	Chemical analysis reported	0 ug/L / 0.42 ug/L / 4.2 ug/L / 42 ug/L	Cellular (Genetics-Glucocorticoid receptor mRNA, Response Site: Ovaries)	NOEC (42 ug/L)	Mechanistic: Cell signaling/function; Oxidative stress (including redox biology); Reproductive/Teratogenic	Medium	9419241
28553-12-0	21 Day(s), (21 Day(s))	*Danio rerio* (Zebra Danio), Adult, 1 Year(s), Female, Not reported (NR)	Fresh water, Aqueous (aquatic habitat), Static, Not Reported	Chemical analysis reported	0 ug/L / 0.42 ug/L / 4.2 ug/L / 42 ug/L	Cellular (Genetics-Fas ligand (TNF superfamily, member 6) mRNA, Response Site: Ovaries)	NOEC (42 ug/L)	Mechanistic: Cell signaling/function; Oxidative stress (including redox biology); Reproductive/Teratogenic	Medium	9419241
28553-12-0	21 Day(s), (21 Day(s))	*Danio rerio* (Zebra Danio), Adult, 1 Year(s), Female, Not reported (NR)	Fresh water, Aqueous (aquatic habitat), Static, Not Reported	Chemical analysis reported	0 ug/L / 0.42 ug/L / 4.2 ug/L / 42 ug/L	Cellular (Genetics-Catalase mRNA, Response Site: Ovaries)	NOEC (42 ug/L)	Mechanistic: Cell signaling/function; Oxidative stress (including redox biology); Reproductive/Teratogenic	Medium	9419241
28553-12-0	21 Day(s), (21 Day(s))	*Danio rerio* (Zebra Danio), Adult, 1 Year(s), Female, Not reported (NR)	Fresh water, Aqueous (aquatic habitat), Static, Not Reported	Chemical analysis reported	0 ug/L / 0.42 ug/L / 4.2 ug/L / 42 ug/L	Cellular (Genetics-Caspase-3 mRNA, Response Site: Ovarian follicle)	NOEC (42 ug/L)	Reproductive/Teratogenic	Medium	9419241

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CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
28553-12-0	21 Day(s), (21 Day(s))	*Danio rerio* (Zebra Danio), Adult, 1 Year(s), Female, Not reported (NR)	Fresh water, Aqueous (aquatic habitat), Static, Not Reported	Chemical analysis reported	0 ug/L / 0.42 ug/L / 4.2 ug/L / 42 ug/L	Cellular (Genetics-Caspase 8 mRNA, Response Site: Ovaries)	NOEC (42 ug/L)	Mechanistic: Cell signaling/function; Oxidative stress (including redox biology); Reproductive/Teratogenic	Medium	9419241
28553-12-0	21 Day(s), (21 Day(s))	*Danio rerio* (Zebra Danio), Adult, 1 Year(s), Female, Not reported (NR)	Fresh water, Aqueous (aquatic habitat), Static, Not Reported	Chemical analysis reported	0 ug/L / 0.42 ug/L / 4.2 ug/L / 42 ug/L	Cellular (Genetics-Caspase 3a mRNA, Response Site: Ovaries)	NOEC (42 ug/L)	Mechanistic: Cell signaling/function; Oxidative stress (including redox biology); Reproductive/Teratogenic	Medium	9419241
28553-12-0	21 Day(s), (21 Day(s))	*Danio rerio* (Zebra Danio), Adult, 1 Year(s), Female, Not reported (NR)	Fresh water, Aqueous (aquatic habitat), Static, Not Reported	Chemical analysis reported	0 ug/L / 0.42 ug/L / 4.2 ug/L / 42 ug/L	Cellular (Genetics-Beclin-1 mRNA, Response Site: Ovaries)	NOEC (42 ug/L)	Mechanistic: Cell signaling/function; Oxidative stress (including redox biology); Reproductive/Teratogenic	Medium	9419241
28553-12-0	21 Day(s), (21 Day(s))	*Danio rerio* (Zebra Danio), Adult, 1 Year(s), Female, Not reported (NR)	Fresh water, Aqueous (aquatic habitat), Static, Not Reported	Chemical analysis reported	0 ug/L / 0.42 ug/L / 4.2 ug/L / 42 ug/L	Cellular (Genetics-BH3 interacting domain death agonist mRNA, Response Site: Ovaries)	NOEC (42 ug/L)	Mechanistic: Cell signaling/function; Oxidative stress (including redox biology); Reproductive/Teratogenic	Medium	9419241
28553-12-0	21 Day(s), (21 Day(s))	*Danio rerio* (Zebra Danio), Adult, 1 Year(s), Female, Not reported (NR)	Fresh water, Aqueous (aquatic habitat), Static, Not Reported	Chemical analysis reported	0 ug/L / 0.42 ug/L / 4.2 ug/L / 42 ug/L	Cellular (Genetics-Glutathione S-transferase omega-1 mRNA, Response Site: Ovaries)	NOEC (42 ug/L)	Mechanistic: Cell signaling/function; Oxidative stress (including redox biology); Reproductive/Teratogenic	Medium	9419241
28553-12-0	21 Day(s), (21 Day(s))	*Danio rerio* (Zebra Danio), Adult, 1 Year(s), Female, Not reported (NR)	Fresh water, Aqueous (aquatic habitat), Static, Not Reported	Chemical analysis reported	0 ug/L / 0.42 ug/L / 4.2 ug/L / 42 ug/L	Cellular (Genetics-Glutathione peroxidase 1a mRNA, Response Site: Ovaries)	NOEC (42 ug/L)	Mechanistic: Cell signaling/function; Oxidative stress (including redox biology); Reproductive/Teratogenic	Medium	9419241

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CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
28553-12-0	21 Day(s), (21 Day(s))	*Danio rerio* (Zebra Danio), Adult, 1 Year(s), Female, Not reported (NR)	Fresh water, Aqueous (aquatic habitat), Static, Not Reported	Chemical analysis reported	0 ug/L / 0.42 ug/L / 4.2 ug/L / 42 ug/L	Cellular (Genetics-Mechanistic target of rapamycin kinase mRNA, Response Site: Ovaries)	NOEC (42 ug/L)	Mechanistic: Cell signaling/function; Oxidative stress (including redox biology); Reproductive/Teratogenic	Medium	9419241
28553-12-0	21 Day(s), (21 Day(s))	*Danio rerio* (Zebra Danio), Adult, 1 Year(s), Female, Not reported (NR)	Fresh water, Aqueous (aquatic habitat), Static, Not Reported	Chemical analysis reported	0 ug/L / 0.42 ug/L / 4.2 ug/L / 42 ug/L	Cellular (Genetics-Glutathione reductase mRNA, Response Site: Ovaries)	NOEC (42 ug/L)	Mechanistic: Cell signaling/function; Oxidative stress (including redox biology); Reproductive/Teratogenic	Medium	9419241
28553-12-0	21 Day(s), (21 Day(s))	*Danio rerio* (Zebra Danio), Adult, 1 Year(s), Female, Not reported (NR)	Fresh water, Aqueous (aquatic habitat), Static, Not Reported	Chemical analysis reported	0 ug/L / 0.42 ug/L / 4.2 ug/L / 42 ug/L	Cellular (Genetics-UV radiation resistance associated gene mRNA, Response Site: Ovaries)	NOEC (42 ug/L)	Mechanistic: Cell signaling/function; Oxidative stress (including redox biology); Reproductive/Teratogenic	Medium	9419241
28553-12-0	21 Day(s), (21 Day(s))	*Danio rerio* (Zebra Danio), Adult, 1 Year(s), Female, Not reported (NR)	Fresh water, Aqueous (aquatic habitat), Static, Not Reported	Chemical analysis reported	0 ug/L / 0.42 ug/L / 4.2 ug/L / 42 ug/L	Cellular (Genetics-Apoptotic protease-activating factor 1 mRNA, Response Site: Ovaries)	NOEC (42 ug/L)	Mechanistic: Cell signaling/function; Oxidative stress (including redox biology); Reproductive/Teratogenic	Medium	9419241
28553-12-0	21 Day(s), (21 Day(s))	*Danio rerio* (Zebra Danio), Adult, 1 Year(s), Female, Not reported (NR)	Fresh water, Aqueous (aquatic habitat), Static, Not Reported	Chemical analysis reported	0 ug/L / 0.42 ug/L / 4.2 ug/L / 42 ug/L	Cellular (Genetics-Protein kinase, AMP-activated, alpha 1 catalytic subunit mRNA, Response Site: Ovaries)	NR (0.42-42 ug/L)	Mechanistic: Cell signaling/function; Oxidative stress (including redox biology); Reproductive/Teratogenic	Medium	9419241
28553-12-0	21 Day(s), (21 Day(s))	*Danio rerio* (Zebra Danio), Adult, 1 Year(s), Female, Not reported (NR)	Fresh water, Aqueous (aquatic habitat), Static, Not Reported	Chemical analysis reported	0 ug/L / 0.42 ug/L / 4.2 ug/L / 42 ug/L	Cellular (Genetics-Caspase-3 mRNA, Response Site: Ovarian follicle)	NR (0.42-42 ug/L)	Reproductive/Teratogenic	Medium	9419241

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28553-12-0	21 Day(s), (21 Day(s))	*Danio rerio* (Zebra Danio), Adult, 1 Year(s), Female, Not reported (NR)	Fresh water, Aqueous (aquatic habitat), Static, Not Reported	Chemical analysis reported	0 ug/L / 0.42 ug/L / 4.2 ug/L / 42 ug/L	Cellular (Genetics-BCL2 associated agonist of cell death mRNA, Response Site: Ovaries)	NR (0.42-42 ug/L)	Mechanistic: Cell signaling/function; Oxidative stress (including redox biology); Reproductive/Teratogenic	Medium	9419241
28553-12-0	21 Day(s), (21 Day(s))	*Danio rerio* (Zebra Danio), Adult, 1 Year(s), Female, Not reported (NR)	Fresh water, Aqueous (aquatic habitat), Static, Not Reported	Chemical analysis reported	0 ug/L / 0.42 ug/L / 4.2 ug/L / 42 ug/L	Cellular (Genetics-Apoptosis, Response Site: Ovarian follicle)	NR (0.42-42 ug/L)	Reproductive/Teratogenic	Medium	9419241
28553-12-0	21 Day(s), (21 Day(s))	*Danio rerio* (Zebra Danio), Adult, 1 Year(s), Female, Not reported (NR)	Fresh water, Aqueous (aquatic habitat), Static, Not Reported	Chemical analysis reported	0 ug/L / 0.42 ug/L / 4.2 ug/L / 42 ug/L	Cellular (Genetics-Superoxide dismutase 2 mRNA, Response Site: Ovaries)	NOEC (42 ug/L)	Mechanistic: Cell signaling/function; Oxidative stress (including redox biology); Reproductive/Teratogenic	Medium	9419241
28553-12-0	21 Day(s), (21 Day(s))	*Danio rerio* (Zebra Danio), Adult, 1 Year(s), Female, Not reported (NR)	Fresh water, Aqueous (aquatic habitat), Static, Not Reported	Chemical analysis reported	0 ug/L / 0.42 ug/L / 4.2 ug/L / 42 ug/L	Cellular (Genetics-Apoptosis regulator Bcl-2 mRNA, Response Site: Ovaries)	NOEC (42 ug/L)	Mechanistic: Cell signaling/function; Oxidative stress (including redox biology); Reproductive/Teratogenic	Medium	9419241
28553-12-0	21 Day(s), (21 Day(s))	*Danio rerio* (Zebra Danio), Adult, 1 Year(s), Female, Not reported (NR)	Fresh water, Aqueous (aquatic habitat), Static, Not Reported	Chemical analysis reported	0 ug/L / 0.42 ug/L / 4.2 ug/L / 42 ug/L	Cellular (Genetics-Microtubule-associated protein 1 light chain 3 beta mRNA, Response Site: Ovaries)	NOEC (42 ug/L)	Mechanistic: Cell signaling/function; Oxidative stress (including redox biology); Reproductive/Teratogenic	Medium	9419241
28553-12-0	21 Day(s), (21 Day(s))	*Danio rerio* (Zebra Danio), Adult, 1 Year(s), Female, Not reported (NR)	Fresh water, Aqueous (aquatic habitat), Static, Not Reported	Chemical analysis reported	0 ug/L / 0.42 ug/L / 4.2 ug/L / 42 ug/L	Cellular (Genetics-Tumor necrosis factor mRNA, Response Site: Ovaries)	NR (0.42-42 ug/L)	Mechanistic: Cell signaling/function; Oxidative stress (including redox biology); Reproductive/Teratogenic	Medium	9419241

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CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
28553-12-0	21 Day(s), (21 Day(s))	*Danio rerio* (Zebra Danio), Adult, 1 Year(s), Female, Not reported (NR)	Fresh water, Aqueous (aquatic habitat), Static, Not Reported	Chemical analysis reported	0 ug/L / 0.42 ug/L / 4.2 ug/L / 42 ug/L	Cellular (Genetics-Superoxide dismutase 1 mRNA, Response Site: Ovaries)	NR (0.42-42 ug/L)	Mechanistic: Cell signaling/function; Oxidative stress (including redox biology); Reproductive/Teratogenic	Medium	9419241
28553-12-0	8 Day(s), (21 Day(s))	*Danio rerio* (Zebra Danio), Adult, Female, Laboratory	Fresh water, Aqueous (aquatic habitat), Static, Not Reported	Unmeasured	0 ug/L / 0.42 ug/L / 4.2 ug/L / 42 ug/L / 420 ug/L / 4200 ug/L	Reproduction (Reproduction-Fecundity, Response Site: Not reported)	NOEC (4200 ug/L)	Reproductive/Teratogenic	High	4198672
28553-12-0	11 Day(s), (21 Day(s))	*Danio rerio* (Zebra Danio), Adult, Female, Laboratory	Fresh water, Aqueous (aquatic habitat), Static, Not Reported	Unmeasured	0 ug/L / 0.42 ug/L / 4.2 ug/L / 42 ug/L / 420 ug/L / 4200 ug/L	Reproduction (Reproduction-Fecundity, Response Site: Not reported)	NOEC (4200 ug/L)	Reproductive/Teratogenic	High	4198672
28553-12-0	14 Day(s), (21 Day(s))	*Danio rerio* (Zebra Danio), Adult, Female, Laboratory	Fresh water, Aqueous (aquatic habitat), Static, Not Reported	Unmeasured	0 ug/L / 0.42 ug/L / 4.2 ug/L / 42 ug/L / 420 ug/L / 4200 ug/L	Reproduction (Reproduction-Fecundity, Response Site: Not reported)	NOEC (4200 ug/L)	Reproductive/Teratogenic	High	4198672
28553-12-0	17 Day(s), (21 Day(s))	*Danio rerio* (Zebra Danio), Adult, Female, Laboratory	Fresh water, Aqueous (aquatic habitat), Static, Not Reported	Unmeasured	0 ug/L / 0.42 ug/L / 4.2 ug/L / 42 ug/L / 420 ug/L / 4200 ug/L	Reproduction (Reproduction-Fecundity, Response Site: Not reported)	NOEC (4200 ug/L)	Reproductive/Teratogenic	High	4198672
28553-12-0	20 Day(s), (21 Day(s))	*Danio rerio* (Zebra Danio), Adult, Female, Laboratory	Fresh water, Aqueous (aquatic habitat), Static, Not Reported	Unmeasured	0 ug/L / 0.42 ug/L / 4.2 ug/L / 42 ug/L / 420 ug/L / 4200 ug/L	Reproduction (Reproduction-Fecundity, Response Site: Not reported)	LOEC (0.42 ug/L)	Reproductive/Teratogenic	High	4198672
28553-12-0	21 Day(s), (21 Day(s))	*Danio rerio* (Zebra Danio), Adult, Female, Laboratory	Fresh water, Aqueous (aquatic habitat), Static, Not Reported	Unmeasured	0 ug/L / 0.42 ug/L / 4.2 ug/L / 42 ug/L / 420 ug/L / 4200 ug/L	Cellular (Genetics-Progesterone receptor membrane component 2 mRNA, Response Site: Ovaries)	LOEC (4200 ug/L)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Reproductive/Teratogenic	High	4198672

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CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
28553-12-0	21 Day(s), (21 Day(s))	*Danio rerio* (Zebra Danio), Adult, Female, Laboratory	Fresh water, Aqueous (aquatic habitat), Static, Not Reported	Unmeasured	0 ug/L / 0.42 ug/L / 4.2 ug/L / 42 ug/L / 420 ug/L / 4200 ug/L	Biochemical (Biochemistry-Organic acids, Response Site: Ovaries)	NR (0.42-420 ug/L)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Reproductive/Teratogenic	High	4198672
28553-12-0	21 Day(s), (21 Day(s))	*Danio rerio* (Zebra Danio), Adult, Female, Laboratory	Fresh water, Aqueous (aquatic habitat), Static, Not Reported	Unmeasured	0 ug/L / 0.42 ug/L / 4.2 ug/L / 42 ug/L / 420 ug/L / 4200 ug/L	Biochemical (Biochemistry-Protein content, Response Site: Ovaries)	NR (0.42-420 ug/L)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Reproductive/Teratogenic	High	4198672
28553-12-0	21 Day(s), (21 Day(s))	*Danio rerio* (Zebra Danio), Adult, Female, Laboratory	Fresh water, Aqueous (aquatic habitat), Static, Not Reported	Unmeasured	0 ug/L / 0.42 ug/L / 4.2 ug/L / 42 ug/L / 420 ug/L / 4200 ug/L	Cellular (Genetics-Progesterone receptor membrane component 2 mRNA, Response Site: Ovaries)	NOEC (420 ug/L)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Reproductive/Teratogenic	High	4198672
28553-12-0	21 Day(s), (21 Day(s))	*Danio rerio* (Zebra Danio), Adult, Female, Laboratory	Fresh water, Aqueous (aquatic habitat), Static, Not Reported	Unmeasured	0 ug/L / 0.42 ug/L / 4.2 ug/L / 42 ug/L / 420 ug/L / 4200 ug/L	Cellular (Genetics-p53 mRNA, Response Site: Ovaries)	NOEC (4200 ug/L)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Reproductive/Teratogenic	High	4198672
28553-12-0	21 Day(s), (21 Day(s))	*Danio rerio* (Zebra Danio), Adult, Female, Laboratory	Fresh water, Aqueous (aquatic habitat), Static, Not Reported	Unmeasured	0 ug/L / 0.42 ug/L / 4.2 ug/L / 42 ug/L / 420 ug/L / 4200 ug/L	Cellular (Genetics-Beclin-1 mRNA, Response Site: Ovaries)	NOEC (4200 ug/L)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Reproductive/Teratogenic	High	4198672
28553-12-0	21 Day(s), (21 Day(s))	*Danio rerio* (Zebra Danio), Adult, Female, Laboratory	Fresh water, Aqueous (aquatic habitat), Static, Not Reported	Unmeasured	0 ug/L / 0.42 ug/L / 4.2 ug/L / 42 ug/L / 420 ug/L / 4200 ug/L	Cellular (Genetics-Caspase 3B mRNA, Response Site: Ovaries)	NOEC (4200 ug/L)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Reproductive/Teratogenic	High	4198672

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CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
28553-12-0	21 Day(s), (21 Day(s))	*Danio rerio* (Zebra Danio), Adult, Female, Laboratory	Fresh water, Aqueous (aquatic habitat), Static, Not Reported	Unmeasured	0 ug/L / 0.42 ug/L / 4.2 ug/L / 42 ug/L / 420 ug/L / 4200 ug/L	Reproduction (Reproduction-Fecundity, Response Site: Not reported)	LOEC (0.42 ug/L)	Reproductive/Teratogenic	High	4198672
28553-12-0	21 Day(s), (21 Day(s))	*Danio rerio* (Zebra Danio), Adult, Female, Laboratory	Fresh water, Aqueous (aquatic habitat), Static, Not Reported	Unmeasured	0 ug/L / 0.42 ug/L / 4.2 ug/L / 42 ug/L / 420 ug/L / 4200 ug/L	Biochemical (Biochemistry-Lipid, Response Site: Ovaries)	LOEC (0.42 ug/L)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Reproductive/Teratogenic	High	4198672
28553-12-0	21 Day(s), (21 Day(s))	*Danio rerio* (Zebra Danio), Adult, Female, Laboratory	Fresh water, Aqueous (aquatic habitat), Static, Not Reported	Unmeasured	0 ug/L / 0.42 ug/L / 4.2 ug/L / 42 ug/L / 420 ug/L / 4200 ug/L	Cellular (Genetics-Growth and differentiation factor 9 mRNA, Response Site: Ovaries)	NOEC (4200 ug/L)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Reproductive/Teratogenic	High	4198672
28553-12-0	21 Day(s), (21 Day(s))	*Danio rerio* (Zebra Danio), Adult, Female, Laboratory	Fresh water, Aqueous (aquatic habitat), Static, Not Reported	Unmeasured	0 ug/L / 0.42 ug/L / 4.2 ug/L / 42 ug/L / 420 ug/L / 4200 ug/L	Cellular (Genetics-Progesterone receptor membrane component 1 mRNA, Response Site: Ovaries)	NOEC (4200 ug/L)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Reproductive/Teratogenic	High	4198672
28553-12-0	21 Day(s), (21 Day(s))	*Danio rerio* (Zebra Danio), Adult, Female, Laboratory	Fresh water, Aqueous (aquatic habitat), Static, Not Reported	Unmeasured	0 ug/L / 0.42 ug/L / 4.2 ug/L / 42 ug/L / 420 ug/L / 4200 ug/L	Biochemical (Biochemistry-Organic acids, Response Site: Ovaries)	LOEC (0.42 ug/L)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Reproductive/Teratogenic	High	4198672
28553-12-0	21 Day(s), (21 Day(s))	*Danio rerio* (Zebra Danio), Adult, Female, Laboratory	Fresh water, Aqueous (aquatic habitat), Static, Not Reported	Unmeasured	0 ug/L / 0.42 ug/L / 4.2 ug/L / 42 ug/L / 420 ug/L / 4200 ug/L	Biochemical (Biochemistry-Phosphate, Response Site: Ovaries)	NR (0.42-420 ug/L)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Reproductive/Teratogenic	High	4198672

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CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
28553-12-0	21 Day(s), (21 Day(s))	*Danio rerio* (Zebra Danio), Adult, Female, Laboratory	Fresh water, Aqueous (aquatic habitat), Static, Not Reported	Unmeasured	0 ug/L / 0.42 ug/L / 4.2 ug/L / 42 ug/L / 420 ug/L / 4200 ug/L	Cellular (Genetics-Cytochrome P450, family 11, subfamily C, polypeptide 1 mRNA, Response Site: Ovaries)	NR (0.42-4200 ug/L)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Reproductive/Teratogenic	High	4198672
28553-12-0	21 Day(s), (21 Day(s))	*Danio rerio* (Zebra Danio), Adult, Female, Laboratory	Fresh water, Aqueous (aquatic habitat), Static, Not Reported	Unmeasured	0 ug/L / 0.42 ug/L / 4.2 ug/L / 42 ug/L / 420 ug/L / 4200 ug/L	Cellular (Genetics-Estrogen receptor alpha 2 mRNA, Response Site: Ovaries)	NR (0.42-4200 ug/L)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Reproductive/Teratogenic	High	4198672
28553-12-0	21 Day(s), (21 Day(s))	*Danio rerio* (Zebra Danio), Adult, Female, Laboratory	Fresh water, Aqueous (aquatic habitat), Static, Not Reported	Unmeasured	0 ug/L / 0.42 ug/L / 4.2 ug/L / 42 ug/L / 420 ug/L / 4200 ug/L	Cellular (Genetics-Estrogen receptor alpha mRNA, Response Site: Ovaries)	NR (0.42-4200 ug/L)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Reproductive/Teratogenic	High	4198672
28553-12-0	21 Day(s), (21 Day(s))	*Danio rerio* (Zebra Danio), Adult, Female, Laboratory	Fresh water, Aqueous (aquatic habitat), Static, Not Reported	Unmeasured	0 ug/L / 0.42 ug/L / 4.2 ug/L / 42 ug/L / 420 ug/L / 4200 ug/L	Cellular (Genetics-Estrogen receptor beta2 protein mRNA, Response Site: Ovaries)	NR (0.42-4200 ug/L)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Reproductive/Teratogenic	High	4198672
28553-12-0	21 Day(s), (21 Day(s))	*Danio rerio* (Zebra Danio), Adult, Female, Laboratory	Fresh water, Aqueous (aquatic habitat), Static, Not Reported	Unmeasured	0 ug/L / 0.42 ug/L / 4.2 ug/L / 42 ug/L / 420 ug/L / 4200 ug/L	Cellular (Genetics-Follicle-stimulating hormone receptor mRNA, Response Site: Ovaries)	NR (0.42-4200 ug/L)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Reproductive/Teratogenic	High	4198672
28553-12-0	21 Day(s), (21 Day(s))	*Danio rerio* (Zebra Danio), Adult, Female, Laboratory	Fresh water, Aqueous (aquatic habitat), Static, Not Reported	Unmeasured	0 ug/L / 0.42 ug/L / 4.2 ug/L / 42 ug/L / 420 ug/L / 4200 ug/L	Cellular (Genetics-Luteinizing hormone receptor mRNA, Response Site: Ovaries)	NR (0.42-4200 ug/L)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Reproductive/Teratogenic	High	4198672

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28553-12-0	21 Day(s), (21 Day(s))	*Danio rerio* (Zebra Danio), Adult, Female, Laboratory	Fresh water, Aqueous (aquatic habitat), Static, Not Reported	Unmeasured	0 ug/L / 0.42 ug/L / 4.2 ug/L / 42 ug/L / 420 ug/L / 4200 ug/L	Cellular (Genetics-Steroidogenic Acute Regulatory protein mRNA, Response Site: Ovaries)	NR (0.42-4200 ug/L)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Reproductive/Teratogenic	High	4198672
28553-12-0	21 Day(s), (21 Day(s))	*Danio rerio* (Zebra Danio), Adult, Female, Laboratory	Fresh water, Aqueous (aquatic habitat), Static, Not Reported	Unmeasured	0 ug/L / 0.42 ug/L / 4.2 ug/L / 42 ug/L / 420 ug/L / 4200 ug/L	Growth (Morphology-Organ weight in relationship to body weight, Response Site: Gonad(s))	NR (0.42-4200 ug/L)	Reproductive/Teratogenic	High	4198672
28553-12-0	21 Day(s), (21 Day(s))	*Danio rerio* (Zebra Danio), Adult, Female, Laboratory	Fresh water, Aqueous (aquatic habitat), Static, Not Reported	Unmeasured	0 ug/L / 0.42 ug/L / 4.2 ug/L / 42 ug/L / 420 ug/L / 4200 ug/L	Reproduction (Reproduction-Final vitellogenic oocyte, Response Site: Ovaries)	NR (0.42-4200 ug/L)	Reproductive/Teratogenic	High	4198672
28553-12-0	21 Day(s), (21 Day(s))	*Danio rerio* (Zebra Danio), Adult, Female, Laboratory	Fresh water, Aqueous (aquatic habitat), Static, Not Reported	Unmeasured	0 ug/L / 0.42 ug/L / 4.2 ug/L / 42 ug/L / 420 ug/L / 4200 ug/L	Cellular (Genetics-Bone morphogenetic protein-15 mRNA, Response Site: Ovaries)	NR (0.42-4200 ug/L)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Reproductive/Teratogenic	High	4198672
28553-12-0	21 Day(s), (21 Day(s))	*Danio rerio* (Zebra Danio), Adult, Female, Laboratory	Fresh water, Aqueous (aquatic habitat), Static, Not Reported	Unmeasured	0 ug/L / 0.42 ug/L / 4.2 ug/L / 42 ug/L / 420 ug/L / 4200 ug/L	Reproduction (Reproduction-Fully developed oocytes, Response Site: Ovaries)	NR (0.42-4200 ug/L)	Reproductive/Teratogenic	High	4198672
28553-12-0	21 Day(s), (21 Day(s))	*Danio rerio* (Zebra Danio), Adult, Female, Laboratory	Fresh water, Aqueous (aquatic habitat), Static, Not Reported	Unmeasured	0 ug/L / 0.42 ug/L / 4.2 ug/L / 42 ug/L / 420 ug/L / 4200 ug/L	Reproduction (Reproduction-Previtellogenic oocyte, Response Site: Ovaries)	NR (0.42-4200 ug/L)	Reproductive/Teratogenic	High	4198672
28553-12-0	21 Day(s), (21 Day(s))	*Danio rerio* (Zebra Danio), Adult, Female, Laboratory	Fresh water, Aqueous (aquatic habitat), Static, Not Reported	Unmeasured	0 ug/L / 0.42 ug/L / 4.2 ug/L / 42 ug/L / 420 ug/L / 4200 ug/L	Cellular (Genetics-Activating molecule in beclin-1-regulated autophagy mRNA, Response Site: Ovaries)	NR (0.42-4200 ug/L)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Reproductive/Teratogenic	High	4198672

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CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
28553-12-0	96 Hour(s), (96 Hour(s))	*Lepomis macrochirus* (Bluegill), Juvenile, Not Reported, Not reported (NR)	Fresh water, Aqueous (aquatic habitat), Static, Not Reported	Measured	NR / NR	Mortality (Mortality-Mortality, Response Site: Not reported)	LC50 (>0.14 mg/L)	Mortality	High	1321996
28553-12-0	24 Hour(s), (96 Hour(s))	*Lepomis macrochirus* (Bluegill), Not reported, Not Reported, Laboratory (COMMERCIAL FISH SUPPLIERS IN CONNECTICUT AND MISSOURI)	Fresh water, Aqueous (aquatic habitat), Static, Not Reported	Measured	<0.013 mg/L / 0.10-0.17 mg/L	Mortality (Mortality-Mortality, Response Site: Not reported)	LC50 (>0.17 mg/L)	Mortality	High	1316201
28553-12-0	48 Hour(s), (96 Hour(s))	*Lepomis macrochirus* (Bluegill), Not reported, Not Reported, Laboratory (COMMERCIAL FISH SUPPLIERS IN CONNECTICUT AND MISSOURI)	Fresh water, Aqueous (aquatic habitat), Static, Not Reported	Measured	<0.013 mg/L / 0.10-0.17 mg/L	Mortality (Mortality-Mortality, Response Site: Not reported)	LC50 (>0.17 mg/L)	Mortality	High	1316201
28553-12-0	72 Hour(s), (96 Hour(s))	*Lepomis macrochirus* (Bluegill), Not reported, Not Reported, Laboratory (COMMERCIAL FISH SUPPLIERS IN CONNECTICUT AND MISSOURI)	Fresh water, Aqueous (aquatic habitat), Static, Not Reported	Measured	<0.013 mg/L / 0.10-0.17 mg/L	Mortality (Mortality-Mortality, Response Site: Not reported)	LC50 (>0.17 mg/L)	Mortality	High	1316201

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CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
28553-12-0	96 Hour(s), (96 Hour(s))	*Lepomis macrochirus* (Bluegill), Not reported, Not Reported, Laboratory (COMMERCIAL FISH SUPPLIERS IN CONNECTICUT AND MISSOURI)	Fresh water, Aqueous (aquatic habitat), Static, Not Reported	Measured	<0.013 mg/L / 0.10-0.17 mg/L	Mortality (Mortality-Mortality, Response Site: Not reported)	LC50 (>0.17 mg/L)	Mortality	High	1316201
28553-12-0	96 Hour(s), (96 Hour(s))	*Oncorhynchus mykiss* (Rainbow Trout), Juvenile, Not Reported, Not reported (NR)	Fresh water, Aqueous (aquatic habitat), Flow-through, Not Reported	Measured	NR / NR	Mortality (Mortality-Mortality, Response Site: Not reported)	LC50 (>0.16 mg/L)	Mortality	High	1321996
28553-12-0	24 Hour(s), (96 Hour(s))	*Oncorhynchus mykiss* (Rainbow Trout), Not reported, Not Reported, Laboratory (OBTAINED FROM COMMERCIAL FISH SUPPLIERS IN MARYLAND AND MONTANA)	Fresh water, Aqueous (aquatic habitat), Flow-through, Not Reported	Measured	<0.0073 (<0.0069-<0.0073) mg/L / 0.0087 (0.0070-0.010) mg/L / 0.019 (0.015-0.024) mg/L / 0.032 (0.027-0.037) mg/L / 0.062 (0.052-0.069) mg/L / 0.16 (0.14-0.20) mg/L	Mortality (Mortality-Mortality, Response Site: Not reported)	LC50 (>0.16 mg/L)	Mortality	High	5530771
28553-12-0	48 Hour(s), (96 Hour(s))	*Oncorhynchus mykiss* (Rainbow Trout), Not reported, Not Reported, Laboratory (OBTAINED FROM COMMERCIAL FISH SUPPLIERS IN MARYLAND AND MONTANA)	Fresh water, Aqueous (aquatic habitat), Flow-through, Not Reported	Measured	<0.0073 (<0.0069-<0.0073) mg/L / 0.0087 (0.0070-0.010) mg/L / 0.019 (0.015-0.024) mg/L / 0.032 (0.027-0.037) mg/L / 0.062 (0.052-0.069) mg/L / 0.16 (0.14-0.20) mg/L	Mortality (Mortality-Mortality, Response Site: Not reported)	LC50 (>0.16 mg/L)	Mortality	High	5530771

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CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
28553-12-0	72 Hour(s), (96 Hour(s))	*Oncorhynchus mykiss* (Rainbow Trout), Not reported, Not Reported, Laboratory (OBTAINED FROM COMMERCIAL FISH SUPPLIERS IN MARYLAND AND MONTANA)	Fresh water, Aqueous (aquatic habitat), Flow-through, Not Reported	Measured	<0.0073 (<0.0069-<0.0073) mg/L / 0.0087 (0.0070-0.010) mg/L / 0.019 (0.015-0.024) mg/L / 0.032 (0.027-0.037) mg/L / 0.062 (0.052-0.069) mg/L / 0.16 (0.14-0.20) mg/L	Mortality (Mortality-Mortality, Response Site: Not reported)	LC50 (>0.16 mg/L)	Mortality	High	5530771
28553-12-0	96 Hour(s), (96 Hour(s))	*Oncorhynchus mykiss* (Rainbow Trout), Not reported, Not Reported, Laboratory (OBTAINED FROM COMMERCIAL FISH SUPPLIERS IN MARYLAND AND MONTANA)	Fresh water, Aqueous (aquatic habitat), Flow-through, Not Reported	Measured	<0.0073 (<0.0069-<0.0073) mg/L / 0.0087 (0.0070-0.010) mg/L / 0.019 (0.015-0.024) mg/L / 0.032 (0.027-0.037) mg/L / 0.062 (0.052-0.069) mg/L / 0.16 (0.14-0.20) mg/L	Mortality (Mortality-Mortality, Response Site: Not reported)	NR-ZERO (0.16 (0.14-0.20) mg/L)	Mortality	High	5530771
28553-12-0	24 Hour(s), (96 Hour(s))	*Oreochromis mossambicus* (Mozambique Tilapia), Not reported, Both (Measured in: Female organisms), Laboratory (COLLECTED FROM A FISH FARM, SAFA AQUARIUM, KOZHIKODE, KERALA, INDIA)	Fresh water, Aqueous (aquatic habitat), Static, NA Female organisms	Unmeasured	0 ppm / 0 ppm / 300 ppm	Biochemical (Enzyme(s)-3-beta Hydroxysteroid dehydrogenase, Response Site: Ovaries)	LOEC (300 ppm)	Mechanistic: Cell signaling/function; Oxidative stress (including redox biology); Reproductive/Teratogenic	Medium	7978601

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CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
28553-12-0	24 Hour(s), (96 Hour(s))	*Oreochromis mossambicus* (Mozambique Tilapia), Not reported, Both (Measured in: Female organisms), Laboratory (COLLECTED FROM A FISH FARM, SAFA AQUARIUM, KOZHIKODE, KERALA, INDIA)	Fresh water, Aqueous (aquatic habitat), Static, NA Female organisms	Unmeasured	0 ppm / 0 ppm / 300 ppm	Growth (Morphology-Weight, Response Site: Ovaries)	NOEC (300 ppm)	Reproductive/Teratogenic	Medium	7978601
28553-12-0	24 Hour(s), (96 Hour(s))	*Oreochromis mossambicus* (Mozambique Tilapia), Not reported, Both (Measured in: Female organisms), Laboratory (COLLECTED FROM A FISH FARM, SAFA AQUARIUM, KOZHIKODE, KERALA, INDIA)	Fresh water, Aqueous (aquatic habitat), Static, NA Female organisms	Unmeasured	0 ppm / 0 ppm / 300 ppm	Biochemical (Enzyme(s)-17beta-Hydroxysteroid dehydrogenase, Response Site: Ovaries)	NOEC (300 ppm)	Mechanistic: Cell signaling/function; Oxidative stress (including redox biology); Reproductive/Teratogenic	Medium	7978601
28553-12-0	24 Hour(s), (96 Hour(s))	*Oreochromis mossambicus* (Mozambique Tilapia), Not reported, Both (Measured in: Male organisms), Laboratory (COLLECTED FROM A FISH FARM, SAFA AQUARIUM, KOZHIKODE, KERALA, INDIA)	Fresh water, Aqueous (aquatic habitat), Static, NA Male organisms	Unmeasured	0 ppm / 0 ppm / 300 ppm	Biochemical (Enzyme(s)-17beta-Hydroxysteroid dehydrogenase, Response Site: Testes)	NOEC (300 ppm)	Mechanistic: Cell signaling/function; Oxidative stress (including redox biology); Reproductive/Teratogenic	Medium	7978601

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CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
28553-12-0	24 Hour(s), (96 Hour(s))	*Oreochromis mossambicus* (Mozambique Tilapia), Not reported, Both (Measured in: Male organisms), Laboratory (COLLECTED FROM A FISH FARM, SAFA AQUARIUM, KOZHIKODE, KERALA, INDIA)	Fresh water, Aqueous (aquatic habitat), Static, NA Male organisms	Unmeasured	0 ppm / 0 ppm / 300 ppm	Biochemical (Enzyme(s)-3-beta Hydroxysteroid dehydrogenase, Response Site: Testes)	NOEC (300 ppm)	Mechanistic: Cell signaling/function; Oxidative stress (including redox biology); Reproductive/Teratogenic	Medium	7978601
28553-12-0	24 Hour(s), (96 Hour(s))	*Oreochromis mossambicus* (Mozambique Tilapia), Not reported, Both (Measured in: Female organisms), Laboratory (COLLECTED FROM A FISH FARM, SAFA AQUARIUM, KOZHIKODE, KERALA, INDIA)	Fresh water, Aqueous (aquatic habitat), Static, NA Female organisms	Unmeasured	0 ppm / 0 ppm / 300 ppm	Biochemical (Enzyme(s)-Catalase, Response Site: Ovaries)	NOEC (300 ppm)	Mechanistic: Cell signaling/function; Oxidative stress (including redox biology); Reproductive/Teratogenic	Medium	7978601
28553-12-0	24 Hour(s), (96 Hour(s))	*Oreochromis mossambicus* (Mozambique Tilapia), Not reported, Both (Measured in: Male organisms), Laboratory (COLLECTED FROM A FISH FARM, SAFA AQUARIUM, KOZHIKODE, KERALA, INDIA)	Fresh water, Aqueous (aquatic habitat), Static, NA Male organisms	Unmeasured	0 ppm / 0 ppm / 300 ppm	Biochemical (Enzyme(s)-Catalase, Response Site: Testes)	NOEC (300 ppm)	Mechanistic: Cell signaling/function; Oxidative stress (including redox biology); Reproductive/Teratogenic	Medium	7978601

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CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
28553-12-0	24 Hour(s), (96 Hour(s))	*Oreochromis mossambicus* (Mozambique Tilapia), Not reported, Both (Measured in: Female organisms), Laboratory (COLLECTED FROM A FISH FARM, SAFA AQUARIUM, KOZHIKODE, KERALA, INDIA)	Fresh water, Aqueous (aquatic habitat), Static, NA Female organisms	Unmeasured	0 ppm / 0 ppm / 300 ppm	Biochemical (Enzyme(s)-Glutathione peroxidase, Response Site: Ovaries)	NOEC (300 ppm)	Mechanistic: Cell signaling/function; Oxidative stress (including redox biology); Reproductive/Teratogenic	Medium	7978601
28553-12-0	24 Hour(s), (96 Hour(s))	*Oreochromis mossambicus* (Mozambique Tilapia), Not reported, Both (Measured in: Male organisms), Laboratory (COLLECTED FROM A FISH FARM, SAFA AQUARIUM, KOZHIKODE, KERALA, INDIA)	Fresh water, Aqueous (aquatic habitat), Static, NA Male organisms	Unmeasured	0 ppm / 0 ppm / 300 ppm	Biochemical (Enzyme(s)-Glutathione peroxidase, Response Site: Testes)	NOEC (300 ppm)	Mechanistic: Cell signaling/function; Oxidative stress (including redox biology); Reproductive/Teratogenic	Medium	7978601
28553-12-0	24 Hour(s), (96 Hour(s))	*Oreochromis mossambicus* (Mozambique Tilapia), Not reported, Both (Measured in: Male organisms), Laboratory (COLLECTED FROM A FISH FARM, SAFA AQUARIUM, KOZHIKODE, KERALA, INDIA)	Fresh water, Aqueous (aquatic habitat), Static, NA Male organisms	Unmeasured	0 ppm / 0 ppm / 300 ppm	Biochemical (Enzyme(s)-Glutathione reductase, Response Site: Testes)	NOEC (300 ppm)	Mechanistic: Cell signaling/function; Oxidative stress (including redox biology); Reproductive/Teratogenic	Medium	7978601

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CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
28553-12-0	24 Hour(s), (96 Hour(s))	*Oreochromis mossambicus* (Mozambique Tilapia), Not reported, Both (Measured in: Female organisms), Laboratory (COLLECTED FROM A FISH FARM, SAFA AQUARIUM, KOZHIKODE, KERALA, INDIA)	Fresh water, Aqueous (aquatic habitat), Static, NA Female organisms	Unmeasured	0 ppm / 0 ppm / 300 ppm	Biochemical (Enzyme(s)-Superoxide dismutase (SOD) enzyme activity, Response Site: Ovaries)	NOEC (300 ppm)	Mechanistic: Cell signaling/function; Oxidative stress (including redox biology); Reproductive/Teratogenic	Medium	7978601
28553-12-0	24 Hour(s), (96 Hour(s))	*Oreochromis mossambicus* (Mozambique Tilapia), Not reported, Both (Measured in: Male organisms), Laboratory (COLLECTED FROM A FISH FARM, SAFA AQUARIUM, KOZHIKODE, KERALA, INDIA)	Fresh water, Aqueous (aquatic habitat), Static, NA Male organisms	Unmeasured	0 ppm / 0 ppm / 300 ppm	Biochemical (Enzyme(s)-Superoxide dismutase (SOD) enzyme activity, Response Site: Testes)	NOEC (300 ppm)	Mechanistic: Cell signaling/function; Oxidative stress (including redox biology); Reproductive/Teratogenic	Medium	7978601
28553-12-0	24 Hour(s), (96 Hour(s))	*Oreochromis mossambicus* (Mozambique Tilapia), Not reported, Both (Measured in: Female organisms), Laboratory (COLLECTED FROM A FISH FARM, SAFA AQUARIUM, KOZHIKODE, KERALA, INDIA)	Fresh water, Aqueous (aquatic habitat), Static, NA Female organisms	Unmeasured	0 ppm / 0 ppm / 300 ppm	Biochemical (Enzyme(s)-Glutathione reductase, Response Site: Ovaries)	NOEC (300 ppm)	Mechanistic: Cell signaling/function; Oxidative stress (including redox biology); Reproductive/Teratogenic	Medium	7978601

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CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
28553-12-0	24 Hour(s), (96 Hour(s))	*Oreochromis mossambicus* (Mozambique Tilapia), Not reported, Both (Measured in: Female organisms), Laboratory (COLLECTED FROM A FISH FARM, SAFA AQUARIUM, KOZHIKODE, KERALA, INDIA)	Fresh water, Aqueous (aquatic habitat), Static, NA Female organisms	Unmeasured	0 ppm / 0 ppm / 300 ppm	Physiology (Physiology-Lipid peroxidation, Response Site: Ovaries)	NOEC (300 ppm)	Mechanistic: Cell signaling/function; Oxidative stress (including redox biology); Reproductive/Teratogenic	Medium	7978601
28553-12-0	24 Hour(s), (96 Hour(s))	*Oreochromis mossambicus* (Mozambique Tilapia), Not reported, Both (Measured in: Male organisms), Laboratory (COLLECTED FROM A FISH FARM, SAFA AQUARIUM, KOZHIKODE, KERALA, INDIA)	Fresh water, Aqueous (aquatic habitat), Static, NA Male organisms	Unmeasured	0 ppm / 0 ppm / 300 ppm	Physiology (Physiology-Lipid peroxidation, Response Site: Testes)	NOEC (300 ppm)	Mechanistic: Cell signaling/function; Oxidative stress (including redox biology); Reproductive/Teratogenic	Medium	7978601
28553-12-0	24 Hour(s), (96 Hour(s))	*Oreochromis mossambicus* (Mozambique Tilapia), Not reported, Both (Measured in: Male organisms), Laboratory (COLLECTED FROM A FISH FARM, SAFA AQUARIUM, KOZHIKODE, KERALA, INDIA)	Fresh water, Aqueous (aquatic habitat), Static, NA Male organisms	Unmeasured	0 ppm / 0 ppm / 300 ppm	Growth (Morphology-Weight, Response Site: Testes)	NOEC (300 ppm)	Reproductive/Teratogenic	Medium	7978601

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CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
28553-12-0	48 Hour(s), (96 Hour(s))	*Oreochromis mossambicus* (Mozambique Tilapia), Not reported, Both (Measured in: Female organisms), Laboratory (COLLECTED FROM A FISH FARM, SAFA AQUARIUM, KOZHIKODE, KERALA, INDIA)	Fresh water, Aqueous (aquatic habitat), Static, NA Female organisms	Unmeasured	0 ppm / 0 ppm / 300 ppm	Biochemical (Enzyme(s)-Catalase, Response Site: Ovaries)	LOEC (300 ppm)	Mechanistic: Cell signaling/function; Oxidative stress (including redox biology); Reproductive/Teratogenic	Medium	7978601
28553-12-0	48 Hour(s), (96 Hour(s))	*Oreochromis mossambicus* (Mozambique Tilapia), Not reported, Both (Measured in: Female organisms), Laboratory (COLLECTED FROM A FISH FARM, SAFA AQUARIUM, KOZHIKODE, KERALA, INDIA)	Fresh water, Aqueous (aquatic habitat), Static, NA Female organisms	Unmeasured	0 ppm / 0 ppm / 300 ppm	Biochemical (Enzyme(s)-Glutathione reductase, Response Site: Ovaries)	LOEC (300 ppm)	Mechanistic: Cell signaling/function; Oxidative stress (including redox biology); Reproductive/Teratogenic	Medium	7978601
28553-12-0	48 Hour(s), (96 Hour(s))	*Oreochromis mossambicus* (Mozambique Tilapia), Not reported, Both (Measured in: Male organisms), Laboratory (COLLECTED FROM A FISH FARM, SAFA AQUARIUM, KOZHIKODE, KERALA, INDIA)	Fresh water, Aqueous (aquatic habitat), Static, NA Male organisms	Unmeasured	0 ppm / 0 ppm / 300 ppm	Physiology (Physiology-Lipid peroxidation, Response Site: Testes)	LOEC (300 ppm)	Mechanistic: Cell signaling/function; Oxidative stress (including redox biology); Reproductive/Teratogenic	Medium	7978601

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CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
28553-12-0	48 Hour(s), (96 Hour(s))	*Oreochromis mossambicus* (Mozambique Tilapia), Not reported, Both (Measured in: Female organisms), Laboratory (COLLECTED FROM A FISH FARM, SAFA AQUARIUM, KOZHIKODE, KERALA, INDIA)	Fresh water, Aqueous (aquatic habitat), Static, NA Female organisms	Unmeasured	0 ppm / 0 ppm / 300 ppm	Biochemical (Enzyme(s)-Glutathione peroxidase, Response Site: Ovaries)	NOEC (300 ppm)	Mechanistic: Cell signaling/function; Oxidative stress (including redox biology); Reproductive/Teratogenic	Medium	7978601
28553-12-0	48 Hour(s), (96 Hour(s))	*Oreochromis mossambicus* (Mozambique Tilapia), Not reported, Both (Measured in: Male organisms), Laboratory (COLLECTED FROM A FISH FARM, SAFA AQUARIUM, KOZHIKODE, KERALA, INDIA)	Fresh water, Aqueous (aquatic habitat), Static, NA Male organisms	Unmeasured	0 ppm / 0 ppm / 300 ppm	Biochemical (Enzyme(s)-17beta-Hydroxysteroid dehydrogenase, Response Site: Testes)	NOEC (300 ppm)	Mechanistic: Cell signaling/function; Oxidative stress (including redox biology); Reproductive/Teratogenic	Medium	7978601
28553-12-0	48 Hour(s), (96 Hour(s))	*Oreochromis mossambicus* (Mozambique Tilapia), Not reported, Both (Measured in: Female organisms), Laboratory (COLLECTED FROM A FISH FARM, SAFA AQUARIUM, KOZHIKODE, KERALA, INDIA)	Fresh water, Aqueous (aquatic habitat), Static, NA Female organisms	Unmeasured	0 ppm / 0 ppm / 300 ppm	Growth (Morphology-Weight, Response Site: Ovaries)	NOEC (300 ppm)	Reproductive/Teratogenic	Medium	7978601

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28553-12-0	48 Hour(s), (96 Hour(s))	*Oreochromis mossambicus* (Mozambique Tilapia), Not reported, Both (Measured in: Female organisms), Laboratory (COLLECTED FROM A FISH FARM, SAFA AQUARIUM, KOZHIKODE, KERALA, INDIA)	Fresh water, Aqueous (aquatic habitat), Static, NA Female organisms	Unmeasured	0 ppm / 0 ppm / 300 ppm	Physiology (Physiology-Lipid peroxidation, Response Site: Ovaries)	NOEC (300 ppm)	Mechanistic: Cell signaling/function; Oxidative stress (including redox biology); Reproductive/Teratogenic	Medium	7978601
28553-12-0	48 Hour(s), (96 Hour(s))	*Oreochromis mossambicus* (Mozambique Tilapia), Not reported, Both (Measured in: Male organisms), Laboratory (COLLECTED FROM A FISH FARM, SAFA AQUARIUM, KOZHIKODE, KERALA, INDIA)	Fresh water, Aqueous (aquatic habitat), Static, NA Male organisms	Unmeasured	0 ppm / 0 ppm / 300 ppm	Biochemical (Enzyme(s)-Superoxide dismutase (SOD) enzyme activity, Response Site: Testes)	NOEC (300 ppm)	Mechanistic: Cell signaling/function; Oxidative stress (including redox biology); Reproductive/Teratogenic	Medium	7978601
28553-12-0	48 Hour(s), (96 Hour(s))	*Oreochromis mossambicus* (Mozambique Tilapia), Not reported, Both (Measured in: Female organisms), Laboratory (COLLECTED FROM A FISH FARM, SAFA AQUARIUM, KOZHIKODE, KERALA, INDIA)	Fresh water, Aqueous (aquatic habitat), Static, NA Female organisms	Unmeasured	0 ppm / 0 ppm / 300 ppm	Biochemical (Enzyme(s)-Superoxide dismutase (SOD) enzyme activity, Response Site: Ovaries)	NOEC (300 ppm)	Mechanistic: Cell signaling/function; Oxidative stress (including redox biology); Reproductive/Teratogenic	Medium	7978601

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CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
28553-12-0	48 Hour(s), (96 Hour(s))	*Oreochromis mossambicus* (Mozambique Tilapia), Not reported, Both (Measured in: Male organisms), Laboratory (COLLECTED FROM A FISH FARM, SAFA AQUARIUM, KOZHIKODE, KERALA, INDIA)	Fresh water, Aqueous (aquatic habitat), Static, NA Male organisms	Unmeasured	0 ppm / 0 ppm / 300 ppm	Biochemical (Enzyme(s)-Glutathione reductase, Response Site: Testes)	NOEC (300 ppm)	Mechanistic: Cell signaling/function; Oxidative stress (including redox biology); Reproductive/Teratogenic	Medium	7978601
28553-12-0	48 Hour(s), (96 Hour(s))	*Oreochromis mossambicus* (Mozambique Tilapia), Not reported, Both (Measured in: Male organisms), Laboratory (COLLECTED FROM A FISH FARM, SAFA AQUARIUM, KOZHIKODE, KERALA, INDIA)	Fresh water, Aqueous (aquatic habitat), Static, NA Male organisms	Unmeasured	0 ppm / 0 ppm / 300 ppm	Biochemical (Enzyme(s)-Glutathione peroxidase, Response Site: Testes)	NOEC (300 ppm)	Mechanistic: Cell signaling/function; Oxidative stress (including redox biology); Reproductive/Teratogenic	Medium	7978601
28553-12-0	48 Hour(s), (96 Hour(s))	*Oreochromis mossambicus* (Mozambique Tilapia), Not reported, Both (Measured in: Male organisms), Laboratory (COLLECTED FROM A FISH FARM, SAFA AQUARIUM, KOZHIKODE, KERALA, INDIA)	Fresh water, Aqueous (aquatic habitat), Static, NA Male organisms	Unmeasured	0 ppm / 0 ppm / 300 ppm	Biochemical (Enzyme(s)-Catalase, Response Site: Testes)	NOEC (300 ppm)	Mechanistic: Cell signaling/function; Oxidative stress (including redox biology); Reproductive/Teratogenic	Medium	7978601

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CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
28553-12-0	48 Hour(s), (96 Hour(s))	*Oreochromis mossambicus* (Mozambique Tilapia), Not reported, Both (Measured in: Female organisms), Laboratory (COLLECTED FROM A FISH FARM, SAFA AQUARIUM, KOZHIKODE, KERALA, INDIA)	Fresh water, Aqueous (aquatic habitat), Static, NA Female organisms	Unmeasured	0 ppm / 0 ppm / 300 ppm	Biochemical (Enzyme(s)-3-beta Hydroxysteroid dehydrogenase, Response Site: Ovaries)	LOEC (300 ppm)	Mechanistic: Cell signaling/function; Oxidative stress (including redox biology); Reproductive/Teratogenic	Medium	7978601
28553-12-0	48 Hour(s), (96 Hour(s))	*Oreochromis mossambicus* (Mozambique Tilapia), Not reported, Both (Measured in: Male organisms), Laboratory (COLLECTED FROM A FISH FARM, SAFA AQUARIUM, KOZHIKODE, KERALA, INDIA)	Fresh water, Aqueous (aquatic habitat), Static, NA Male organisms	Unmeasured	0 ppm / 0 ppm / 300 ppm	Biochemical (Enzyme(s)-3-beta Hydroxysteroid dehydrogenase, Response Site: Testes)	NOEC (300 ppm)	Mechanistic: Cell signaling/function; Oxidative stress (including redox biology); Reproductive/Teratogenic	Medium	7978601
28553-12-0	48 Hour(s), (96 Hour(s))	*Oreochromis mossambicus* (Mozambique Tilapia), Not reported, Both (Measured in: Male organisms), Laboratory (COLLECTED FROM A FISH FARM, SAFA AQUARIUM, KOZHIKODE, KERALA, INDIA)	Fresh water, Aqueous (aquatic habitat), Static, NA Male organisms	Unmeasured	0 ppm / 0 ppm / 300 ppm	Growth (Morphology-Weight, Response Site: Testes)	NOEC (300 ppm)	Reproductive/Teratogenic	Medium	7978601

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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
28553-12-0	48 Hour(s), (96 Hour(s))	*Oreochromis mossambicus* (Mozambique Tilapia), Not reported, Both (Measured in: Female organisms), Laboratory (COLLECTED FROM A FISH FARM, SAFA AQUARIUM, KOZHIKODE, KERALA, INDIA)	Fresh water, Aqueous (aquatic habitat), Static, NA Female organisms	Unmeasured	0 ppm / 0 ppm / 300 ppm	Biochemical (Enzyme(s)-17beta-Hydroxysteroid dehydrogenase, Response Site: Ovaries)	LOEC (300 ppm)	Mechanistic: Cell signaling/function; Oxidative stress (including redox biology); Reproductive/Teratogenic	Medium	7978601
28553-12-0	72 Hour(s), (96 Hour(s))	*Oreochromis mossambicus* (Mozambique Tilapia), Not reported, Both (Measured in: Male organisms), Laboratory (COLLECTED FROM A FISH FARM, SAFA AQUARIUM, KOZHIKODE, KERALA, INDIA)	Fresh water, Aqueous (aquatic habitat), Static, NA Male organisms	Unmeasured	0 ppm / 0 ppm / 300 ppm	Biochemical (Enzyme(s)-Superoxide dismutase (SOD) enzyme activity, Response Site: Testes)	NOEC (300 ppm)	Mechanistic: Cell signaling/function; Oxidative stress (including redox biology); Reproductive/Teratogenic	Medium	7978601
28553-12-0	72 Hour(s), (96 Hour(s))	*Oreochromis mossambicus* (Mozambique Tilapia), Not reported, Both (Measured in: Female organisms), Laboratory (COLLECTED FROM A FISH FARM, SAFA AQUARIUM, KOZHIKODE, KERALA, INDIA)	Fresh water, Aqueous (aquatic habitat), Static, NA Female organisms	Unmeasured	0 ppm / 0 ppm / 300 ppm	Growth (Morphology-Weight, Response Site: Ovaries)	NOEC (300 ppm)	Reproductive/Teratogenic	Medium	7978601

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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
28553-12-0	72 Hour(s), (96 Hour(s))	*Oreochromis mossambicus* (Mozambique Tilapia), Not reported, Both (Measured in: Male organisms), Laboratory (COLLECTED FROM A FISH FARM, SAFA AQUARIUM, KOZHIKODE, KERALA, INDIA)	Fresh water, Aqueous (aquatic habitat), Static, NA Male organisms	Unmeasured	0 ppm / 0 ppm / 300 ppm	Biochemical (Enzyme(s)-3-beta Hydroxysteroid dehydrogenase, Response Site: Testes)	LOEC (300 ppm)	Mechanistic: Cell signaling/function; Oxidative stress (including redox biology); Reproductive/Teratogenic	Medium	7978601
28553-12-0	72 Hour(s), (96 Hour(s))	*Oreochromis mossambicus* (Mozambique Tilapia), Not reported, Both (Measured in: Male organisms), Laboratory (COLLECTED FROM A FISH FARM, SAFA AQUARIUM, KOZHIKODE, KERALA, INDIA)	Fresh water, Aqueous (aquatic habitat), Static, NA Male organisms	Unmeasured	0 ppm / 0 ppm / 300 ppm	Biochemical (Enzyme(s)-17beta-Hydroxysteroid dehydrogenase, Response Site: Testes)	LOEC (300 ppm)	Mechanistic: Cell signaling/function; Oxidative stress (including redox biology); Reproductive/Teratogenic	Medium	7978601
28553-12-0	72 Hour(s), (96 Hour(s))	*Oreochromis mossambicus* (Mozambique Tilapia), Not reported, Both (Measured in: Female organisms), Laboratory (COLLECTED FROM A FISH FARM, SAFA AQUARIUM, KOZHIKODE, KERALA, INDIA)	Fresh water, Aqueous (aquatic habitat), Static, NA Female organisms	Unmeasured	0 ppm / 0 ppm / 300 ppm	Biochemical (Enzyme(s)-3-beta Hydroxysteroid dehydrogenase, Response Site: Ovaries)	LOEC (300 ppm)	Mechanistic: Cell signaling/function; Oxidative stress (including redox biology); Reproductive/Teratogenic	Medium	7978601

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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
28553-12-0	72 Hour(s), (96 Hour(s))	*Oreochromis mossambicus* (Mozambique Tilapia), Not reported, Both (Measured in: Male organisms), Laboratory (COLLECTED FROM A FISH FARM, SAFA AQUARIUM, KOZHIKODE, KERALA, INDIA)	Fresh water, Aqueous (aquatic habitat), Static, NA Male organisms	Unmeasured	0 ppm / 0 ppm / 300 ppm	Biochemical (Enzyme(s)-Catalase, Response Site: Testes)	LOEC (300 ppm)	Mechanistic: Cell signaling/function; Oxidative stress (including redox biology); Reproductive/Teratogenic	Medium	7978601
28553-12-0	72 Hour(s), (96 Hour(s))	*Oreochromis mossambicus* (Mozambique Tilapia), Not reported, Both (Measured in: Female organisms), Laboratory (COLLECTED FROM A FISH FARM, SAFA AQUARIUM, KOZHIKODE, KERALA, INDIA)	Fresh water, Aqueous (aquatic habitat), Static, NA Female organisms	Unmeasured	0 ppm / 0 ppm / 300 ppm	Biochemical (Enzyme(s)-17beta-Hydroxysteroid dehydrogenase, Response Site: Ovaries)	LOEC (300 ppm)	Mechanistic: Cell signaling/function; Oxidative stress (including redox biology); Reproductive/Teratogenic	Medium	7978601
28553-12-0	72 Hour(s), (96 Hour(s))	*Oreochromis mossambicus* (Mozambique Tilapia), Not reported, Both (Measured in: Female organisms), Laboratory (COLLECTED FROM A FISH FARM, SAFA AQUARIUM, KOZHIKODE, KERALA, INDIA)	Fresh water, Aqueous (aquatic habitat), Static, NA Female organisms	Unmeasured	0 ppm / 0 ppm / 300 ppm	Biochemical (Enzyme(s)-Superoxide dismutase (SOD) enzyme activity, Response Site: Ovaries)	LOEC (300 ppm)	Mechanistic: Cell signaling/function; Oxidative stress (including redox biology); Reproductive/Teratogenic	Medium	7978601

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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
28553-12-0	72 Hour(s), (96 Hour(s))	*Oreochromis mossambicus* (Mozambique Tilapia), Not reported, Both (Measured in: Male organisms), Laboratory (COLLECTED FROM A FISH FARM, SAFA AQUARIUM, KOZHIKODE, KERALA, INDIA)	Fresh water, Aqueous (aquatic habitat), Static, NA Male organisms	Unmeasured	0 ppm / 0 ppm / 300 ppm	Physiology (Physiology-Lipid peroxidation, Response Site: Testes)	LOEC (300 ppm)	Mechanistic: Cell signaling/function; Oxidative stress (including redox biology); Reproductive/Teratogenic	Medium	7978601
28553-12-0	72 Hour(s), (96 Hour(s))	*Oreochromis mossambicus* (Mozambique Tilapia), Not reported, Both (Measured in: Female organisms), Laboratory (COLLECTED FROM A FISH FARM, SAFA AQUARIUM, KOZHIKODE, KERALA, INDIA)	Fresh water, Aqueous (aquatic habitat), Static, NA Female organisms	Unmeasured	0 ppm / 0 ppm / 300 ppm	Physiology (Physiology-Lipid peroxidation, Response Site: Ovaries)	LOEC (300 ppm)	Mechanistic: Cell signaling/function; Oxidative stress (including redox biology); Reproductive/Teratogenic	Medium	7978601
28553-12-0	72 Hour(s), (96 Hour(s))	*Oreochromis mossambicus* (Mozambique Tilapia), Not reported, Both (Measured in: Male organisms), Laboratory (COLLECTED FROM A FISH FARM, SAFA AQUARIUM, KOZHIKODE, KERALA, INDIA)	Fresh water, Aqueous (aquatic habitat), Static, NA Male organisms	Unmeasured	0 ppm / 0 ppm / 300 ppm	Biochemical (Enzyme(s)-Glutathione peroxidase, Response Site: Testes)	LOEC (300 ppm)	Mechanistic: Cell signaling/function; Oxidative stress (including redox biology); Reproductive/Teratogenic	Medium	7978601

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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
28553-12-0	72 Hour(s), (96 Hour(s))	*Oreochromis mossambicus* (Mozambique Tilapia), Not reported, Both (Measured in: Female organisms), Laboratory (COLLECTED FROM A FISH FARM, SAFA AQUARIUM, KOZHIKODE, KERALA, INDIA)	Fresh water, Aqueous (aquatic habitat), Static, NA Female organisms	Unmeasured	0 ppm / 0 ppm / 300 ppm	Biochemical (Enzyme(s)-Catalase, Response Site: Ovaries)	LOEC (300 ppm)	Mechanistic: Cell signaling/function; Oxidative stress (including redox biology); Reproductive/Teratogenic	Medium	7978601
28553-12-0	72 Hour(s), (96 Hour(s))	*Oreochromis mossambicus* (Mozambique Tilapia), Not reported, Both (Measured in: Male organisms), Laboratory (COLLECTED FROM A FISH FARM, SAFA AQUARIUM, KOZHIKODE, KERALA, INDIA)	Fresh water, Aqueous (aquatic habitat), Static, NA Male organisms	Unmeasured	0 ppm / 0 ppm / 300 ppm	Growth (Morphology-Weight, Response Site: Testes)	LOEC (300 ppm)	Reproductive/Teratogenic	Medium	7978601
28553-12-0	72 Hour(s), (96 Hour(s))	*Oreochromis mossambicus* (Mozambique Tilapia), Not reported, Both (Measured in: Female organisms), Laboratory (COLLECTED FROM A FISH FARM, SAFA AQUARIUM, KOZHIKODE, KERALA, INDIA)	Fresh water, Aqueous (aquatic habitat), Static, NA Female organisms	Unmeasured	0 ppm / 0 ppm / 300 ppm	Biochemical (Enzyme(s)-Glutathione reductase, Response Site: Ovaries)	LOEC (300 ppm)	Mechanistic: Cell signaling/function; Oxidative stress (including redox biology); Reproductive/Teratogenic	Medium	7978601

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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
28553-12-0	72 Hour(s), (96 Hour(s))	*Oreochromis mossambicus* (Mozambique Tilapia), Not reported, Both (Measured in: Male organisms), Laboratory (COLLECTED FROM A FISH FARM, SAFA AQUARIUM, KOZHIKODE, KERALA, INDIA)	Fresh water, Aqueous (aquatic habitat), Static, NA Male organisms	Unmeasured	0 ppm / 0 ppm / 300 ppm	Biochemical (Enzyme(s)-Glutathione reductase, Response Site: Testes)	LOEC (300 ppm)	Mechanistic: Cell signaling/function; Oxidative stress (including redox biology); Reproductive/Teratogenic	Medium	7978601
28553-12-0	72 Hour(s), (96 Hour(s))	*Oreochromis mossambicus* (Mozambique Tilapia), Not reported, Both (Measured in: Female organisms), Laboratory (COLLECTED FROM A FISH FARM, SAFA AQUARIUM, KOZHIKODE, KERALA, INDIA)	Fresh water, Aqueous (aquatic habitat), Static, NA Female organisms	Unmeasured	0 ppm / 0 ppm / 300 ppm	Biochemical (Enzyme(s)-Glutathione peroxidase, Response Site: Ovaries)	LOEC (300 ppm)	Mechanistic: Cell signaling/function; Oxidative stress (including redox biology); Reproductive/Teratogenic	Medium	7978601
28553-12-0	96 Hour(s), (96 Hour(s))	*Oreochromis mossambicus* (Mozambique Tilapia), Not reported, Both (Measured in: Female organisms), Laboratory (COLLECTED FROM A FISH FARM, SAFA AQUARIUM, KOZHIKODE, KERALA, INDIA)	Fresh water, Aqueous (aquatic habitat), Static, NA Female organisms	Unmeasured	0 ppm / 0 ppm / 300 ppm	Growth (Morphology-Weight, Response Site: Ovaries)	LOEC (300 ppm)	Reproductive/Teratogenic	Medium	7978601

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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
28553-12-0	96 Hour(s), (96 Hour(s))	*Oreochromis mossambicus* (Mozambique Tilapia), Not reported, Both (Measured in: Male organisms), Laboratory (COLLECTED FROM A FISH FARM, SAFA AQUARIUM, KOZHIKODE, KERALA, INDIA)	Fresh water, Aqueous (aquatic habitat), Static, NA Male organisms	Unmeasured	0 ppm / 0 ppm / 300 ppm	Physiology (Physiology-Lipid peroxidation, Response Site: Testes)	LOEC (300 ppm)	Mechanistic: Cell signaling/function; Oxidative stress (including redox biology); Reproductive/Teratogenic	Medium	7978601
28553-12-0	96 Hour(s), (96 Hour(s))	*Oreochromis mossambicus* (Mozambique Tilapia), Not reported, Both (Measured in: Male organisms), Laboratory (COLLECTED FROM A FISH FARM, SAFA AQUARIUM, KOZHIKODE, KERALA, INDIA)	Fresh water, Aqueous (aquatic habitat), Static, NA Male organisms	Unmeasured	0 ppm / 0 ppm / 300 ppm	Growth (Morphology-Weight, Response Site: Testes)	LOEC (300 ppm)	Reproductive/Teratogenic	Medium	7978601
28553-12-0	96 Hour(s), (96 Hour(s))	*Oreochromis mossambicus* (Mozambique Tilapia), Not reported, Both (Measured in: Female organisms), Laboratory (COLLECTED FROM A FISH FARM, SAFA AQUARIUM, KOZHIKODE, KERALA, INDIA)	Fresh water, Aqueous (aquatic habitat), Static, NA Female organisms	Unmeasured	0 ppm / 0 ppm / 300 ppm	Biochemical (Enzyme(s)-17beta-Hydroxysteroid dehydrogenase, Response Site: Ovaries)	LOEC (300 ppm)	Mechanistic: Cell signaling/function; Oxidative stress (including redox biology); Reproductive/Teratogenic	Medium	7978601

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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
28553-12-0	96 Hour(s), (96 Hour(s))	*Oreochromis mossambicus* (Mozambique Tilapia), Not reported, Both (Measured in: Male organisms), Laboratory (COLLECTED FROM A FISH FARM, SAFA AQUARIUM, KOZHIKODE, KERALA, INDIA)	Fresh water, Aqueous (aquatic habitat), Static, NA Male organisms	Unmeasured	0 ppm / 0 ppm / 300 ppm	Biochemical (Enzyme(s)-Superoxide dismutase (SOD) enzyme activity, Response Site: Testes)	LOEC (300 ppm)	Mechanistic: Cell signaling/function; Oxidative stress (including redox biology); Reproductive/Teratogenic	Medium	7978601
28553-12-0	96 Hour(s), (96 Hour(s))	*Oreochromis mossambicus* (Mozambique Tilapia), Not reported, Both (Measured in: Male organisms), Laboratory (COLLECTED FROM A FISH FARM, SAFA AQUARIUM, KOZHIKODE, KERALA, INDIA)	Fresh water, Aqueous (aquatic habitat), Static, NA Male organisms	Unmeasured	0 ppm / 0 ppm / 300 ppm	Biochemical (Enzyme(s)-17beta-Hydroxysteroid dehydrogenase, Response Site: Testes)	LOEC (300 ppm)	Mechanistic: Cell signaling/function; Oxidative stress (including redox biology); Reproductive/Teratogenic	Medium	7978601
28553-12-0	96 Hour(s), (96 Hour(s))	*Oreochromis mossambicus* (Mozambique Tilapia), Not reported, Both (Measured in: Female organisms), Laboratory (COLLECTED FROM A FISH FARM, SAFA AQUARIUM, KOZHIKODE, KERALA, INDIA)	Fresh water, Aqueous (aquatic habitat), Static, NA Female organisms	Unmeasured	0 ppm / 0 ppm / 300 ppm	Biochemical (Enzyme(s)-3-beta Hydroxysteroid dehydrogenase, Response Site: Ovaries)	LOEC (300 ppm)	Mechanistic: Cell signaling/function; Oxidative stress (including redox biology); Reproductive/Teratogenic	Medium	7978601

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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
28553-12-0	96 Hour(s), (96 Hour(s))	*Oreochromis mossambicus* (Mozambique Tilapia), Not reported, Both (Measured in: Female organisms), Laboratory (COLLECTED FROM A FISH FARM, SAFA AQUARIUM, KOZHIKODE, KERALA, INDIA)	Fresh water, Aqueous (aquatic habitat), Static, NA Female organisms	Unmeasured	0 ppm / 0 ppm / 300 ppm	Physiology (Physiology-Lipid peroxidation, Response Site: Ovaries)	LOEC (300 ppm)	Mechanistic: Cell signaling/function; Oxidative stress (including redox biology); Reproductive/Teratogenic	Medium	7978601
28553-12-0	96 Hour(s), (96 Hour(s))	*Oreochromis mossambicus* (Mozambique Tilapia), Not reported, Both (Measured in: Female organisms), Laboratory (COLLECTED FROM A FISH FARM, SAFA AQUARIUM, KOZHIKODE, KERALA, INDIA)	Fresh water, Aqueous (aquatic habitat), Static, NA Female organisms	Unmeasured	0 ppm / 0 ppm / 300 ppm	Biochemical (Enzyme(s)-Catalase, Response Site: Ovaries)	LOEC (300 ppm)	Mechanistic: Cell signaling/function; Oxidative stress (including redox biology); Reproductive/Teratogenic	Medium	7978601
28553-12-0	96 Hour(s), (96 Hour(s))	*Oreochromis mossambicus* (Mozambique Tilapia), Not reported, Both (Measured in: Male organisms), Laboratory (COLLECTED FROM A FISH FARM, SAFA AQUARIUM, KOZHIKODE, KERALA, INDIA)	Fresh water, Aqueous (aquatic habitat), Static, NA Male organisms	Unmeasured	0 ppm / 0 ppm / 300 ppm	Biochemical (Enzyme(s)-Catalase, Response Site: Testes)	LOEC (300 ppm)	Mechanistic: Cell signaling/function; Oxidative stress (including redox biology); Reproductive/Teratogenic	Medium	7978601

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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
28553-12-0	96 Hour(s), (96 Hour(s))	*Oreochromis mossambicus* (Mozambique Tilapia), Not reported, Both (Measured in: Female organisms), Laboratory (COLLECTED FROM A FISH FARM, SAFA AQUARIUM, KOZHIKODE, KERALA, INDIA)	Fresh water, Aqueous (aquatic habitat), Static, NA Female organisms	Unmeasured	0 ppm / 0 ppm / 300 ppm	Biochemical (Enzyme(s)-Glutathione peroxidase, Response Site: Ovaries)	LOEC (300 ppm)	Mechanistic: Cell signaling/function; Oxidative stress (including redox biology); Reproductive/Teratogenic	Medium	7978601
28553-12-0	96 Hour(s), (96 Hour(s))	*Oreochromis mossambicus* (Mozambique Tilapia), Not reported, Both (Measured in: Male organisms), Laboratory (COLLECTED FROM A FISH FARM, SAFA AQUARIUM, KOZHIKODE, KERALA, INDIA)	Fresh water, Aqueous (aquatic habitat), Static, NA Male organisms	Unmeasured	0 ppm / 0 ppm / 300 ppm	Biochemical (Enzyme(s)-Glutathione peroxidase, Response Site: Testes)	LOEC (300 ppm)	Mechanistic: Cell signaling/function; Oxidative stress (including redox biology); Reproductive/Teratogenic	Medium	7978601
28553-12-0	96 Hour(s), (96 Hour(s))	*Oreochromis mossambicus* (Mozambique Tilapia), Not reported, Both (Measured in: Female organisms), Laboratory (COLLECTED FROM A FISH FARM, SAFA AQUARIUM, KOZHIKODE, KERALA, INDIA)	Fresh water, Aqueous (aquatic habitat), Static, NA Female organisms	Unmeasured	0 ppm / 0 ppm / 300 ppm	Biochemical (Enzyme(s)-Glutathione reductase, Response Site: Ovaries)	LOEC (300 ppm)	Mechanistic: Cell signaling/function; Oxidative stress (including redox biology); Reproductive/Teratogenic	Medium	7978601

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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
28553-12-0	96 Hour(s), (96 Hour(s))	*Oreochromis mossambicus* (Mozambique Tilapia), Not reported, Both (Measured in: Female organisms), Laboratory (COLLECTED FROM A FISH FARM, SAFA AQUARIUM, KOZHIKODE, KERALA, INDIA)	Fresh water, Aqueous (aquatic habitat), Static, NA Female organisms	Unmeasured	0 ppm / 0 ppm / 300 ppm	Biochemical (Enzyme(s)-Superoxide dismutase (SOD) enzyme activity, Response Site: Ovaries)	LOEC (300 ppm)	Mechanistic: Cell signaling/function; Oxidative stress (including redox biology); Reproductive/Teratogenic	Medium	7978601
28553-12-0	96 Hour(s), (96 Hour(s))	*Oreochromis mossambicus* (Mozambique Tilapia), Not reported, Both (Measured in: Male organisms), Laboratory (COLLECTED FROM A FISH FARM, SAFA AQUARIUM, KOZHIKODE, KERALA, INDIA)	Fresh water, Aqueous (aquatic habitat), Static, NA Male organisms	Unmeasured	0 ppm / 0 ppm / 300 ppm	Biochemical (Enzyme(s)-Glutathione reductase, Response Site: Testes)	LOEC (300 ppm)	Mechanistic: Cell signaling/function; Oxidative stress (including redox biology); Reproductive/Teratogenic	Medium	7978601
28553-12-0	96 Hour(s), (96 Hour(s))	*Oreochromis mossambicus* (Mozambique Tilapia), Not reported, Both (Measured in: Male organisms), Laboratory (COLLECTED FROM A FISH FARM, SAFA AQUARIUM, KOZHIKODE, KERALA, INDIA)	Fresh water, Aqueous (aquatic habitat), Static, NA Male organisms	Unmeasured	0 ppm / 0 ppm / 300 ppm	Biochemical (Enzyme(s)-3-beta Hydroxysteroid dehydrogenase, Response Site: Testes)	LOEC (300 ppm)	Mechanistic: Cell signaling/function; Oxidative stress (including redox biology); Reproductive/Teratogenic	Medium	7978601

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CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
28553-12-0	7 Day(s), (60 Day(s))	*Oreochromis mossambicus* (Mozambique Tilapia), Not reported, Both (Measured in: Female organisms), Laboratory (COLLECTED FROM A FISH FARM, SAFA AQUARIUM, KOZHIKODE, KERALA, INDIA)	Fresh water, Aqueous (aquatic habitat), Static, NA Female organisms	Unmeasured	0 ppm / 0 ppm / 300 ppm	Biochemical (Enzyme(s)-Catalase, Response Site: Ovaries)	LOEC (300 ppm)	Mechanistic: Cell signaling/function; Oxidative stress (including redox biology); Reproductive/Teratogenic	Medium	7978601
28553-12-0	7 Day(s), (60 Day(s))	*Oreochromis mossambicus* (Mozambique Tilapia), Not reported, Both (Measured in: Female organisms), Laboratory (COLLECTED FROM A FISH FARM, SAFA AQUARIUM, KOZHIKODE, KERALA, INDIA)	Fresh water, Aqueous (aquatic habitat), Static, NA Female organisms	Unmeasured	0 ppm / 0 ppm / 300 ppm	Biochemical (Enzyme(s)-Superoxide dismutase (SOD) enzyme activity, Response Site: Ovaries)	LOEC (300 ppm)	Mechanistic: Cell signaling/function; Oxidative stress (including redox biology); Reproductive/Teratogenic	Medium	7978601
28553-12-0	7 Day(s), (60 Day(s))	*Oreochromis mossambicus* (Mozambique Tilapia), Not reported, Both (Measured in: Male organisms), Laboratory (COLLECTED FROM A FISH FARM, SAFA AQUARIUM, KOZHIKODE, KERALA, INDIA)	Fresh water, Aqueous (aquatic habitat), Static, NA Male organisms	Unmeasured	0 ppm / 0 ppm / 300 ppm	Biochemical (Enzyme(s)-Catalase, Response Site: Testes)	LOEC (300 ppm)	Mechanistic: Cell signaling/function; Oxidative stress (including redox biology); Reproductive/Teratogenic	Medium	7978601

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CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
28553-12-0	7 Day(s), (60 Day(s))	*Oreochromis mossambicus* (Mozambique Tilapia), Not reported, Both (Measured in: Female organisms), Laboratory (COLLECTED FROM A FISH FARM, SAFA AQUARIUM, KOZHIKODE, KERALA, INDIA)	Fresh water, Aqueous (aquatic habitat), Static, NA Female organisms	Unmeasured	0 ppm / 0 ppm / 300 ppm	Biochemical (Enzyme(s)-Glutathione peroxidase, Response Site: Ovaries)	LOEC (300 ppm)	Mechanistic: Cell signaling/function; Oxidative stress (including redox biology); Reproductive/Teratogenic	Medium	7978601
28553-12-0	7 Day(s), (60 Day(s))	*Oreochromis mossambicus* (Mozambique Tilapia), Not reported, Both (Measured in: Male organisms), Laboratory (COLLECTED FROM A FISH FARM, SAFA AQUARIUM, KOZHIKODE, KERALA, INDIA)	Fresh water, Aqueous (aquatic habitat), Static, NA Male organisms	Unmeasured	0 ppm / 0 ppm / 300 ppm	Growth (Morphology-Weight, Response Site: Testes)	LOEC (300 ppm)	Reproductive/Teratogenic	Medium	7978601
28553-12-0	7 Day(s), (60 Day(s))	*Oreochromis mossambicus* (Mozambique Tilapia), Not reported, Both (Measured in: Female organisms), Laboratory (COLLECTED FROM A FISH FARM, SAFA AQUARIUM, KOZHIKODE, KERALA, INDIA)	Fresh water, Aqueous (aquatic habitat), Static, NA Female organisms	Unmeasured	0 ppm / 0 ppm / 300 ppm	Growth (Morphology-Weight, Response Site: Ovaries)	LOEC (300 ppm)	Reproductive/Teratogenic	Medium	7978601

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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
28553-12-0	7 Day(s), (60 Day(s))	*Oreochromis mossambicus* (Mozambique Tilapia), Not reported, Both (Measured in: Male organisms), Laboratory (COLLECTED FROM A FISH FARM, SAFA AQUARIUM, KOZHIKODE, KERALA, INDIA)	Fresh water, Aqueous (aquatic habitat), Static, NA Male organisms	Unmeasured	0 ppm / 0 ppm / 300 ppm	Biochemical (Enzyme(s)-Glutathione peroxidase, Response Site: Testes)	LOEC (300 ppm)	Mechanistic: Cell signaling/function; Oxidative stress (including redox biology); Reproductive/Teratogenic	Medium	7978601
28553-12-0	7 Day(s), (60 Day(s))	*Oreochromis mossambicus* (Mozambique Tilapia), Not reported, Both (Measured in: Male organisms), Laboratory (COLLECTED FROM A FISH FARM, SAFA AQUARIUM, KOZHIKODE, KERALA, INDIA)	Fresh water, Aqueous (aquatic habitat), Static, NA Male organisms	Unmeasured	0 ppm / 0 ppm / 300 ppm	Physiology (Physiology-Lipid peroxidation, Response Site: Testes)	LOEC (300 ppm)	Mechanistic: Cell signaling/function; Oxidative stress (including redox biology); Reproductive/Teratogenic	Medium	7978601
28553-12-0	7 Day(s), (60 Day(s))	*Oreochromis mossambicus* (Mozambique Tilapia), Not reported, Both (Measured in: Male organisms), Laboratory (COLLECTED FROM A FISH FARM, SAFA AQUARIUM, KOZHIKODE, KERALA, INDIA)	Fresh water, Aqueous (aquatic habitat), Static, NA Male organisms	Unmeasured	0 ppm / 0 ppm / 300 ppm	Biochemical (Enzyme(s)-Superoxide dismutase (SOD) enzyme activity, Response Site: Testes)	LOEC (300 ppm)	Mechanistic: Cell signaling/function; Oxidative stress (including redox biology); Reproductive/Teratogenic	Medium	7978601

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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
28553-12-0	7 Day(s), (60 Day(s))	*Oreochromis mossambicus* (Mozambique Tilapia), Not reported, Both (Measured in: Male organisms), Laboratory (COLLECTED FROM A FISH FARM, SAFA AQUARIUM, KOZHIKODE, KERALA, INDIA)	Fresh water, Aqueous (aquatic habitat), Static, NA Male organisms	Unmeasured	0 ppm / 0 ppm / 300 ppm	Biochemical (Enzyme(s)-3-beta Hydroxysteroid dehydrogenase, Response Site: Testes)	LOEC (300 ppm)	Mechanistic: Cell signaling/function; Oxidative stress (including redox biology); Reproductive/Teratogenic	Medium	7978601
28553-12-0	7 Day(s), (60 Day(s))	*Oreochromis mossambicus* (Mozambique Tilapia), Not reported, Both (Measured in: Female organisms), Laboratory (COLLECTED FROM A FISH FARM, SAFA AQUARIUM, KOZHIKODE, KERALA, INDIA)	Fresh water, Aqueous (aquatic habitat), Static, NA Female organisms	Unmeasured	0 ppm / 0 ppm / 300 ppm	Physiology (Physiology-Lipid peroxidation, Response Site: Ovaries)	LOEC (300 ppm)	Mechanistic: Cell signaling/function; Oxidative stress (including redox biology); Reproductive/Teratogenic	Medium	7978601
28553-12-0	7 Day(s), (60 Day(s))	*Oreochromis mossambicus* (Mozambique Tilapia), Not reported, Both (Measured in: Male organisms), Laboratory (COLLECTED FROM A FISH FARM, SAFA AQUARIUM, KOZHIKODE, KERALA, INDIA)	Fresh water, Aqueous (aquatic habitat), Static, NA Male organisms	Unmeasured	0 ppm / 0 ppm / 300 ppm	Biochemical (Enzyme(s)-17beta-Hydroxysteroid dehydrogenase, Response Site: Testes)	LOEC (300 ppm)	Mechanistic: Cell signaling/function; Oxidative stress (including redox biology); Reproductive/Teratogenic	Medium	7978601

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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
28553-12-0	7 Day(s), (60 Day(s))	*Oreochromis mossambicus* (Mozambique Tilapia), Not reported, Both (Measured in: Female organisms), Laboratory (COLLECTED FROM A FISH FARM, SAFA AQUARIUM, KOZHIKODE, KERALA, INDIA)	Fresh water, Aqueous (aquatic habitat), Static, NA Female organisms	Unmeasured	0 ppm / 0 ppm / 300 ppm	Biochemical (Enzyme(s)-17beta-Hydroxysteroid dehydrogenase, Response Site: Ovaries)	LOEC (300 ppm)	Mechanistic: Cell signaling/function; Oxidative stress (including redox biology); Reproductive/Teratogenic	Medium	7978601
28553-12-0	7 Day(s), (60 Day(s))	*Oreochromis mossambicus* (Mozambique Tilapia), Not reported, Both (Measured in: Male organisms), Laboratory (COLLECTED FROM A FISH FARM, SAFA AQUARIUM, KOZHIKODE, KERALA, INDIA)	Fresh water, Aqueous (aquatic habitat), Static, NA Male organisms	Unmeasured	0 ppm / 0 ppm / 300 ppm	Biochemical (Enzyme(s)-Glutathione reductase, Response Site: Testes)	LOEC (300 ppm)	Mechanistic: Cell signaling/function; Oxidative stress (including redox biology); Reproductive/Teratogenic	Medium	7978601
28553-12-0	7 Day(s), (60 Day(s))	*Oreochromis mossambicus* (Mozambique Tilapia), Not reported, Both (Measured in: Female organisms), Laboratory (COLLECTED FROM A FISH FARM, SAFA AQUARIUM, KOZHIKODE, KERALA, INDIA)	Fresh water, Aqueous (aquatic habitat), Static, NA Female organisms	Unmeasured	0 ppm / 0 ppm / 300 ppm	Biochemical (Enzyme(s)-3-beta Hydroxysteroid dehydrogenase, Response Site: Ovaries)	LOEC (300 ppm)	Mechanistic: Cell signaling/function; Oxidative stress (including redox biology); Reproductive/Teratogenic	Medium	7978601

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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
28553-12-0	7 Day(s), (60 Day(s))	*Oreochromis mossambicus* (Mozambique Tilapia), Not reported, Both (Measured in: Female organisms), Laboratory (COLLECTED FROM A FISH FARM, SAFA AQUARIUM, KOZHIKODE, KERALA, INDIA)	Fresh water, Aqueous (aquatic habitat), Static, NA Female organisms	Unmeasured	0 ppm / 0 ppm / 300 ppm	Biochemical (Enzyme(s)-Glutathione reductase, Response Site: Ovaries)	LOEC (300 ppm)	Mechanistic: Cell signaling/function; Oxidative stress (including redox biology); Reproductive/Teratogenic	Medium	7978601
28553-12-0	14 Day(s), (60 Day(s))	*Oreochromis mossambicus* (Mozambique Tilapia), Not reported, Both (Measured in: Male organisms), Laboratory (COLLECTED FROM A FISH FARM, SAFA AQUARIUM, KOZHIKODE, KERALA, INDIA)	Fresh water, Aqueous (aquatic habitat), Static, NA Male organisms	Unmeasured	0 ppm / 0 ppm / 300 ppm	Biochemical (Enzyme(s)-Glutathione peroxidase, Response Site: Testes)	LOEC (300 ppm)	Mechanistic: Cell signaling/function; Oxidative stress (including redox biology); Reproductive/Teratogenic	Medium	7978601
28553-12-0	14 Day(s), (60 Day(s))	*Oreochromis mossambicus* (Mozambique Tilapia), Not reported, Both (Measured in: Male organisms), Laboratory (COLLECTED FROM A FISH FARM, SAFA AQUARIUM, KOZHIKODE, KERALA, INDIA)	Fresh water, Aqueous (aquatic habitat), Static, NA Male organisms	Unmeasured	0 ppm / 0 ppm / 300 ppm	Biochemical (Enzyme(s)-Catalase, Response Site: Testes)	LOEC (300 ppm)	Mechanistic: Cell signaling/function; Oxidative stress (including redox biology); Reproductive/Teratogenic	Medium	7978601

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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
28553-12-0	14 Day(s), (60 Day(s))	*Oreochromis mossambicus* (Mozambique Tilapia), Not reported, Both (Measured in: Female organisms), Laboratory (COLLECTED FROM A FISH FARM, SAFA AQUARIUM, KOZHIKODE, KERALA, INDIA)	Fresh water, Aqueous (aquatic habitat), Static, NA Female organisms	Unmeasured	0 ppm / 0 ppm / 300 ppm	Biochemical (Enzyme(s)-Glutathione peroxidase, Response Site: Ovaries)	LOEC (300 ppm)	Mechanistic: Cell signaling/function; Oxidative stress (including redox biology); Reproductive/Teratogenic	Medium	7978601
28553-12-0	14 Day(s), (60 Day(s))	*Oreochromis mossambicus* (Mozambique Tilapia), Not reported, Both (Measured in: Female organisms), Laboratory (COLLECTED FROM A FISH FARM, SAFA AQUARIUM, KOZHIKODE, KERALA, INDIA)	Fresh water, Aqueous (aquatic habitat), Static, NA Female organisms	Unmeasured	0 ppm / 0 ppm / 300 ppm	Biochemical (Enzyme(s)-17beta-Hydroxysteroid dehydrogenase, Response Site: Ovaries)	LOEC (300 ppm)	Mechanistic: Cell signaling/function; Oxidative stress (including redox biology); Reproductive/Teratogenic	Medium	7978601
28553-12-0	14 Day(s), (60 Day(s))	*Oreochromis mossambicus* (Mozambique Tilapia), Not reported, Both (Measured in: Male organisms), Laboratory (COLLECTED FROM A FISH FARM, SAFA AQUARIUM, KOZHIKODE, KERALA, INDIA)	Fresh water, Aqueous (aquatic habitat), Static, NA Male organisms	Unmeasured	0 ppm / 0 ppm / 300 ppm	Biochemical (Enzyme(s)-17beta-Hydroxysteroid dehydrogenase, Response Site: Testes)	LOEC (300 ppm)	Mechanistic: Cell signaling/function; Oxidative stress (including redox biology); Reproductive/Teratogenic	Medium	7978601

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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
28553-12-0	14 Day(s), (60 Day(s))	*Oreochromis mossambicus* (Mozambique Tilapia), Not reported, Both (Measured in: Female organisms), Laboratory (COLLECTED FROM A FISH FARM, SAFA AQUARIUM, KOZHIKODE, KERALA, INDIA)	Fresh water, Aqueous (aquatic habitat), Static, NA Female organisms	Unmeasured	0 ppm / 0 ppm / 300 ppm	Biochemical (Enzyme(s)-3-beta Hydroxysteroid dehydrogenase, Response Site: Ovaries)	LOEC (300 ppm)	Mechanistic: Cell signaling/function; Oxidative stress (including redox biology); Reproductive/Teratogenic	Medium	7978601
28553-12-0	14 Day(s), (60 Day(s))	*Oreochromis mossambicus* (Mozambique Tilapia), Not reported, Both (Measured in: Male organisms), Laboratory (COLLECTED FROM A FISH FARM, SAFA AQUARIUM, KOZHIKODE, KERALA, INDIA)	Fresh water, Aqueous (aquatic habitat), Static, NA Male organisms	Unmeasured	0 ppm / 0 ppm / 300 ppm	Biochemical (Enzyme(s)-3-beta Hydroxysteroid dehydrogenase, Response Site: Testes)	LOEC (300 ppm)	Mechanistic: Cell signaling/function; Oxidative stress (including redox biology); Reproductive/Teratogenic	Medium	7978601
28553-12-0	14 Day(s), (60 Day(s))	*Oreochromis mossambicus* (Mozambique Tilapia), Not reported, Both (Measured in: Female organisms), Laboratory (COLLECTED FROM A FISH FARM, SAFA AQUARIUM, KOZHIKODE, KERALA, INDIA)	Fresh water, Aqueous (aquatic habitat), Static, NA Female organisms	Unmeasured	0 ppm / 0 ppm / 300 ppm	Biochemical (Enzyme(s)-Catalase, Response Site: Ovaries)	LOEC (300 ppm)	Mechanistic: Cell signaling/function; Oxidative stress (including redox biology); Reproductive/Teratogenic	Medium	7978601

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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
28553-12-0	14 Day(s), (60 Day(s))	*Oreochromis mossambicus* (Mozambique Tilapia), Not reported, Both (Measured in: Female organisms), Laboratory (COLLECTED FROM A FISH FARM, SAFA AQUARIUM, KOZHIKODE, KERALA, INDIA)	Fresh water, Aqueous (aquatic habitat), Static, NA Female organisms	Unmeasured	0 ppm / 0 ppm / 300 ppm	Biochemical (Enzyme(s)-Superoxide dismutase (SOD) enzyme activity, Response Site: Ovaries)	LOEC (300 ppm)	Mechanistic: Cell signaling/function; Oxidative stress (including redox biology); Reproductive/Teratogenic	Medium	7978601
28553-12-0	14 Day(s), (60 Day(s))	*Oreochromis mossambicus* (Mozambique Tilapia), Not reported, Both (Measured in: Female organisms), Laboratory (COLLECTED FROM A FISH FARM, SAFA AQUARIUM, KOZHIKODE, KERALA, INDIA)	Fresh water, Aqueous (aquatic habitat), Static, NA Female organisms	Unmeasured	0 ppm / 0 ppm / 300 ppm	Biochemical (Enzyme(s)-Glutathione reductase, Response Site: Ovaries)	LOEC (300 ppm)	Mechanistic: Cell signaling/function; Oxidative stress (including redox biology); Reproductive/Teratogenic	Medium	7978601
28553-12-0	14 Day(s), (60 Day(s))	*Oreochromis mossambicus* (Mozambique Tilapia), Not reported, Both (Measured in: Male organisms), Laboratory (COLLECTED FROM A FISH FARM, SAFA AQUARIUM, KOZHIKODE, KERALA, INDIA)	Fresh water, Aqueous (aquatic habitat), Static, NA Male organisms	Unmeasured	0 ppm / 0 ppm / 300 ppm	Physiology (Physiology-Lipid peroxidation, Response Site: Testes)	LOEC (300 ppm)	Mechanistic: Cell signaling/function; Oxidative stress (including redox biology); Reproductive/Teratogenic	Medium	7978601

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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
28553-12-0	14 Day(s), (60 Day(s))	*Oreochromis mossambicus* (Mozambique Tilapia), Not reported, Both (Measured in: Female organisms), Laboratory (COLLECTED FROM A FISH FARM, SAFA AQUARIUM, KOZHIKODE, KERALA, INDIA)	Fresh water, Aqueous (aquatic habitat), Static, NA Female organisms	Unmeasured	0 ppm / 0 ppm / 300 ppm	Physiology (Physiology-Lipid peroxidation, Response Site: Ovaries)	LOEC (300 ppm)	Mechanistic: Cell signaling/function; Oxidative stress (including redox biology); Reproductive/Teratogenic	Medium	7978601
28553-12-0	14 Day(s), (60 Day(s))	*Oreochromis mossambicus* (Mozambique Tilapia), Not reported, Both (Measured in: Male organisms), Laboratory (COLLECTED FROM A FISH FARM, SAFA AQUARIUM, KOZHIKODE, KERALA, INDIA)	Fresh water, Aqueous (aquatic habitat), Static, NA Male organisms	Unmeasured	0 ppm / 0 ppm / 300 ppm	Growth (Morphology-Weight, Response Site: Testes)	LOEC (300 ppm)	Reproductive/Teratogenic	Medium	7978601
28553-12-0	14 Day(s), (60 Day(s))	*Oreochromis mossambicus* (Mozambique Tilapia), Not reported, Both (Measured in: Female organisms), Laboratory (COLLECTED FROM A FISH FARM, SAFA AQUARIUM, KOZHIKODE, KERALA, INDIA)	Fresh water, Aqueous (aquatic habitat), Static, NA Female organisms	Unmeasured	0 ppm / 0 ppm / 300 ppm	Growth (Morphology-Weight, Response Site: Ovaries)	LOEC (300 ppm)	Reproductive/Teratogenic	Medium	7978601

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CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
28553-12-0	14 Day(s), (60 Day(s))	*Oreochromis mossambicus* (Mozambique Tilapia), Not reported, Both (Measured in: Male organisms), Laboratory (COLLECTED FROM A FISH FARM, SAFA AQUARIUM, KOZHIKODE, KERALA, INDIA)	Fresh water, Aqueous (aquatic habitat), Static, NA Male organisms	Unmeasured	0 ppm / 0 ppm / 300 ppm	Biochemical (Enzyme(s)-Superoxide dismutase (SOD) enzyme activity, Response Site: Testes)	LOEC (300 ppm)	Mechanistic: Cell signaling/function; Oxidative stress (including redox biology); Reproductive/Teratogenic	Medium	7978601
28553-12-0	14 Day(s), (60 Day(s))	*Oreochromis mossambicus* (Mozambique Tilapia), Not reported, Both (Measured in: Male organisms), Laboratory (COLLECTED FROM A FISH FARM, SAFA AQUARIUM, KOZHIKODE, KERALA, INDIA)	Fresh water, Aqueous (aquatic habitat), Static, NA Male organisms	Unmeasured	0 ppm / 0 ppm / 300 ppm	Biochemical (Enzyme(s)-Glutathione reductase, Response Site: Testes)	LOEC (300 ppm)	Mechanistic: Cell signaling/function; Oxidative stress (including redox biology); Reproductive/Teratogenic	Medium	7978601
28553-12-0	30 Day(s), (60 Day(s))	*Oreochromis mossambicus* (Mozambique Tilapia), Not reported, Both (Measured in: Male organisms), Laboratory (COLLECTED FROM A FISH FARM, SAFA AQUARIUM, KOZHIKODE, KERALA, INDIA)	Fresh water, Aqueous (aquatic habitat), Static, NA Male organisms	Unmeasured	0 ppm / 0 ppm / 300 ppm	Biochemical (Enzyme(s)-Superoxide dismutase (SOD) enzyme activity, Response Site: Testes)	LOEC (300 ppm)	Mechanistic: Cell signaling/function; Oxidative stress (including redox biology); Reproductive/Teratogenic	Medium	7978601

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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
28553-12-0	30 Day(s), (60 Day(s))	*Oreochromis mossambicus* (Mozambique Tilapia), Not reported, Both (Measured in: Female organisms), Laboratory (COLLECTED FROM A FISH FARM, SAFA AQUARIUM, KOZHIKODE, KERALA, INDIA)	Fresh water, Aqueous (aquatic habitat), Static, NA Female organisms	Unmeasured	0 ppm / 0 ppm / 300 ppm	Biochemical (Enzyme(s)-Glutathione peroxidase, Response Site: Ovaries)	LOEC (300 ppm)	Mechanistic: Cell signaling/function; Oxidative stress (including redox biology); Reproductive/Teratogenic	Medium	7978601
28553-12-0	30 Day(s), (60 Day(s))	*Oreochromis mossambicus* (Mozambique Tilapia), Not reported, Both (Measured in: Male organisms), Laboratory (COLLECTED FROM A FISH FARM, SAFA AQUARIUM, KOZHIKODE, KERALA, INDIA)	Fresh water, Aqueous (aquatic habitat), Static, NA Male organisms	Unmeasured	0 ppm / 0 ppm / 300 ppm	Biochemical (Enzyme(s)-Glutathione peroxidase, Response Site: Testes)	LOEC (300 ppm)	Mechanistic: Cell signaling/function; Oxidative stress (including redox biology); Reproductive/Teratogenic	Medium	7978601
28553-12-0	30 Day(s), (60 Day(s))	*Oreochromis mossambicus* (Mozambique Tilapia), Not reported, Both (Measured in: Female organisms), Laboratory (COLLECTED FROM A FISH FARM, SAFA AQUARIUM, KOZHIKODE, KERALA, INDIA)	Fresh water, Aqueous (aquatic habitat), Static, NA Female organisms	Unmeasured	0 ppm / 0 ppm / 300 ppm	Biochemical (Enzyme(s)-3-beta Hydroxysteroid dehydrogenase, Response Site: Ovaries)	LOEC (300 ppm)	Mechanistic: Cell signaling/function; Oxidative stress (including redox biology); Reproductive/Teratogenic	Medium	7978601

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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
28553-12-0	30 Day(s), (60 Day(s))	*Oreochromis mossambicus* (Mozambique Tilapia), Not reported, Both (Measured in: Female organisms), Laboratory (COLLECTED FROM A FISH FARM, SAFA AQUARIUM, KOZHIKODE, KERALA, INDIA)	Fresh water, Aqueous (aquatic habitat), Static, NA Female organisms	Unmeasured	0 ppm / 0 ppm / 300 ppm	Biochemical (Enzyme(s)-Superoxide dismutase (SOD) enzyme activity, Response Site: Ovaries)	LOEC (300 ppm)	Mechanistic: Cell signaling/function; Oxidative stress (including redox biology); Reproductive/Teratogenic	Medium	7978601
28553-12-0	30 Day(s), (60 Day(s))	*Oreochromis mossambicus* (Mozambique Tilapia), Not reported, Both (Measured in: Male organisms), Laboratory (COLLECTED FROM A FISH FARM, SAFA AQUARIUM, KOZHIKODE, KERALA, INDIA)	Fresh water, Aqueous (aquatic habitat), Static, NA Male organisms	Unmeasured	0 ppm / 0 ppm / 300 ppm	Biochemical (Enzyme(s)-3-beta Hydroxysteroid dehydrogenase, Response Site: Testes)	LOEC (300 ppm)	Mechanistic: Cell signaling/function; Oxidative stress (including redox biology); Reproductive/Teratogenic	Medium	7978601
28553-12-0	30 Day(s), (60 Day(s))	*Oreochromis mossambicus* (Mozambique Tilapia), Not reported, Both (Measured in: Female organisms), Laboratory (COLLECTED FROM A FISH FARM, SAFA AQUARIUM, KOZHIKODE, KERALA, INDIA)	Fresh water, Aqueous (aquatic habitat), Static, NA Female organisms	Unmeasured	0 ppm / 0 ppm / 300 ppm	Biochemical (Enzyme(s)-Glutathione reductase, Response Site: Ovaries)	LOEC (300 ppm)	Mechanistic: Cell signaling/function; Oxidative stress (including redox biology); Reproductive/Teratogenic	Medium	7978601

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CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
28553-12-0	30 Day(s), (60 Day(s))	*Oreochromis mossambicus* (Mozambique Tilapia), Not reported, Both (Measured in: Male organisms), Laboratory (COLLECTED FROM A FISH FARM, SAFA AQUARIUM, KOZHIKODE, KERALA, INDIA)	Fresh water, Aqueous (aquatic habitat), Static, NA Male organisms	Unmeasured	0 ppm / 0 ppm / 300 ppm	Biochemical (Enzyme(s)-17beta-Hydroxysteroid dehydrogenase, Response Site: Testes)	LOEC (300 ppm)	Mechanistic: Cell signaling/function; Oxidative stress (including redox biology); Reproductive/Teratogenic	Medium	7978601
28553-12-0	30 Day(s), (60 Day(s))	*Oreochromis mossambicus* (Mozambique Tilapia), Not reported, Both (Measured in: Male organisms), Laboratory (COLLECTED FROM A FISH FARM, SAFA AQUARIUM, KOZHIKODE, KERALA, INDIA)	Fresh water, Aqueous (aquatic habitat), Static, NA Male organisms	Unmeasured	0 ppm / 0 ppm / 300 ppm	Biochemical (Enzyme(s)-Glutathione reductase, Response Site: Testes)	LOEC (300 ppm)	Mechanistic: Cell signaling/function; Oxidative stress (including redox biology); Reproductive/Teratogenic	Medium	7978601
28553-12-0	30 Day(s), (60 Day(s))	*Oreochromis mossambicus* (Mozambique Tilapia), Not reported, Both (Measured in: Male organisms), Laboratory (COLLECTED FROM A FISH FARM, SAFA AQUARIUM, KOZHIKODE, KERALA, INDIA)	Fresh water, Aqueous (aquatic habitat), Static, NA Male organisms	Unmeasured	0 ppm / 0 ppm / 300 ppm	Biochemical (Enzyme(s)-Catalase, Response Site: Testes)	LOEC (300 ppm)	Mechanistic: Cell signaling/function; Oxidative stress (including redox biology); Reproductive/Teratogenic	Medium	7978601

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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
28553-12-0	30 Day(s), (60 Day(s))	*Oreochromis mossambicus* (Mozambique Tilapia), Not reported, Both (Measured in: Male organisms), Laboratory (COLLECTED FROM A FISH FARM, SAFA AQUARIUM, KOZHIKODE, KERALA, INDIA)	Fresh water, Aqueous (aquatic habitat), Static, NA Male organisms	Unmeasured	0 ppm / 0 ppm / 300 ppm	Physiology (Physiology-Lipid peroxidation, Response Site: Testes)	LOEC (300 ppm)	Mechanistic: Cell signaling/function; Oxidative stress (including redox biology); Reproductive/Teratogenic	Medium	7978601
28553-12-0	30 Day(s), (60 Day(s))	*Oreochromis mossambicus* (Mozambique Tilapia), Not reported, Both (Measured in: Female organisms), Laboratory (COLLECTED FROM A FISH FARM, SAFA AQUARIUM, KOZHIKODE, KERALA, INDIA)	Fresh water, Aqueous (aquatic habitat), Static, NA Female organisms	Unmeasured	0 ppm / 0 ppm / 300 ppm	Growth (Morphology-Weight, Response Site: Ovaries)	LOEC (300 ppm)	Reproductive/Teratogenic	Medium	7978601
28553-12-0	30 Day(s), (60 Day(s))	*Oreochromis mossambicus* (Mozambique Tilapia), Not reported, Both (Measured in: Female organisms), Laboratory (COLLECTED FROM A FISH FARM, SAFA AQUARIUM, KOZHIKODE, KERALA, INDIA)	Fresh water, Aqueous (aquatic habitat), Static, NA Female organisms	Unmeasured	0 ppm / 0 ppm / 300 ppm	Physiology (Physiology-Lipid peroxidation, Response Site: Ovaries)	LOEC (300 ppm)	Mechanistic: Cell signaling/function; Oxidative stress (including redox biology); Reproductive/Teratogenic	Medium	7978601

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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
28553-12-0	30 Day(s), (60 Day(s))	*Oreochromis mossambicus* (Mozambique Tilapia), Not reported, Both (Measured in: Female organisms), Laboratory (COLLECTED FROM A FISH FARM, SAFA AQUARIUM, KOZHIKODE, KERALA, INDIA)	Fresh water, Aqueous (aquatic habitat), Static, NA Female organisms	Unmeasured	0 ppm / 0 ppm / 300 ppm	Biochemical (Enzyme(s)-17beta-Hydroxysteroid dehydrogenase, Response Site: Ovaries)	LOEC (300 ppm)	Mechanistic: Cell signaling/function; Oxidative stress (including redox biology); Reproductive/Teratogenic	Medium	7978601
28553-12-0	30 Day(s), (60 Day(s))	*Oreochromis mossambicus* (Mozambique Tilapia), Not reported, Both (Measured in: Male organisms), Laboratory (COLLECTED FROM A FISH FARM, SAFA AQUARIUM, KOZHIKODE, KERALA, INDIA)	Fresh water, Aqueous (aquatic habitat), Static, NA Male organisms	Unmeasured	0 ppm / 0 ppm / 300 ppm	Growth (Morphology-Weight, Response Site: Testes)	LOEC (300 ppm)	Reproductive/Teratogenic	Medium	7978601
28553-12-0	30 Day(s), (60 Day(s))	*Oreochromis mossambicus* (Mozambique Tilapia), Not reported, Both (Measured in: Female organisms), Laboratory (COLLECTED FROM A FISH FARM, SAFA AQUARIUM, KOZHIKODE, KERALA, INDIA)	Fresh water, Aqueous (aquatic habitat), Static, NA Female organisms	Unmeasured	0 ppm / 0 ppm / 300 ppm	Biochemical (Enzyme(s)-Catalase, Response Site: Ovaries)	LOEC (300 ppm)	Mechanistic: Cell signaling/function; Oxidative stress (including redox biology); Reproductive/Teratogenic	Medium	7978601

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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
28553-12-0	60 Day(s), (60 Day(s))	*Oreochromis mossambicus* (Mozambique Tilapia), Not reported, Both (Measured in: Male organisms), Laboratory (COLLECTED FROM A FISH FARM, SAFA AQUARIUM, KOZHIKODE, KERALA, INDIA)	Fresh water, Aqueous (aquatic habitat), Static, NA Male organisms	Unmeasured	0 ppm / 0 ppm / 300 ppm	Growth (Morphology-Weight, Response Site: Testes)	LOEC (300 ppm)	Reproductive/Teratogenic	Medium	7978601
28553-12-0	60 Day(s), (60 Day(s))	*Oreochromis mossambicus* (Mozambique Tilapia), Not reported, Both (Measured in: Female organisms), Laboratory (COLLECTED FROM A FISH FARM, SAFA AQUARIUM, KOZHIKODE, KERALA, INDIA)	Fresh water, Aqueous (aquatic habitat), Static, NA Female organisms	Unmeasured	0 ppm / 0 ppm / 300 ppm	Biochemical (Enzyme(s)-17beta-Hydroxysteroid dehydrogenase, Response Site: Ovaries)	LOEC (300 ppm)	Mechanistic: Cell signaling/function; Oxidative stress (including redox biology); Reproductive/Teratogenic	Medium	7978601
28553-12-0	60 Day(s), (60 Day(s))	*Oreochromis mossambicus* (Mozambique Tilapia), Not reported, Both (Measured in: Female organisms), Laboratory (COLLECTED FROM A FISH FARM, SAFA AQUARIUM, KOZHIKODE, KERALA, INDIA)	Fresh water, Aqueous (aquatic habitat), Static, NA Female organisms	Unmeasured	0 ppm / 0 ppm / 300 ppm	Physiology (Physiology-Lipid peroxidation, Response Site: Ovaries)	LOEC (300 ppm)	Mechanistic: Cell signaling/function; Oxidative stress (including redox biology); Reproductive/Teratogenic	Medium	7978601

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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
28553-12-0	60 Day(s), (60 Day(s))	*Oreochromis mossambicus* (Mozambique Tilapia), Not reported, Both (Measured in: Female organisms), Laboratory (COLLECTED FROM A FISH FARM, SAFA AQUARIUM, KOZHIKODE, KERALA, INDIA)	Fresh water, Aqueous (aquatic habitat), Static, NA Female organisms	Unmeasured	0 ppm / 0 ppm / 300 ppm	Biochemical (Enzyme(s)-3-beta Hydroxysteroid dehydrogenase, Response Site: Ovaries)	LOEC (300 ppm)	Mechanistic: Cell signaling/function; Oxidative stress (including redox biology); Reproductive/Teratogenic	Medium	7978601
28553-12-0	60 Day(s), (60 Day(s))	*Oreochromis mossambicus* (Mozambique Tilapia), Not reported, Both (Measured in: Female organisms), Laboratory (COLLECTED FROM A FISH FARM, SAFA AQUARIUM, KOZHIKODE, KERALA, INDIA)	Fresh water, Aqueous (aquatic habitat), Static, NA Female organisms	Unmeasured	0 ppm / 0 ppm / 300 ppm	Biochemical (Enzyme(s)-Catalase, Response Site: Ovaries)	LOEC (300 ppm)	Mechanistic: Cell signaling/function; Oxidative stress (including redox biology); Reproductive/Teratogenic	Medium	7978601
28553-12-0	60 Day(s), (60 Day(s))	*Oreochromis mossambicus* (Mozambique Tilapia), Not reported, Both (Measured in: Male organisms), Laboratory (COLLECTED FROM A FISH FARM, SAFA AQUARIUM, KOZHIKODE, KERALA, INDIA)	Fresh water, Aqueous (aquatic habitat), Static, NA Male organisms	Unmeasured	0 ppm / 0 ppm / 300 ppm	Biochemical (Enzyme(s)-Catalase, Response Site: Testes)	LOEC (300 ppm)	Mechanistic: Cell signaling/function; Oxidative stress (including redox biology); Reproductive/Teratogenic	Medium	7978601

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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
28553-12-0	60 Day(s), (60 Day(s))	*Oreochromis mossambicus* (Mozambique Tilapia), Not reported, Both (Measured in: Female organisms), Laboratory (COLLECTED FROM A FISH FARM, SAFA AQUARIUM, KOZHIKODE, KERALA, INDIA)	Fresh water, Aqueous (aquatic habitat), Static, NA Female organisms	Unmeasured	0 ppm / 0 ppm / 300 ppm	Biochemical (Enzyme(s)-Glutathione peroxidase, Response Site: Ovaries)	LOEC (300 ppm)	Mechanistic: Cell signaling/function; Oxidative stress (including redox biology); Reproductive/Teratogenic	Medium	7978601
28553-12-0	60 Day(s), (60 Day(s))	*Oreochromis mossambicus* (Mozambique Tilapia), Not reported, Both (Measured in: Female organisms), Laboratory (COLLECTED FROM A FISH FARM, SAFA AQUARIUM, KOZHIKODE, KERALA, INDIA)	Fresh water, Aqueous (aquatic habitat), Static, NA Female organisms	Unmeasured	0 ppm / 0 ppm / 300 ppm	Biochemical (Enzyme(s)-Glutathione reductase, Response Site: Ovaries)	LOEC (300 ppm)	Mechanistic: Cell signaling/function; Oxidative stress (including redox biology); Reproductive/Teratogenic	Medium	7978601
28553-12-0	60 Day(s), (60 Day(s))	*Oreochromis mossambicus* (Mozambique Tilapia), Not reported, Both (Measured in: Male organisms), Laboratory (COLLECTED FROM A FISH FARM, SAFA AQUARIUM, KOZHIKODE, KERALA, INDIA)	Fresh water, Aqueous (aquatic habitat), Static, NA Male organisms	Unmeasured	0 ppm / 0 ppm / 300 ppm	Biochemical (Enzyme(s)-Glutathione reductase, Response Site: Testes)	LOEC (300 ppm)	Mechanistic: Cell signaling/function; Oxidative stress (including redox biology); Reproductive/Teratogenic	Medium	7978601

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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
28553-12-0	60 Day(s), (60 Day(s))	*Oreochromis mossambicus* (Mozambique Tilapia), Not reported, Both (Measured in: Female organisms), Laboratory (COLLECTED FROM A FISH FARM, SAFA AQUARIUM, KOZHIKODE, KERALA, INDIA)	Fresh water, Aqueous (aquatic habitat), Static, NA Female organisms	Unmeasured	0 ppm / 0 ppm / 300 ppm	Biochemical (Enzyme(s)-Superoxide dismutase (SOD) enzyme activity, Response Site: Ovaries)	LOEC (300 ppm)	Mechanistic: Cell signaling/function; Oxidative stress (including redox biology); Reproductive/Teratogenic	Medium	7978601
28553-12-0	60 Day(s), (60 Day(s))	*Oreochromis mossambicus* (Mozambique Tilapia), Not reported, Both (Measured in: Male organisms), Laboratory (COLLECTED FROM A FISH FARM, SAFA AQUARIUM, KOZHIKODE, KERALA, INDIA)	Fresh water, Aqueous (aquatic habitat), Static, NA Male organisms	Unmeasured	0 ppm / 0 ppm / 300 ppm	Physiology (Physiology-Lipid peroxidation, Response Site: Testes)	LOEC (300 ppm)	Mechanistic: Cell signaling/function; Oxidative stress (including redox biology); Reproductive/Teratogenic	Medium	7978601
28553-12-0	60 Day(s), (60 Day(s))	*Oreochromis mossambicus* (Mozambique Tilapia), Not reported, Both (Measured in: Male organisms), Laboratory (COLLECTED FROM A FISH FARM, SAFA AQUARIUM, KOZHIKODE, KERALA, INDIA)	Fresh water, Aqueous (aquatic habitat), Static, NA Male organisms	Unmeasured	0 ppm / 0 ppm / 300 ppm	Biochemical (Enzyme(s)-Superoxide dismutase (SOD) enzyme activity, Response Site: Testes)	LOEC (300 ppm)	Mechanistic: Cell signaling/function; Oxidative stress (including redox biology); Reproductive/Teratogenic	Medium	7978601

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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
28553-12-0	60 Day(s), (60 Day(s))	*Oreochromis mossambicus* (Mozambique Tilapia), Not reported, Both (Measured in: Female organisms), Laboratory (COLLECTED FROM A FISH FARM, SAFA AQUARIUM, KOZHIKODE, KERALA, INDIA)	Fresh water, Aqueous (aquatic habitat), Static, NA Female organisms	Unmeasured	0 ppm / 0 ppm / 300 ppm	Growth (Morphology-Weight, Response Site: Ovaries)	LOEC (300 ppm)	Reproductive/Teratogenic	Medium	7978601
28553-12-0	60 Day(s), (60 Day(s))	*Oreochromis mossambicus* (Mozambique Tilapia), Not reported, Both (Measured in: Male organisms), Laboratory (COLLECTED FROM A FISH FARM, SAFA AQUARIUM, KOZHIKODE, KERALA, INDIA)	Fresh water, Aqueous (aquatic habitat), Static, NA Male organisms	Unmeasured	0 ppm / 0 ppm / 300 ppm	Biochemical (Enzyme(s)-3-beta Hydroxysteroid dehydrogenase, Response Site: Testes)	LOEC (300 ppm)	Mechanistic: Cell signaling/function; Oxidative stress (including redox biology); Reproductive/Teratogenic	Medium	7978601
28553-12-0	60 Day(s), (60 Day(s))	*Oreochromis mossambicus* (Mozambique Tilapia), Not reported, Both (Measured in: Male organisms), Laboratory (COLLECTED FROM A FISH FARM, SAFA AQUARIUM, KOZHIKODE, KERALA, INDIA)	Fresh water, Aqueous (aquatic habitat), Static, NA Male organisms	Unmeasured	0 ppm / 0 ppm / 300 ppm	Biochemical (Enzyme(s)-17beta-Hydroxysteroid dehydrogenase, Response Site: Testes)	LOEC (300 ppm)	Mechanistic: Cell signaling/function; Oxidative stress (including redox biology); Reproductive/Teratogenic	Medium	7978601

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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
28553-12-0	60 Day(s), (60 Day(s))	*Oreochromis mossambicus* (Mozambique Tilapia), Not reported, Both (Measured in: Male organisms), Laboratory (COLLECTED FROM A FISH FARM, SAFA AQUARIUM, KOZHIKODE, KERALA, INDIA)	Fresh water, Aqueous (aquatic habitat), Static, NA Male organisms	Unmeasured	0 ppm / 0 ppm / 300 ppm	Biochemical (Enzyme(s)-Glutathione peroxidase, Response Site: Testes)	LOEC (300 ppm)	Mechanistic: Cell signaling/function; Oxidative stress (including redox biology); Reproductive/Teratogenic	Medium	7978601
28553-12-0	154 Days post-hatch, (300 Day(s))	*Oryzias latipes* (Japanese Medaka), Juvenile, 2 Week(s) (Measured in: male, 1st generation), Both (Measured in: male, 1st generation), Laboratory (ESTABLISHED BREEDING COLONY, ORIGINALLY SUPPLIED FROM THE CAROLINA BIOLOGICAL SUPPLY COMPANY, (BURLINGTON, NC))	Fresh water, Oral (diet, drink, gavage), Food, 20 male, 1st generation	Measured	0 mg/kg / 0 mg/kg / 18.4-24.5 mg/kg	Biochemical (Biochemistry-Vitellogenin, Response Site: Liver)	NR (18.5-24.5 mg/kg)	Mechanistic: Biomarkers (exposure and effect)	Low	5489073

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CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
28553-12-0	154 Days post-hatch, (300 Day(s))	*Oryzias latipes* (Japanese Medaka), Juvenile, 2 Week(s) (Measured in: female, 1st generation), Both (Measured in: female, 1st generation), Laboratory (ESTABLISHED BREEDING COLONY, ORIGINALLY SUPPLIED FROM THE CAROLINA BIOLOGICAL SUPPLY COMPANY, (BURLINGTON, NC))	Fresh water, Oral (diet, drink, gavage), Food, 20 female, 1st generation	Measured	0 mg/kg / 0 mg/kg / 18.4-24.5 mg/kg	Biochemical (Biochemistry-Vitellogenin, Response Site: Liver)	NR (18.5-24.5 mg/kg)	Mechanistic: Biomarkers (exposure and effect)	Low	5489073
28553-12-0	<=17 Day(s), (~17 Day(s))	*Oryzias latipes* (Japanese Medaka), Blastula, Not Reported, Laboratory (ESTABLISHED BREEDING COLONY, ORIGINALLY SUPPLIED FROM CAROLINA BIOLOGICAL SUPPLY, BURLINGTON, NC)	Fresh water, Aqueous (aquatic habitat), Static, Not Reported	Unmeasured	0 mg/L / 0 mg/L / <=209.5 mg/L	Mortality (Mortality-Mortality, Response Site: Not reported)	NR (<=209.5 mg/L)	Mortality	Uninformative	5489073

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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
28553-12-0	<=17 Day(s), (~17 Day(s))	*Oryzias latipes* (Japanese Medaka), Blastula, Not Reported, Laboratory (ESTABLISHED BREEDING COLONY, ORIGINALLY SUPPLIED FROM CAROLINA BIOLOGICAL SUPPLY, BURLINGTON, NC)	Fresh water, Aqueous (aquatic habitat), Static, Not Reported	Unmeasured	0 mg/L / 0 mg/L / <=209.5 mg/L	Cellular (Histology-Lesions, Response Site: Whole organism)	NR (<=209.5 mg/L)	Development/Growth	Uninformative	5489073
28553-12-0	140 Day(s), (300 Day(s))	*Oryzias latipes* (Japanese Medaka), Juvenile, 2 Week(s), Both, Laboratory (ESTABLISHED BREEDING COLONY, ORIGINALLY SUPPLIED FROM THE CAROLINA BIOLOGICAL SUPPLY COMPANY, (BURLINGTON, NC))	Fresh water, Oral (diet, drink, gavage), Food, 20 female, 0th (parental) generation	Measured	0 mg/kg / 0 mg/kg / 18.4-24.5 mg/kg	Biochemical (Biochemistry-Vitellogenin, Response Site: Liver)	NR (18.5-24.5 mg/kg)	Mechanistic: Biomarkers (exposure and effect)	Low	5489073

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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
28553-12-0	140 Day(s), (300 Day(s))	*Oryzias latipes* (Japanese Medaka), Juvenile, 2 Week(s), Both, Laboratory (ESTABLISHED BREEDING COLONY, ORIGINALLY SUPPLIED FROM THE CAROLINA BIOLOGICAL SUPPLY COMPANY, (BURLINGTON, NC))	Fresh water, Oral (diet, drink, gavage), Food, 20 male, 0th (parental) generation	Measured	0 mg/kg / 0 mg/kg / 18.4-24.5 mg/kg	Biochemical (Biochemistry-Vitellogenin, Response Site: Liver)	NR (18.5-24.5 mg/kg)	Mechanistic: Biomarkers (exposure and effect)	Low	5489073
68515-48-0	126 Day(s), (300 Day(s))	*Oryzias latipes* (Japanese Medaka), Juvenile, >14 Day(s), Both (Measured in: Female organisms), Laboratory (ORIGINALLY FROM CAROLINA BIOLOGICAL SUPPLY CO., BURLINGTON, NC TO ESTABLISH THE BREEDING COLONY)	Fresh water, Oral (diet, drink, gavage), Food, 29 Female organisms	Chemical analysis reported	0 ug/g bdwt/d / 0 ug/g bdwt/d / 1 ug/g bdwt/d	Growth (Growth-Weight, Response Site: Whole organism)	NOEC (1 ug/g bdwt/d)	Development/Growth	High	680110

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CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
68515-48-0	126 Day(s), (300 Day(s))	*Oryzias latipes* (Japanese Medaka), Juvenile, >14 Day(s), Both (Measured in: Male organisms), Laboratory (ORIGINALLY FROM CAROLINA BIOLOGICAL SUPPLY CO., BURLINGTON, NC TO ESTABLISH THE BREEDING COLONY)	Fresh water, Oral (diet, drink, gavage), Food, 47 Male organisms	Chemical analysis reported	0 ug/g bdwt/d / 0 ug/g bdwt/d / 1 ug/g bdwt/d	Growth (Growth-Weight, Response Site: Whole organism)	NOEC (1 ug/g bdwt/d)	Development/Growth	High	680110
68515-48-0	126 Day(s), (300 Day(s))	*Oryzias latipes* (Japanese Medaka), Juvenile, >14 Day(s), Both (Measured in: Female organisms), Laboratory (ORIGINALLY FROM CAROLINA BIOLOGICAL SUPPLY CO., BURLINGTON, NC TO ESTABLISH THE BREEDING COLONY)	Fresh water, Oral (diet, drink, gavage), Food, 23 Female organisms	Chemical analysis reported	0 ug/g bdwt/d / 0 ug/g bdwt/d / 1 ug/g bdwt/d	Growth (Morphology-Organ weight in relationship to body weight, Response Site: Gonad(s))	NOEC (1 ug/g bdwt/d)	Development/Growth	High	680110

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CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
68515-48-0	126 Day(s), (300 Day(s))	*Oryzias latipes* (Japanese Medaka), Juvenile, >14 Day(s), Both (Measured in: Male organisms), Laboratory (ORIGINALLY FROM CAROLINA BIOLOGICAL SUPPLY CO., BURLINGTON, NC TO ESTABLISH THE BREEDING COLONY)	Fresh water, Oral (diet, drink, gavage), Food, 25 Male organisms	Chemical analysis reported	0 ug/g bdwt/d / 0 ug/g bdwt/d / 1 ug/g bdwt/d	Growth (Morphology-Organ weight in relationship to body weight, Response Site: Gonad(s))	NOEC (1 ug/g bdwt/d)	Development/Growth	High	680110
68515-48-0	126 Day(s), (300 Day(s))	*Oryzias latipes* (Japanese Medaka), Juvenile, >14 Day(s), Both (Measured in: Female organisms), Laboratory (ORIGINALLY FROM CAROLINA BIOLOGICAL SUPPLY CO., BURLINGTON, NC TO ESTABLISH THE BREEDING COLONY)	Fresh water, Oral (diet, drink, gavage), Food, 23 Female organisms	Chemical analysis reported	0 ug/g bdwt/d / 0 ug/g bdwt/d / 1 ug/g bdwt/d	Growth (Morphology-Weight, Response Site: Gonad(s))	NOEC (1 ug/g bdwt/d)	Development/Growth	High	680110

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CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
68515-48-0	126 Day(s), (300 Day(s))	*Oryzias latipes* (Japanese Medaka), Juvenile, >14 Day(s), Both (Measured in: Male organisms), Laboratory (ORIGINALLY FROM CAROLINA BIOLOGICAL SUPPLY CO., BURLINGTON, NC TO ESTABLISH THE BREEDING COLONY)	Fresh water, Oral (diet, drink, gavage), Food, 25 Male organisms	Chemical analysis reported	0 ug/g bdwt/d / 0 ug/g bdwt/d / 1 ug/g bdwt/d	Growth (Morphology-Weight, Response Site: Gonad(s))	NOEC (1 ug/g bdwt/d)	Development/Growth	High	680110
68515-48-0	126 Day(s), (300 Day(s))	*Oryzias latipes* (Japanese Medaka), Juvenile, >14 Day(s) (Measured in: F0 generation), Both, Laboratory (ORIGINALLY FROM CAROLINA BIOLOGICAL SUPPLY CO., BURLINGTON, NC TO ESTABLISH THE BREEDING COLONY)	Fresh water, Oral (diet, drink, gavage), Food, 250 F0 generation	Chemical analysis reported	0 ug/g bdwt/d / 0 ug/g bdwt/d / 1 ug/g bdwt/d	Mortality (Mortality-Survival, Response Site: Not reported)	NOEC (1 ug/g bdwt/d)	Mortality	High	680110

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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
68515-48-0	126 Day(s), (300 Day(s))	*Oryzias latipes* (Japanese Medaka), Juvenile, >14 Day(s), Both (Measured in: Female organisms), Laboratory (ORIGINALLY FROM CAROLINA BIOLOGICAL SUPPLY CO., BURLINGTON, NC TO ESTABLISH THE BREEDING COLONY)	Fresh water, Oral (diet, drink, gavage), Food, 5 Female organisms	Chemical analysis reported	0 ug/g bdwt/d / 0 ug/g bdwt/d / 1 ug/g bdwt/d	Reproduction (Reproduction-Progeny counts/numbers, Response Site: Not reported)	NOEC (1 ug/g bdwt/d)	Reproductive/Teratogenic	High	680110
68515-48-0	167-207 Day(s), (300 Day(s))	*Oryzias latipes* (Japanese Medaka), Juvenile, >14 Day(s) (Measured in: F1 generation), Both, Laboratory (ORIGINALLY FROM CAROLINA BIOLOGICAL SUPPLY CO., BURLINGTON, NC TO ESTABLISH THE BREEDING COLONY)	Fresh water, Oral (diet, drink, gavage), Food, 50 F1 generation	Chemical analysis reported	0 ug/g bdwt/d / 0 ug/g bdwt/d / 1 ug/g bdwt/d	Physiology (Physiology-Pigmentation, Response Site: Not reported)	LOEC (1 ug/g bdwt/d)	Mechanistic: Biomarkers (exposure and effect); Immune/Hematological	High	680110

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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
68515-48-0	167-207 Day(s), (300 Day(s))	*Oryzias latipes* (Japanese Medaka), Juvenile, >14 Day(s) (Measured in: F1 generation), Both, Laboratory (ORIGINALLY FROM CAROLINA BIOLOGICAL SUPPLY CO., BURLINGTON, NC TO ESTABLISH THE BREEDING COLONY)	Fresh water, Oral (diet, drink, gavage), Food, 50 F1 generation	Chemical analysis reported	0 ug/g bdwt/d / 0 ug/g bdwt/d / 1 ug/g bdwt/d	Mortality (Mortality-Survival, Response Site: Not reported)	NOEC (1 ug/g bdwt/d)	Mortality	High	680110
68515-48-0	167-207 Day(s), (300 Day(s))	*Oryzias latipes* (Japanese Medaka), Juvenile, >14 Day(s) (Measured in: female, 1st generation), Both (Measured in: female, 1st generation), Laboratory (ORIGINALLY FROM CAROLINA BIOLOGICAL SUPPLY CO., BURLINGTON, NC TO ESTABLISH THE BREEDING COLONY)	Fresh water, Oral (diet, drink, gavage), Food, 5 female, 1st generation	Chemical analysis reported	0 ug/g bdwt/d / 0 ug/g bdwt/d / 1 ug/g bdwt/d	Reproduction (Reproduction-Progeny counts/numbers, Response Site: Not reported)	NOEC (1 ug/g bdwt/d)	Reproductive/Teratogenic	High	680110

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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
68515-48-0	168-207 Day(s), (300 Day(s))	*Oryzias latipes* (Japanese Medaka), Juvenile, >14 Day(s) (Measured in: female, 1st generation), Both (Measured in: female, 1st generation), Laboratory (ORIGINALLY FROM CAROLINA BIOLOGICAL SUPPLY CO., BURLINGTON, NC TO ESTABLISH THE BREEDING COLONY)	Fresh water, Oral (diet, drink, gavage), Food, 42 female, 1st generation	Chemical analysis reported	0 ug/g bdwt/d / 0 ug/g bdwt/d / 1 ug/g bdwt/d	Growth (Growth-Weight, Response Site: Whole organism)	NOEC (1 ug/g bdwt/d)	Development/Growth	High	680110
68515-48-0	168-207 Day(s), (300 Day(s))	*Oryzias latipes* (Japanese Medaka), Juvenile, >14 Day(s) (Measured in: female, 1st generation), Both (Measured in: female, 1st generation), Laboratory (ORIGINALLY FROM CAROLINA BIOLOGICAL SUPPLY CO., BURLINGTON, NC TO ESTABLISH THE BREEDING COLONY)	Fresh water, Oral (diet, drink, gavage), Food, 50 female, 1st generation	Chemical analysis reported	0 ug/g bdwt/d / 0 ug/g bdwt/d / 1 ug/g bdwt/d	Growth (Morphology-Organ weight in relationship to body weight, Response Site: Gonad(s))	NOEC (1 ug/g bdwt/d)	Development/Growth	High	680110

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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
68515-48-0	168-207 Day(s), (300 Day(s))	*Oryzias latipes* (Japanese Medaka), Juvenile, >14 Day(s) (Measured in: female, 1st generation), Both (Measured in: female, 1st generation), Laboratory (ORIGINALLY FROM CAROLINA BIOLOGICAL SUPPLY CO., BURLINGTON, NC TO ESTABLISH THE BREEDING COLONY)	Fresh water, Oral (diet, drink, gavage), Food, 50 female, 1st generation	Chemical analysis reported	0 ug/g bdwt/d / 0 ug/g bdwt/d / 1 ug/g bdwt/d	Growth (Morphology-Weight, Response Site: Gonad(s))	NOEC (1 ug/g bdwt/d)	Development/Growth	High	680110
68515-48-0	168-207 Day(s), (300 Day(s))	*Oryzias latipes* (Japanese Medaka), Juvenile, >14 Day(s) (Measured in: male, 1st generation), Both (Measured in: male, 1st generation), Laboratory (ORIGINALLY FROM CAROLINA BIOLOGICAL SUPPLY CO., BURLINGTON, NC TO ESTABLISH THE BREEDING COLONY)	Fresh water, Oral (diet, drink, gavage), Food, 48 male, 1st generation	Chemical analysis reported	0 ug/g bdwt/d / 0 ug/g bdwt/d / 1 ug/g bdwt/d	Growth (Morphology-Weight, Response Site: Gonad(s))	NOEC (1 ug/g bdwt/d)	Development/Growth	High	680110

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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
68515-48-0	168-207 Day(s), (300 Day(s))	*Oryzias latipes* (Japanese Medaka), Juvenile, >14 Day(s) (Measured in: female, 1st generation), Both (Measured in: female, 1st generation), Laboratory (ORIGINALLY FROM CAROLINA BIOLOGICAL SUPPLY CO., BURLINGTON, NC TO ESTABLISH THE BREEDING COLONY)	Fresh water, Oral (diet, drink, gavage), Food, 5 female, 1st generation	Chemical analysis reported	0 ug/g bdwt/d / 0 ug/g bdwt/d / 1 ug/g bdwt/d	Reproduction (Reproduction-Progeny counts/numbers, Response Site: Not reported)	NOEC (1 ug/g bdwt/d)	Reproductive/Teratogenic	High	680110
68515-48-0	126-207 Day(s), (300 Day(s))	*Oryzias latipes* (Japanese Medaka), Juvenile, >14 Day(s), Both, Laboratory (ORIGINALLY FROM CAROLINA BIOLOGICAL SUPPLY CO., BURLINGTON, NC TO ESTABLISH THE BREEDING COLONY)	Fresh water, Oral (diet, drink, gavage), Food, NA Multiple	Chemical analysis reported	0 ug/g bdwt/d / 0 ug/g bdwt/d / 1 ug/g bdwt/d	Biochemical (Enzyme(s)-Cytochrome P1A,7-Ethoxyresorufin O-deethylase, Response Site: Liver)	NR (1 ug/g bdwt/d)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Immune/Hematological	High	680110

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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
68515-48-0	126-207 Day(s), (300 Day(s))	*Oryzias latipes* (Japanese Medaka), Juvenile, >14 Day(s), Both, Laboratory (ORIGINALLY FROM CAROLINA BIOLOGICAL SUPPLY CO., BURLINGTON, NC TO ESTABLISH THE BREEDING COLONY)	Fresh water, Oral (diet, drink, gavage), Food, NA Multiple	Chemical analysis reported	0 ug/g bdwt/d / 0 ug/g bdwt/d / 1 ug/g bdwt/d	Biochemical (Hormone(s)-Testosterone, Response Site: Liver)	NR (1 ug/g bdwt/d)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Immune/Hematological	High	680110
68515-48-0	168-207 Day(s), (300 Day(s))	*Oryzias latipes* (Japanese Medaka), Juvenile, >14 Day(s) (Measured in: male, 1st generation), Both (Measured in: male, 1st generation), Laboratory (ORIGINALLY FROM CAROLINA BIOLOGICAL SUPPLY CO., BURLINGTON, NC TO ESTABLISH THE BREEDING COLONY)	Fresh water, Oral (diet, drink, gavage), Food, 48 male, 1st generation	Chemical analysis reported	0 ug/g bdwt/d / 0 ug/g bdwt/d / 1 ug/g bdwt/d	Growth (Morphology-Organ weight in relationship to body weight, Response Site: Gonad(s))	NOEC (1 ug/g bdwt/d)	Development/Growth	High	680110

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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
68515-48-0	168-207 Day(s), (300 Day(s))	*Oryzias latipes* (Japanese Medaka), Juvenile, >14 Day(s) (Measured in: male, 1st generation), Both (Measured in: male, 1st generation), Laboratory (ORIGINALLY FROM CAROLINA BIOLOGICAL SUPPLY CO., BURLINGTON, NC TO ESTABLISH THE BREEDING COLONY)	Fresh water, Oral (diet, drink, gavage), Food, 45 male, 1st generation	Chemical analysis reported	0 ug/g bdwt/d / 0 ug/g bdwt/d / 1 ug/g bdwt/d	Growth (Growth-Weight, Response Site: Whole organism)	NOEC (1 ug/g bdwt/d)	Development/Growth	High	680110
68515-48-0	167-207 Day(s), (300 Day(s))	*Oryzias latipes* (Japanese Medaka), Juvenile, >14 Day(s) (Measured in: F1 generation), Both, Laboratory (ORIGINALLY FROM CAROLINA BIOLOGICAL SUPPLY CO., BURLINGTON, NC TO ESTABLISH THE BREEDING COLONY)	Fresh water, Oral (diet, drink, gavage), Food, 50 F1 generation	Chemical analysis reported	0 ug/g bdwt/d / 0 ug/g bdwt/d / 1 ug/g bdwt/d	Mortality (Mortality-Survival, Response Site: Not reported)	LOEC (1 ug/g bdwt/d)	Mortality	High	680110

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CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
68515-48-0	266 Day(s), (300 Day(s))	*Oryzias latipes* (Japanese Medaka), Juvenile, >14 Day(s) (Measured in: F2 generation), Both, Laboratory (ORIGINALLY FROM CAROLINA BIOLOGICAL SUPPLY CO., BURLINGTON, NC TO ESTABLISH THE BREEDING COLONY)	Fresh water, Oral (diet, drink, gavage), Food, 50 F2 generation	Chemical analysis reported	0 ug/g bdwt/d / 0 ug/g bdwt/d / 1 ug/g bdwt/d	Mortality (Mortality-Survival, Response Site: Not reported)	NOEC (1 ug/g bdwt/d)	Mortality	High	680110
68515-48-0	266 Day(s), (300 Day(s))	*Oryzias latipes* (Japanese Medaka), Juvenile, >14 Day(s) (Measured in: F2 generation), Both, Laboratory (ORIGINALLY FROM CAROLINA BIOLOGICAL SUPPLY CO., BURLINGTON, NC TO ESTABLISH THE BREEDING COLONY)	Fresh water, Oral (diet, drink, gavage), Food, 50 F2 generation	Chemical analysis reported	0 ug/g bdwt/d / 0 ug/g bdwt/d / 1 ug/g bdwt/d	Physiology (Physiology-Pigmentation, Response Site: Not reported)	NOEC (1 ug/g bdwt/d)	Mechanistic: Biomarkers (exposure and effect); Immune/Hematological	High	680110

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CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
68515-48-0	266 Day(s), (300 Day(s))	*Oryzias latipes* (Japanese Medaka), Juvenile, >14 Day(s) (Measured in: F2 generation), Both, Laboratory (ORIGINALLY FROM CAROLINA BIOLOGICAL SUPPLY CO., BURLINGTON, NC TO ESTABLISH THE BREEDING COLONY)	Fresh water, Oral (diet, drink, gavage), Food, 50 F2 generation	Chemical analysis reported	0 ug/g bdwt/d / 0 ug/g bdwt/d / 1 ug/g bdwt/d	Physiology (Physiology-Pigmentation, Response Site: Not reported)	LOEC (1 ug/g bdwt/d)	Mechanistic: Biomarkers (exposure and effect); Immune/Hematological	High	680110
68515-48-0	266 Day(s), (300 Day(s))	*Oryzias latipes* (Japanese Medaka), Juvenile, >14 Day(s) (Measured in: F1 generation), Both, Laboratory (ORIGINALLY FROM CAROLINA BIOLOGICAL SUPPLY CO., BURLINGTON, NC TO ESTABLISH THE BREEDING COLONY)	Fresh water, Oral (diet, drink, gavage), Food, 250 F1 generation	Chemical analysis reported	0 ug/g bdwt/d / 0 ug/g bdwt/d / 1 ug/g bdwt/d	Mortality (Mortality-Survival, Response Site: Not reported)	LOEC (1 ug/g bdwt/d)	Mortality	High	680110

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CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
68515-48-0	300 Day(s), (300 Day(s))	*Oryzias latipes* (Japanese Medaka), Juvenile, >14 Day(s) (Measured in: F2 generation), Both, Laboratory (ORIGINALLY FROM CAROLINA BIOLOGICAL SUPPLY CO., BURLINGTON, NC TO ESTABLISH THE BREEDING COLONY)	Fresh water, Oral (diet, drink, gavage), Food, 250 F2 generation	Chemical analysis reported	0 ug/g bdwt/d / 0 ug/g bdwt/d / 1 ug/g bdwt/d	Mortality (Mortality-Survival, Response Site: Not reported)	NOEC (1 ug/g bdwt/d)	Mortality	High	680110
28553-12-0	24 Hour(s), (24 Hour(s))	*Oryzias melastigma* (Indian Medaka), Embryo, Not Reported, Laboratory	Fresh water, Aqueous (aquatic habitat), Static, Not Reported	Unmeasured	0 ppm / 0 ppm / 0.01 ppm / 0.06 ppm / 0.30 ppm / 0.60 ppm / 1.50 ppm / 10.00 ppm / 50.00 ppm	Biochemical (Hormone(s)-Estrogen (Oestrogen), Response Site: Liver)	NR (0.01-50.00 ppm)	Mechanistic: Receptor binding/ regulation of receptor activity; Endocrine toxicity; Reproductive/Teratogenic	Medium	2298079
28553-12-0	96 Hour(s), (96 Hour(s))	*Pimephales promelas* (Fathead Minnow), Juvenile, Not Reported, Not reported (NR)	Fresh water, Aqueous (aquatic habitat), Flow-through, Not Reported	Measured	NR / NR	Mortality (Mortality-Mortality, Response Site: Not reported)	LC50 (>0.19 mg/L)	Mortality	High	1321996
28553-12-0	96 Hour(s), (96 Hour(s))	*Pimephales promelas* (Fathead Minnow), Juvenile, Not Reported, Not reported (NR)	Fresh water, Aqueous (aquatic habitat), Static, Not Reported	Measured	NR / NR	Mortality (Mortality-Mortality, Response Site: Not reported)	LC50 (>0.10 mg/L)	Mortality	High	1321996

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CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
28553-12-0	24 Hour(s), (96 Hour(s))	*Pimephales promelas* (Fathead Minnow), Not reported, Not Reported, Laboratory (OBTAINED FROM CULTURES MAINTAINED AT EG AND G, BIONOMICS, WAREHAM, MASSACHUSETTS)	Fresh water, Aqueous (aquatic habitat), Static, Not Reported	Measured	<0.013 mg/L / 0.075-0.15 mg/L	Mortality (Mortality-Mortality, Response Site: Not reported)	LC50 (>0.14 mg/L)	Mortality	High	1316188
28553-12-0	48 Hour(s), (96 Hour(s))	*Pimephales promelas* (Fathead Minnow), Not reported, Not Reported, Laboratory (OBTAINED FROM CULTURES MAINTAINED AT EG AND G, BIONOMICS, WAREHAM, MASSACHUSETTS)	Fresh water, Aqueous (aquatic habitat), Static, Not Reported	Measured	<0.013 mg/L / 0.075-0.15 mg/L	Mortality (Mortality-Mortality, Response Site: Not reported)	LC50 (>0.14 mg/L)	Mortality	High	1316188
28553-12-0	72 Hour(s), (96 Hour(s))	*Pimephales promelas* (Fathead Minnow), Not reported, Not Reported, Laboratory (OBTAINED FROM CULTURES MAINTAINED AT EG AND G, BIONOMICS, WAREHAM, MASSACHUSETTS)	Fresh water, Aqueous (aquatic habitat), Static, Not Reported	Measured	<0.013 mg/L / 0.075-0.15 mg/L	Mortality (Mortality-Mortality, Response Site: Not reported)	LC50 (>0.14 mg/L)	Mortality	High	1316188

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CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
28553-12-0	96 Hour(s), (96 Hour(s))	*Pimephales promelas* (Fathead Minnow), Not reported, Not Reported, Laboratory (OBTAINED FROM CULTURES MAINTAINED AT EG AND G, BIONOMICS, WAREHAM, MASSACHUSETTS)	Fresh water, Aqueous (aquatic habitat), Static, Not Reported	Measured	<0.013 mg/L / 0.075-0.15 mg/L	Mortality (Mortality-Mortality, Response Site: Not reported)	LC50 (>0.14 mg/L)	Mortality	High	1316188
28553-12-0	96 Hour(s), (96 Hour(s))	*Pimephales promelas* (Fathead Minnow), Not reported, Not Reported, Laboratory (OBTAINED FROM CULTURES MAINTAINED AT EG AND G, BIONOMICS, WAREHAM, MASSACHUSETTS)	Fresh water, Aqueous (aquatic habitat), Static, Not Reported	Measured	<0.013 mg/L / 0.075-0.15 mg/L	Mortality (Mortality-Mortality, Response Site: Not reported)	NR-ZERO (0.075-0.15 mg/L)	Mortality	High	1316188
28553-12-0	24 Hour(s), (96 Hour(s))	*Pimephales promelas* (Fathead Minnow), Not reported, Not Reported, Laboratory (EG AND G BIONOMICS, WAREHAM, MASSACHUSETTS)	Fresh water, Aqueous (aquatic habitat), Flow-through, Not Reported	Measured	<0.0085 (<0.0068-<0.0085) mg/L / 0.019 (0.015-0.026) mg/L / 0.030 (0.024-0.032) mg/L / 0.047 (0.043-0.050) mg/L / 0.097 (0.092-0.10) mg/L / 0.19 (0.16-0.21) mg/L	Mortality (Mortality-Mortality, Response Site: Not reported)	LC50 (>0.19 mg/L)	Mortality	High	1316189

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CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
28553-12-0	48 Hour(s), (96 Hour(s))	*Pimephales promelas* (Fathead Minnow), Not reported, Not Reported, Laboratory (EG AND G BIONOMICS, WAREHAM, MASSACHUSETTS)	Fresh water, Aqueous (aquatic habitat), Flow-through, Not Reported	Measured	<0.0085 (<0.0068-<0.0085) mg/L / 0.019 (0.015-0.026) mg/L / 0.030 (0.024-0.032) mg/L / 0.047 (0.043-0.050) mg/L / 0.097 (0.092-0.10) mg/L / 0.19 (0.16-0.21) mg/L	Mortality (Mortality-Mortality, Response Site: Not reported)	LC50 (>0.19 mg/L)	Mortality	High	1316189
28553-12-0	72 Hour(s), (96 Hour(s))	*Pimephales promelas* (Fathead Minnow), Not reported, Not Reported, Laboratory (EG AND G BIONOMICS, WAREHAM, MASSACHUSETTS)	Fresh water, Aqueous (aquatic habitat), Flow-through, Not Reported	Measured	<0.0085 (<0.0068-<0.0085) mg/L / 0.019 (0.015-0.026) mg/L / 0.030 (0.024-0.032) mg/L / 0.047 (0.043-0.050) mg/L / 0.097 (0.092-0.10) mg/L / 0.19 (0.16-0.21) mg/L	Mortality (Mortality-Mortality, Response Site: Not reported)	LC50 (>0.19 mg/L)	Mortality	High	1316189
28553-12-0	96 Hour(s), (96 Hour(s))	*Pimephales promelas* (Fathead Minnow), Not reported, Not Reported, Laboratory (EG AND G BIONOMICS, WAREHAM, MASSACHUSETTS)	Fresh water, Aqueous (aquatic habitat), Flow-through, 20 Organism	Measured	<0.0085 (<0.0068-<0.0085) mg/L / 0.019 (0.015-0.026) mg/L / 0.030 (0.024-0.032) mg/L / 0.047 (0.043-0.050) mg/L / 0.097 (0.092-0.10) mg/L / 0.19 (0.16-0.21) mg/L	Mortality (Mortality-Mortality, Response Site: Not reported)	NOEC (0.19 (0.16-0.21) mg/L)	Mortality	High	1316189

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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
28553-12-0	21 Day(s), (21 Day(s))	*Sparus aurata* (Gilthead Seabream), Adult, 2 Year(s), Male, Laboratory (COMMERCIAL AQUACULTURE FACILITY (FORKYS S.A., CRETE, GREECE)	Salt water, Oral (diet, drink, gavage), Food, Not Reported	Unmeasured	0 AI ug/kg bdwt/d / 15 AI ug/kg bdwt/d / 1500 AI ug/kg bdwt/d	Cellular (Genetics-Cathepsin D mRNA, Response Site: Muscle)	LOEC (1500 AI ug/kg bdwt/d)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Musculoskeletal	Medium	5532247
28553-12-0	21 Day(s), (21 Day(s))	*Sparus aurata* (Gilthead Seabream), Adult, 2 Year(s), Male, Laboratory (COMMERCIAL AQUACULTURE FACILITY (FORKYS S.A., CRETE, GREECE)	Salt water, Oral (diet, drink, gavage), Food, Not Reported	Unmeasured	0 AI ug/kg bdwt/d / 15 AI ug/kg bdwt/d / 1500 AI ug/kg bdwt/d	Cellular (Genetics-Calpain small subunit 1-like mRNA, Response Site: Muscle)	LOEC (1500 AI ug/kg bdwt/d)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Musculoskeletal	Medium	5532247
28553-12-0	21 Day(s), (21 Day(s))	*Sparus aurata* (Gilthead Seabream), Adult, 2 Year(s), Male, Laboratory (COMMERCIAL AQUACULTURE FACILITY (FORKYS S.A., CRETE, GREECE)	Salt water, Oral (diet, drink, gavage), Food, Not Reported	Unmeasured	0 AI ug/kg bdwt/d / 15 AI ug/kg bdwt/d / 1500 AI ug/kg bdwt/d	Cellular (Genetics-Calpain small subunit 1 b mRNA, Response Site: Muscle)	LOEC (1500 AI ug/kg bdwt/d)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Musculoskeletal	Medium	5532247
28553-12-0	21 Day(s), (21 Day(s))	*Sparus aurata* (Gilthead Seabream), Adult, 2 Year(s), Male, Laboratory (COMMERCIAL AQUACULTURE FACILITY (FORKYS S.A., CRETE, GREECE)	Salt water, Oral (diet, drink, gavage), Food, Not Reported	Unmeasured	0 AI ug/kg bdwt/d / 15 AI ug/kg bdwt/d / 1500 AI ug/kg bdwt/d	Cellular (Genetics-Calpain 3 mRNA, Response Site: Muscle)	LOEC (1500 AI ug/kg bdwt/d)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Musculoskeletal	Medium	5532247

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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
28553-12-0	21 Day(s), (21 Day(s))	*Sparus aurata* (Gilthead Seabream), Adult, 2 Year(s), Male, Laboratory (COMMERCIAL AQUACULTURE FACILITY (FORKYS S.A., CRETE, GREECE)	Salt water, Oral (diet, drink, gavage), Food, Not Reported	Unmeasured	0 AI ug/kg bdwt/d / 15 AI ug/kg bdwt/d / 1500 AI ug/kg bdwt/d	Biochemical (Enzyme(s)-Cathepsin b, Response Site: Muscle)	LOEC (1500 AI ug/kg bdwt/d)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Musculoskeletal	Medium	5532247
28553-12-0	21 Day(s), (21 Day(s))	*Sparus aurata* (Gilthead Seabream), Adult, 2 Year(s), Male, Laboratory (COMMERCIAL AQUACULTURE FACILITY (FORKYS S.A., CRETE, GREECE)	Salt water, Oral (diet, drink, gavage), Food, Not Reported	Unmeasured	0 AI ug/kg bdwt/d / 15 AI ug/kg bdwt/d / 1500 AI ug/kg bdwt/d	Biochemical (Enzyme(s)-Cathepsin L, Response Site: Muscle)	LOEC (1500 AI ug/kg bdwt/d)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Musculoskeletal	Medium	5532247
28553-12-0	21 Day(s), (21 Day(s))	*Sparus aurata* (Gilthead Seabream), Adult, 2 Year(s), Male, Laboratory (COMMERCIAL AQUACULTURE FACILITY (FORKYS S.A., CRETE, GREECE)	Salt water, Oral (diet, drink, gavage), Food, Not Reported	Unmeasured	0 AI ug/kg bdwt/d / 15 AI ug/kg bdwt/d / 1500 AI ug/kg bdwt/d	Biochemical (Biochemistry-Unsaturated lipid or fat, Response Site: Muscle)	LOEC (15 AI ug/kg bdwt/d)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Musculoskeletal	Medium	5532247
28553-12-0	21 Day(s), (21 Day(s))	*Sparus aurata* (Gilthead Seabream), Adult, 2 Year(s), Male, Laboratory (COMMERCIAL AQUACULTURE FACILITY (FORKYS S.A., CRETE, GREECE)	Salt water, Oral (diet, drink, gavage), Food, Not Reported	Unmeasured	0 AI ug/kg bdwt/d / 15 AI ug/kg bdwt/d / 1500 AI ug/kg bdwt/d	Biochemical (Biochemistry-Triglycerides, Response Site: Muscle)	LOEC (15 AI ug/kg bdwt/d)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Musculoskeletal	Medium	5532247

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CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
28553-12-0	21 Day(s), (21 Day(s))	*Sparus aurata* (Gilthead Seabream), Adult, 2 Year(s), Male, Laboratory (COMMERCIAL AQUACULTURE FACILITY (FORKYS S.A., CRETE, GREECE)	Salt water, Oral (diet, drink, gavage), Food, Not Reported	Unmeasured	0 AI ug/kg bdwt/d / 15 AI ug/kg bdwt/d / 1500 AI ug/kg bdwt/d	Cellular (Genetics-Cathepsin L mRNA, Response Site: Muscle)	LOEC (1500 AI ug/kg bdwt/d)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Musculoskeletal	Medium	5532247
28553-12-0	21 Day(s), (21 Day(s))	*Sparus aurata* (Gilthead Seabream), Adult, 2 Year(s), Male, Laboratory (COMMERCIAL AQUACULTURE FACILITY (FORKYS S.A., CRETE, GREECE)	Salt water, Oral (diet, drink, gavage), Food, Not Reported	Unmeasured	0 AI ug/kg bdwt/d / 15 AI ug/kg bdwt/d / 1500 AI ug/kg bdwt/d	Biochemical (Enzyme(s)-Cathepsin b, Response Site: Muscle)	NOEC (15 AI ug/kg bdwt/d)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Musculoskeletal	Medium	5532247
28553-12-0	21 Day(s), (21 Day(s))	*Sparus aurata* (Gilthead Seabream), Adult, 2 Year(s), Male, Laboratory (COMMERCIAL AQUACULTURE FACILITY (FORKYS S.A., CRETE, GREECE)	Salt water, Oral (diet, drink, gavage), Food, Not Reported	Unmeasured	0 AI ug/kg bdwt/d / 15 AI ug/kg bdwt/d / 1500 AI ug/kg bdwt/d	Biochemical (Biochemistry-Pyruvate, Response Site: Muscle)	NR (15-1500 AI ug/kg bdwt/d)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Musculoskeletal	Medium	5532247
28553-12-0	21 Day(s), (21 Day(s))	*Sparus aurata* (Gilthead Seabream), Adult, 2 Year(s), Male, Laboratory (COMMERCIAL AQUACULTURE FACILITY (FORKYS S.A., CRETE, GREECE)	Salt water, Oral (diet, drink, gavage), Food, Not Reported	Unmeasured	0 AI ug/kg bdwt/d / 15 AI ug/kg bdwt/d / 1500 AI ug/kg bdwt/d	Biochemical (Biochemistry-Protein content, Response Site: Muscle)	NR (15-1500 AI ug/kg bdwt/d)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Musculoskeletal	Medium	5532247

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CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
28553-12-0	21 Day(s), (21 Day(s))	*Sparus aurata* (Gilthead Seabream), Adult, 2 Year(s), Male, Laboratory (COMMERCIAL AQUACULTURE FACILITY (FORKYS S.A., CRETE, GREECE)	Salt water, Oral (diet, drink, gavage), Food, Not Reported	Unmeasured	0 AI ug/kg bdwt/d / 15 AI ug/kg bdwt/d / 1500 AI ug/kg bdwt/d	Cellular (Genetics-N3/PSMB4 mRNA, Response Site: Muscle)	NOEC (1500 AI ug/kg bdwt/d)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Musculoskeletal	Medium	5532247
28553-12-0	21 Day(s), (21 Day(s))	*Sparus aurata* (Gilthead Seabream), Adult, 2 Year(s), Male, Laboratory (COMMERCIAL AQUACULTURE FACILITY (FORKYS S.A., CRETE, GREECE)	Salt water, Oral (diet, drink, gavage), Food, Not Reported	Unmeasured	0 AI ug/kg bdwt/d / 15 AI ug/kg bdwt/d / 1500 AI ug/kg bdwt/d	Cellular (Genetics-Cathepsin B mRNA, Response Site: Muscle)	NOEC (1500 AI ug/kg bdwt/d)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Musculoskeletal	Medium	5532247
28553-12-0	21 Day(s), (21 Day(s))	*Sparus aurata* (Gilthead Seabream), Adult, 2 Year(s), Male, Laboratory (COMMERCIAL AQUACULTURE FACILITY (FORKYS S.A., CRETE, GREECE)	Salt water, Oral (diet, drink, gavage), Food, Not Reported	Unmeasured	0 AI ug/kg bdwt/d / 15 AI ug/kg bdwt/d / 1500 AI ug/kg bdwt/d	Cellular (Genetics-Calpain 2 mRNA, Response Site: Muscle)	NOEC (1500 AI ug/kg bdwt/d)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Musculoskeletal	Medium	5532247
28553-12-0	21 Day(s), (21 Day(s))	*Sparus aurata* (Gilthead Seabream), Adult, 2 Year(s), Male, Laboratory (COMMERCIAL AQUACULTURE FACILITY (FORKYS S.A., CRETE, GREECE)	Salt water, Oral (diet, drink, gavage), Food, Not Reported	Unmeasured	0 AI ug/kg bdwt/d / 15 AI ug/kg bdwt/d / 1500 AI ug/kg bdwt/d	Biochemical (Enzyme(s)-Cathepsin d, Response Site: Muscle)	NOEC (1500 AI ug/kg bdwt/d)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Musculoskeletal	Medium	5532247

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CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
28553-12-0	21 Day(s), (21 Day(s))	*Sparus aurata* (Gilthead Seabream), Adult, 2 Year(s), Male, Laboratory (COMMERCIAL AQUACULTURE FACILITY (FORKYS S.A., CRETE, GREECE)	Salt water, Oral (diet, drink, gavage), Food, Not Reported	Unmeasured	0 AI ug/kg bdwt/d / 15 AI ug/kg bdwt/d / 1500 AI ug/kg bdwt/d	Biochemical (Biochemistry-Protein content, Response Site: Muscle)	NOEC (1500 AI ug/kg bdwt/d)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Musculoskeletal	Medium	5532247
28553-12-0	21 Day(s), (21 Day(s))	*Sparus aurata* (Gilthead Seabream), Adult, 2 Year(s), Male, Laboratory (COMMERCIAL AQUACULTURE FACILITY (FORKYS S.A., CRETE, GREECE)	Salt water, Oral (diet, drink, gavage), Food, Not Reported	Unmeasured	0 AI ug/kg bdwt/d / 15 AI ug/kg bdwt/d / 1500 AI ug/kg bdwt/d	Cellular (Genetics-Calpain small subunit 1-like mRNA, Response Site: Muscle)	NOEC (15 AI ug/kg bdwt/d)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Musculoskeletal	Medium	5532247
28553-12-0	21 Day(s), (21 Day(s))	*Sparus aurata* (Gilthead Seabream), Adult, 2 Year(s), Male, Laboratory (COMMERCIAL AQUACULTURE FACILITY (FORKYS S.A., CRETE, GREECE)	Salt water, Oral (diet, drink, gavage), Food, Not Reported	Unmeasured	0 AI ug/kg bdwt/d / 15 AI ug/kg bdwt/d / 1500 AI ug/kg bdwt/d	Cellular (Genetics-Calpain small subunit 1 b mRNA, Response Site: Muscle)	NOEC (15 AI ug/kg bdwt/d)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Musculoskeletal	Medium	5532247
28553-12-0	21 Day(s), (21 Day(s))	*Sparus aurata* (Gilthead Seabream), Adult, 2 Year(s), Male, Laboratory (COMMERCIAL AQUACULTURE FACILITY (FORKYS S.A., CRETE, GREECE)	Salt water, Oral (diet, drink, gavage), Food, Not Reported	Unmeasured	0 AI ug/kg bdwt/d / 15 AI ug/kg bdwt/d / 1500 AI ug/kg bdwt/d	Biochemical (Biochemistry-Saturated lipid or fat, Response Site: Muscle)	LOEC (15 AI ug/kg bdwt/d)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Musculoskeletal	Medium	5532247

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CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
28553-12-0	21 Day(s), (21 Day(s))	*Sparus aurata* (Gilthead Seabream), Adult, 2 Year(s), Male, Laboratory (COMMERCIAL AQUACULTURE FACILITY (FORKYS S.A., CRETE, GREECE)	Salt water, Oral (diet, drink, gavage), Food, Not Reported	Unmeasured	0 AI ug/kg bdwt/d / 15 AI ug/kg bdwt/d / 1500 AI ug/kg bdwt/d	Biochemical (Biochemistry-Protein content, Response Site: Muscle)	LOEC (15 AI ug/kg bdwt/d)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Musculoskeletal	Medium	5532247
28553-12-0	21 Day(s), (21 Day(s))	*Sparus aurata* (Gilthead Seabream), Adult, 2 Year(s), Male, Laboratory (COMMERCIAL AQUACULTURE FACILITY (FORKYS S.A., CRETE, GREECE)	Salt water, Oral (diet, drink, gavage), Food, Not Reported	Unmeasured	0 AI ug/kg bdwt/d / 15 AI ug/kg bdwt/d / 1500 AI ug/kg bdwt/d	Biochemical (Biochemistry-Lipid, Response Site: Muscle)	LOEC (15 AI ug/kg bdwt/d)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Musculoskeletal	Medium	5532247
28553-12-0	21 Day(s), (21 Day(s))	*Sparus aurata* (Gilthead Seabream), Adult, 2 Year(s), Male, Laboratory (COMMERCIAL AQUACULTURE FACILITY (FORKYS S.A., CRETE, GREECE)	Salt water, Oral (diet, drink, gavage), Food, Not Reported	Unmeasured	0 AI ug/kg bdwt/d / 15 AI ug/kg bdwt/d / 1500 AI ug/kg bdwt/d	Biochemical (Biochemistry-Phosphate, Response Site: Muscle)	LOEC (15 AI ug/kg bdwt/d)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Musculoskeletal	Medium	5532247
28553-12-0	21 Day(s), (21 Day(s))	*Sparus aurata* (Gilthead Seabream), Adult, 2 Year(s), Male, Laboratory (COMMERCIAL AQUACULTURE FACILITY (FORKYS S.A., CRETE, GREECE)	Salt water, Oral (diet, drink, gavage), Food, Not Reported	Unmeasured	0 AI ug/kg bdwt/d / 15 AI ug/kg bdwt/d / 1500 AI ug/kg bdwt/d	Biochemical (Enzyme(s)-Cathepsin L, Response Site: Muscle)	NOEC (15 AI ug/kg bdwt/d)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Musculoskeletal	Medium	5532247

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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
28553-12-0	21 Day(s), (21 Day(s))	*Sparus aurata* (Gilthead Seabream), Adult, 2 Year(s), Male, Laboratory (COMMERCIAL AQUACULTURE FACILITY (FORKYS S.A., CRETE, GREECE)	Salt water, Oral (diet, drink, gavage), Food, Not Reported	Unmeasured	0 AI ug/kg bdwt/d / 15 AI ug/kg bdwt/d / 1500 AI ug/kg bdwt/d	Cellular (Genetics-Calpain 3 mRNA, Response Site: Muscle)	NOEC (15 AI ug/kg bdwt/d)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Musculoskeletal	Medium	5532247
28553-12-0	21 Day(s), (21 Day(s))	*Sparus aurata* (Gilthead Seabream), Adult, 2 Year(s), Male, Laboratory (COMMERCIAL AQUACULTURE FACILITY (FORKYS S.A., CRETE, GREECE)	Salt water, Oral (diet, drink, gavage), Food, Not Reported	Unmeasured	0 AI ug/kg bdwt/d / 15 AI ug/kg bdwt/d / 1500 AI ug/kg bdwt/d	Cellular (Genetics-Calpain 1 mRNA, Response Site: Muscle)	NR (15-1500 AI ug/kg bdwt/d)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Musculoskeletal	Medium	5532247
28553-12-0	21 Day(s), (21 Day(s))	*Sparus aurata* (Gilthead Seabream), Adult, 2 Year(s), Male, Laboratory (COMMERCIAL AQUACULTURE FACILITY (FORKYS S.A., CRETE, GREECE)	Salt water, Oral (diet, drink, gavage), Food, Not Reported	Unmeasured	0 AI ug/kg bdwt/d / 15 AI ug/kg bdwt/d / 1500 AI ug/kg bdwt/d	Biochemical (Biochemistry-Calpain 1, large subunit, Response Site: Muscle)	NOEC (1500 AI ug/kg bdwt/d)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Musculoskeletal	Medium	5532247

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CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
28553-12-0	21 Day(s), (21 Day(s))	*Sparus aurata* (Gilthead Seabream), 2 Year(s), Male, Laboratory (AQUALABS FACILITIES OF THE INST. OF MARINE BIOLOGY, BIOTECHNOLOGY AND AQUACULTURE OF THE HELLENIC CENT. FOR MARINE RES., IRAKLION, CRETE, GREECE)	Fresh water, Oral (diet, drink, gavage), Food, 10 Male organisms	Unmeasured	0 ug/kg bdwt/d / 15 ug/kg bdwt/d / 1500 ug/kg bdwt/d	Cellular (Genetics-Diacylglycerol transferase 2 mRNA, Response Site: Liver)	NOEC (1500 ug/kg bdwt/d)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Liver toxicology; Neurotoxicology	Medium	4829367
28553-12-0	21 Day(s), (21 Day(s))	*Sparus aurata* (Gilthead Seabream), 2 Year(s), Male, Laboratory (AQUALABS FACILITIES OF THE INST. OF MARINE BIOLOGY, BIOTECHNOLOGY AND AQUACULTURE OF THE HELLENIC CENT. FOR MARINE RES., IRAKLION, CRETE, GREECE)	Fresh water, Oral (diet, drink, gavage), Food, 10 Male organisms	Unmeasured	0 ug/kg bdwt/d / 15 ug/kg bdwt/d / 1500 ug/kg bdwt/d	Cellular (Genetics-Peroxisome proliferator-activated receptor beta mRNA, Response Site: Brain)	NR (15-1500 ug/kg bdwt/d)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Liver toxicology; Neurotoxicology	Medium	4829367

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CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
28553-12-0	21 Day(s), (21 Day(s))	*Sparus aurata* (Gilthead Seabream), 2 Year(s), Male, Laboratory (AQUALABS FACILITIES OF THE INST. OF MARINE BIOLOGY, BIOTECHNOLOGY AND AQUACULTURE OF THE HELLENIC CENT. FOR MARINE RES., IRAKLION, CRETE, GREECE)	Fresh water, Oral (diet, drink, gavage), Food, 10 Male organisms	Unmeasured	0 ug/kg bdwt/d / 15 ug/kg bdwt/d / 1500 ug/kg bdwt/d	Cellular (Genetics-Glycerol-3-phosphate acyltransferase 1 mRNA, Response Site: Liver)	NR (15-1500 ug/kg bdwt/d)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Liver toxicology; Neurotoxicology	Medium	4829367
28553-12-0	21 Day(s), (21 Day(s))	*Sparus aurata* (Gilthead Seabream), 2 Year(s), Male, Laboratory (AQUALABS FACILITIES OF THE INST. OF MARINE BIOLOGY, BIOTECHNOLOGY AND AQUACULTURE OF THE HELLENIC CENT. FOR MARINE RES., IRAKLION, CRETE, GREECE)	Fresh water, Oral (diet, drink, gavage), Food, 10 Male organisms	Unmeasured	0 ug/kg bdwt/d / 15 ug/kg bdwt/d / 1500 ug/kg bdwt/d	Cellular (Genetics-Fatty acid synthase mRNA, Response Site: Liver)	NR (15-1500 ug/kg bdwt/d)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Liver toxicology; Neurotoxicology	Medium	4829367

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CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
28553-12-0	21 Day(s), (21 Day(s))	*Sparus aurata* (Gilthead Seabream), 2 Year(s), Male, Laboratory (AQUALABS FACILITIES OF THE INST. OF MARINE BIOLOGY, BIOTECHNOLOGY AND AQUACULTURE OF THE HELLENIC CENT. FOR MARINE RES., IRAKLION, CRETE, GREECE)	Fresh water, Oral (diet, drink, gavage), Food, 10 Male organisms	Unmeasured	0 ug/kg bdwt/d / 15 ug/kg bdwt/d / 1500 ug/kg bdwt/d	Cellular (Genetics-Endocannabinoid receptor type 2 mRNA, Response Site: Liver)	NR (15-1500 ug/kg bdwt/d)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Liver toxicology; Neurotoxicology	Medium	4829367
28553-12-0	21 Day(s), (21 Day(s))	*Sparus aurata* (Gilthead Seabream), 2 Year(s), Male, Laboratory (AQUALABS FACILITIES OF THE INST. OF MARINE BIOLOGY, BIOTECHNOLOGY AND AQUACULTURE OF THE HELLENIC CENT. FOR MARINE RES., IRAKLION, CRETE, GREECE)	Fresh water, Oral (diet, drink, gavage), Food, 10 Male organisms	Unmeasured	0 ug/kg bdwt/d / 15 ug/kg bdwt/d / 1500 ug/kg bdwt/d	Cellular (Genetics-Endocannabinoid receptor type 1 mRNA, Response Site: Brain)	NR (15-1500 ug/kg bdwt/d)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Liver toxicology; Neurotoxicology	Medium	4829367

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CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
28553-12-0	21 Day(s), (21 Day(s))	*Sparus aurata* (Gilthead Seabream), 2 Year(s), Male, Laboratory (AQUALABS FACILITIES OF THE INST. OF MARINE BIOLOGY, BIOTECHNOLOGY AND AQUACULTURE OF THE HELLENIC CENT. FOR MARINE RES., IRAKLION, CRETE, GREECE)	Fresh water, Oral (diet, drink, gavage), Food, 10 Male organisms	Unmeasured	0 ug/kg bdwt/d / 15 ug/kg bdwt/d / 1500 ug/kg bdwt/d	Biochemical (Biochemistry-Triglycerides, Response Site: Liver)	NR (15-1500 ug/kg bdwt/d)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Liver toxicology; Neurotoxicology	Medium	4829367
28553-12-0	21 Day(s), (21 Day(s))	*Sparus aurata* (Gilthead Seabream), 2 Year(s), Male, Laboratory (AQUALABS FACILITIES OF THE INST. OF MARINE BIOLOGY, BIOTECHNOLOGY AND AQUACULTURE OF THE HELLENIC CENT. FOR MARINE RES., IRAKLION, CRETE, GREECE)	Fresh water, Oral (diet, drink, gavage), Food, 10 Male organisms	Unmeasured	0 ug/kg bdwt/d / 15 ug/kg bdwt/d / 1500 ug/kg bdwt/d	Growth (Morphology-Organ weight in relationship to body weight, Response Site: Liver)	NOEC (1500 ug/kg bdwt/d)	Development/Growth	Medium	4829367

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CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
28553-12-0	21 Day(s), (21 Day(s))	*Sparus aurata* (Gilthead Seabream), 2 Year(s), Male, Laboratory (AQUALABS FACILITIES OF THE INST. OF MARINE BIOLOGY, BIOTECHNOLOGY AND AQUACULTURE OF THE HELLENIC CENT. FOR MARINE RES., IRAKLION, CRETE, GREECE)	Fresh water, Oral (diet, drink, gavage), Food, 10 Male organisms	Unmeasured	0 ug/kg bdwt/d / 15 ug/kg bdwt/d / 1500 ug/kg bdwt/d	Cellular (Genetics-Transient receptor potential cation channel subfamily V member 1 mRNA, Response Site: Liver)	NOEC (1500 ug/kg bdwt/d)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Liver toxicology; Neurotoxicology	Medium	4829367
28553-12-0	21 Day(s), (21 Day(s))	*Sparus aurata* (Gilthead Seabream), 2 Year(s), Male, Laboratory (AQUALABS FACILITIES OF THE INST. OF MARINE BIOLOGY, BIOTECHNOLOGY AND AQUACULTURE OF THE HELLENIC CENT. FOR MARINE RES., IRAKLION, CRETE, GREECE)	Fresh water, Oral (diet, drink, gavage), Food, 10 Male organisms	Unmeasured	0 ug/kg bdwt/d / 15 ug/kg bdwt/d / 1500 ug/kg bdwt/d	Cellular (Genetics-Phospholipase A2 mRNA, Response Site: Brain)	NOEC (1500 ug/kg bdwt/d)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Liver toxicology; Neurotoxicology	Medium	4829367

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CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
28553-12-0	21 Day(s), (21 Day(s))	*Sparus aurata* (Gilthead Seabream), 2 Year(s), Male, Laboratory (AQUALABS FACILITIES OF THE INST. OF MARINE BIOLOGY, BIOTECHNOLOGY AND AQUACULTURE OF THE HELLENIC CENT. FOR MARINE RES., IRAKLION, CRETE, GREECE)	Fresh water, Oral (diet, drink, gavage), Food, 10 Male organisms	Unmeasured	0 ug/kg bdwt/d / 15 ug/kg bdwt/d / 1500 ug/kg bdwt/d	Cellular (Genetics-Diacylglycerol lipase, alpha mRNA, Response Site: Liver)	NOEC (1500 ug/kg bdwt/d)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Liver toxicology; Neurotoxicology	Medium	4829367
28553-12-0	21 Day(s), (21 Day(s))	*Sparus aurata* (Gilthead Seabream), 2 Year(s), Male, Laboratory (AQUALABS FACILITIES OF THE INST. OF MARINE BIOLOGY, BIOTECHNOLOGY AND AQUACULTURE OF THE HELLENIC CENT. FOR MARINE RES., IRAKLION, CRETE, GREECE)	Fresh water, Oral (diet, drink, gavage), Food, 10 Male organisms	Unmeasured	0 ug/kg bdwt/d / 15 ug/kg bdwt/d / 1500 ug/kg bdwt/d	Cellular (Genetics-N-acyl phosphatidylethanolamine phospholipase D mRNA, Response Site: Liver)	NOEC (1500 ug/kg bdwt/d)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Liver toxicology; Neurotoxicology	Medium	4829367

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CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
28553-12-0	21 Day(s), (21 Day(s))	*Sparus aurata* (Gilthead Seabream), 2 Year(s), Male, Laboratory (AQUALABS FACILITIES OF THE INST. OF MARINE BIOLOGY, BIOTECHNOLOGY AND AQUACULTURE OF THE HELLENIC CENT. FOR MARINE RES., IRAKLION, CRETE, GREECE)	Fresh water, Oral (diet, drink, gavage), Food, 10 Male organisms	Unmeasured	0 ug/kg bdwt/d / 15 ug/kg bdwt/d / 1500 ug/kg bdwt/d	Cellular (Genetics-Diacylglycerol lipase, alpha mRNA, Response Site: Brain)	NOEC (1500 ug/kg bdwt/d)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Liver toxicology; Neurotoxicology	Medium	4829367
28553-12-0	21 Day(s), (21 Day(s))	*Sparus aurata* (Gilthead Seabream), 2 Year(s), Male, Laboratory (AQUALABS FACILITIES OF THE INST. OF MARINE BIOLOGY, BIOTECHNOLOGY AND AQUACULTURE OF THE HELLENIC CENT. FOR MARINE RES., IRAKLION, CRETE, GREECE)	Fresh water, Oral (diet, drink, gavage), Food, 10 Male organisms	Unmeasured	0 ug/kg bdwt/d / 15 ug/kg bdwt/d / 1500 ug/kg bdwt/d	Biochemical (Biochemistry-Anandamide, Response Site: Liver)	LOEC (1500 ug/kg bdwt/d)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Liver toxicology; Neurotoxicology	Medium	4829367

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CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
28553-12-0	21 Day(s), (21 Day(s))	*Sparus aurata* (Gilthead Seabream), 2 Year(s), Male, Laboratory (AQUALABS FACILITIES OF THE INST. OF MARINE BIOLOGY, BIOTECHNOLOGY AND AQUACULTURE OF THE HELLENIC CENT. FOR MARINE RES., IRAKLION, CRETE, GREECE)	Fresh water, Oral (diet, drink, gavage), Food, 10 Male organisms	Unmeasured	0 ug/kg bdwt/d / 15 ug/kg bdwt/d / 1500 ug/kg bdwt/d	Cellular (Genetics-Cocaine- and amphetamine-regulated transcript protein mRNA, Response Site: Brain)	NOEC (1500 ug/kg bdwt/d)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Liver toxicology; Neurotoxicology	Medium	4829367
28553-12-0	21 Day(s), (21 Day(s))	*Sparus aurata* (Gilthead Seabream), 2 Year(s), Male, Laboratory (AQUALABS FACILITIES OF THE INST. OF MARINE BIOLOGY, BIOTECHNOLOGY AND AQUACULTURE OF THE HELLENIC CENT. FOR MARINE RES., IRAKLION, CRETE, GREECE)	Fresh water, Oral (diet, drink, gavage), Food, 10 Male organisms	Unmeasured	0 ug/kg bdwt/d / 15 ug/kg bdwt/d / 1500 ug/kg bdwt/d	Biochemical (Biochemistry-2-Arachidonoylglycerol, Response Site: Brain)	LOEC (15 ug/kg bdwt/d)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Liver toxicology; Neurotoxicology	Medium	4829367

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CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
28553-12-0	21 Day(s), (21 Day(s))	*Sparus aurata* (Gilthead Seabream), 2 Year(s), Male, Laboratory (AQUALABS FACILITIES OF THE INST. OF MARINE BIOLOGY, BIOTECHNOLOGY AND AQUACULTURE OF THE HELLENIC CENT. FOR MARINE RES., IRAKLION, CRETE, GREECE)	Fresh water, Oral (diet, drink, gavage), Food, 10 Male organisms	Unmeasured	0 ug/kg bdwt/d / 15 ug/kg bdwt/d / 1500 ug/kg bdwt/d	Biochemical (Biochemistry-Anandamide, Response Site: Brain)	LOEC (15 ug/kg bdwt/d)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Liver toxicology; Neurotoxicology	Medium	4829367
28553-12-0	21 Day(s), (21 Day(s))	*Sparus aurata* (Gilthead Seabream), 2 Year(s), Male, Laboratory (AQUALABS FACILITIES OF THE INST. OF MARINE BIOLOGY, BIOTECHNOLOGY AND AQUACULTURE OF THE HELLENIC CENT. FOR MARINE RES., IRAKLION, CRETE, GREECE)	Fresh water, Oral (diet, drink, gavage), Food, 10 Male organisms	Unmeasured	0 ug/kg bdwt/d / 15 ug/kg bdwt/d / 1500 ug/kg bdwt/d	Biochemical (Biochemistry-Fatty acids, Response Site: Liver)	LOEC (15 ug/kg bdwt/d)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Liver toxicology; Neurotoxicology	Medium	4829367

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CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
28553-12-0	21 Day(s), (21 Day(s))	*Sparus aurata* (Gilthead Seabream), 2 Year(s), Male, Laboratory (AQUALABS FACILITIES OF THE INST. OF MARINE BIOLOGY, BIOTECHNOLOGY AND AQUACULTURE OF THE HELLENIC CENT. FOR MARINE RES., IRAKLION, CRETE, GREECE)	Fresh water, Oral (diet, drink, gavage), Food, 10 Male organisms	Unmeasured	0 ug/kg bdwt/d / 15 ug/kg bdwt/d / 1500 ug/kg bdwt/d	Biochemical (Biochemistry-Lipid, Response Site: Liver)	LOEC (15 ug/kg bdwt/d)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Liver toxicology; Neurotoxicology	Medium	4829367
28553-12-0	21 Day(s), (21 Day(s))	*Sparus aurata* (Gilthead Seabream), 2 Year(s), Male, Laboratory (AQUALABS FACILITIES OF THE INST. OF MARINE BIOLOGY, BIOTECHNOLOGY AND AQUACULTURE OF THE HELLENIC CENT. FOR MARINE RES., IRAKLION, CRETE, GREECE)	Fresh water, Oral (diet, drink, gavage), Food, 10 Male organisms	Unmeasured	0 ug/kg bdwt/d / 15 ug/kg bdwt/d / 1500 ug/kg bdwt/d	Biochemical (Biochemistry-Oleoylethanolamine, Response Site: Liver)	LOEC (15 ug/kg bdwt/d)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Liver toxicology; Neurotoxicology	Medium	4829367

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CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
28553-12-0	21 Day(s), (21 Day(s))	*Sparus aurata* (Gilthead Seabream), 2 Year(s), Male, Laboratory (AQUALABS FACILITIES OF THE INST. OF MARINE BIOLOGY, BIOTECHNOLOGY AND AQUACULTURE OF THE HELLENIC CENT. FOR MARINE RES., IRAKLION, CRETE, GREECE)	Fresh water, Oral (diet, drink, gavage), Food, 10 Male organisms	Unmeasured	0 ug/kg bdwt/d / 15 ug/kg bdwt/d / 1500 ug/kg bdwt/d	Biochemical (Biochemistry-Palmitoylethanolamide, Response Site: Brain)	LOEC (15 ug/kg bdwt/d)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Liver toxicology; Neurotoxicology	Medium	4829367
28553-12-0	21 Day(s), (21 Day(s))	*Sparus aurata* (Gilthead Seabream), 2 Year(s), Male, Laboratory (AQUALABS FACILITIES OF THE INST. OF MARINE BIOLOGY, BIOTECHNOLOGY AND AQUACULTURE OF THE HELLENIC CENT. FOR MARINE RES., IRAKLION, CRETE, GREECE)	Fresh water, Oral (diet, drink, gavage), Food, 10 Male organisms	Unmeasured	0 ug/kg bdwt/d / 15 ug/kg bdwt/d / 1500 ug/kg bdwt/d	Biochemical (Biochemistry-Palmitoylethanolamide, Response Site: Liver)	LOEC (15 ug/kg bdwt/d)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Liver toxicology; Neurotoxicology	Medium	4829367

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CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
28553-12-0	21 Day(s), (21 Day(s))	*Sparus aurata* (Gilthead Seabream), 2 Year(s), Male, Laboratory (AQUALABS FACILITIES OF THE INST. OF MARINE BIOLOGY, BIOTECHNOLOGY AND AQUACULTURE OF THE HELLENIC CENT. FOR MARINE RES., IRAKLION, CRETE, GREECE)	Fresh water, Oral (diet, drink, gavage), Food, 10 Male organisms	Unmeasured	0 ug/kg bdwt/d / 15 ug/kg bdwt/d / 1500 ug/kg bdwt/d	Cellular (Genetics-1-acylglycerol-3-phosphate O-acyltransferase 4 mRNA, Response Site: Liver)	LOEC (15 ug/kg bdwt/d)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Liver toxicology; Neurotoxicology	Medium	4829367
28553-12-0	21 Day(s), (21 Day(s))	*Sparus aurata* (Gilthead Seabream), 2 Year(s), Male, Laboratory (AQUALABS FACILITIES OF THE INST. OF MARINE BIOLOGY, BIOTECHNOLOGY AND AQUACULTURE OF THE HELLENIC CENT. FOR MARINE RES., IRAKLION, CRETE, GREECE)	Fresh water, Oral (diet, drink, gavage), Food, 10 Male organisms	Unmeasured	0 ug/kg bdwt/d / 15 ug/kg bdwt/d / 1500 ug/kg bdwt/d	Cellular (Genetics-Endocannabinoid receptor type 1 mRNA, Response Site: Liver)	LOEC (15 ug/kg bdwt/d)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Liver toxicology; Neurotoxicology	Medium	4829367

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CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
28553-12-0	21 Day(s), (21 Day(s))	*Sparus aurata* (Gilthead Seabream), 2 Year(s), Male, Laboratory (AQUALABS FACILITIES OF THE INST. OF MARINE BIOLOGY, BIOTECHNOLOGY AND AQUACULTURE OF THE HELLENIC CENT. FOR MARINE RES., IRAKLION, CRETE, GREECE)	Fresh water, Oral (diet, drink, gavage), Food, 10 Male organisms	Unmeasured	0 ug/kg bdwt/d / 15 ug/kg bdwt/d / 1500 ug/kg bdwt/d	Cellular (Genetics-Peroxisome proliferator-activated receptor gamma mRNA, Response Site: Liver)	NOEC (1500 ug/kg bdwt/d)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Liver toxicology; Neurotoxicology	Medium	4829367
28553-12-0	21 Day(s), (21 Day(s))	*Sparus aurata* (Gilthead Seabream), 2 Year(s), Male, Laboratory (AQUALABS FACILITIES OF THE INST. OF MARINE BIOLOGY, BIOTECHNOLOGY AND AQUACULTURE OF THE HELLENIC CENT. FOR MARINE RES., IRAKLION, CRETE, GREECE)	Fresh water, Oral (diet, drink, gavage), Food, 10 Male organisms	Unmeasured	0 ug/kg bdwt/d / 15 ug/kg bdwt/d / 1500 ug/kg bdwt/d	Cellular (Genetics-Neuropeptide Y mRNA, Response Site: Brain)	LOEC (15 ug/kg bdwt/d)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Liver toxicology; Neurotoxicology	Medium	4829367

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CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
28553-12-0	21 Day(s), (21 Day(s))	*Sparus aurata* (Gilthead Seabream), 2 Year(s), Male, Laboratory (AQUALABS FACILITIES OF THE INST. OF MARINE BIOLOGY, BIOTECHNOLOGY AND AQUACULTURE OF THE HELLENIC CENT. FOR MARINE RES., IRAKLION, CRETE, GREECE)	Fresh water, Oral (diet, drink, gavage), Food, 10 Male organisms	Unmeasured	0 ug/kg bdwt/d / 15 ug/kg bdwt/d / 1500 ug/kg bdwt/d	Cellular (Genetics-Peroxisome proliferator-activated receptor gamma mRNA, Response Site: Brain)	NOEC (1500 ug/kg bdwt/d)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Liver toxicology; Neurotoxicology	Medium	4829367
28553-12-0	21 Day(s), (21 Day(s))	*Sparus aurata* (Gilthead Seabream), 2 Year(s), Male, Laboratory (AQUALABS FACILITIES OF THE INST. OF MARINE BIOLOGY, BIOTECHNOLOGY AND AQUACULTURE OF THE HELLENIC CENT. FOR MARINE RES., IRAKLION, CRETE, GREECE)	Fresh water, Oral (diet, drink, gavage), Food, 10 Male organisms	Unmeasured	0 ug/kg bdwt/d / 15 ug/kg bdwt/d / 1500 ug/kg bdwt/d	Cellular (Genetics-Peroxisome proliferator-activated receptor alpha mRNA, Response Site: Liver)	NOEC (1500 ug/kg bdwt/d)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Liver toxicology; Neurotoxicology	Medium	4829367

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28553-12-0	21 Day(s), (21 Day(s))	*Sparus aurata* (Gilthead Seabream), 2 Year(s), Male, Laboratory (AQUALABS FACILITIES OF THE INST. OF MARINE BIOLOGY, BIOTECHNOLOGY AND AQUACULTURE OF THE HELLENIC CENT. FOR MARINE RES., IRAKLION, CRETE, GREECE)	Fresh water, Oral (diet, drink, gavage), Food, 10 Male organisms	Unmeasured	0 ug/kg bdwt/d / 15 ug/kg bdwt/d / 1500 ug/kg bdwt/d	Cellular (Genetics-Monoacylglycerol lipase abhd12A mRNA, Response Site: Liver)	NOEC (1500 ug/kg bdwt/d)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Liver toxicology; Neurotoxicology	Medium	4829367
28553-12-0	21 Day(s), (21 Day(s))	*Sparus aurata* (Gilthead Seabream), 2 Year(s), Male, Laboratory (AQUALABS FACILITIES OF THE INST. OF MARINE BIOLOGY, BIOTECHNOLOGY AND AQUACULTURE OF THE HELLENIC CENT. FOR MARINE RES., IRAKLION, CRETE, GREECE)	Fresh water, Oral (diet, drink, gavage), Food, 10 Male organisms	Unmeasured	0 ug/kg bdwt/d / 15 ug/kg bdwt/d / 1500 ug/kg bdwt/d	Cellular (Genetics-Monoacylglycerol lipase abhd6A mRNA, Response Site: Brain)	NOEC (1500 ug/kg bdwt/d)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Liver toxicology; Neurotoxicology	Medium	4829367

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CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
28553-12-0	21 Day(s), (21 Day(s))	*Sparus aurata* (Gilthead Seabream), 2 Year(s), Male, Laboratory (AQUALABS FACILITIES OF THE INST. OF MARINE BIOLOGY, BIOTECHNOLOGY AND AQUACULTURE OF THE HELLENIC CENT. FOR MARINE RES., IRAKLION, CRETE, GREECE)	Fresh water, Oral (diet, drink, gavage), Food, 10 Male organisms	Unmeasured	0 ug/kg bdwt/d / 15 ug/kg bdwt/d / 1500 ug/kg bdwt/d	Cellular (Genetics-Monoacylglycerol lipase abhd12A mRNA, Response Site: Brain)	NOEC (1500 ug/kg bdwt/d)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Liver toxicology; Neurotoxicology	Medium	4829367
28553-12-0	21 Day(s), (21 Day(s))	*Sparus aurata* (Gilthead Seabream), 2 Year(s), Male, Laboratory (AQUALABS FACILITIES OF THE INST. OF MARINE BIOLOGY, BIOTECHNOLOGY AND AQUACULTURE OF THE HELLENIC CENT. FOR MARINE RES., IRAKLION, CRETE, GREECE)	Fresh water, Oral (diet, drink, gavage), Food, 10 Male organisms	Unmeasured	0 ug/kg bdwt/d / 15 ug/kg bdwt/d / 1500 ug/kg bdwt/d	Cellular (Genetics-Leptin receptor mRNA, Response Site: Brain)	NOEC (1500 ug/kg bdwt/d)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Liver toxicology; Neurotoxicology	Medium	4829367

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CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
28553-12-0	21 Day(s), (21 Day(s))	*Sparus aurata* (Gilthead Seabream), 2 Year(s), Male, Laboratory (AQUALABS FACILITIES OF THE INST. OF MARINE BIOLOGY, BIOTECHNOLOGY AND AQUACULTURE OF THE HELLENIC CENT. FOR MARINE RES., IRAKLION, CRETE, GREECE)	Fresh water, Oral (diet, drink, gavage), Food, 10 Male organisms	Unmeasured	0 ug/kg bdwt/d / 15 ug/kg bdwt/d / 1500 ug/kg bdwt/d	Cellular (Genetics-Hepatic lipase mRNA, Response Site: Liver)	NOEC (1500 ug/kg bdwt/d)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Liver toxicology; Neurotoxicology	Medium	4829367
28553-12-0	21 Day(s), (21 Day(s))	*Sparus aurata* (Gilthead Seabream), 2 Year(s), Male, Laboratory (AQUALABS FACILITIES OF THE INST. OF MARINE BIOLOGY, BIOTECHNOLOGY AND AQUACULTURE OF THE HELLENIC CENT. FOR MARINE RES., IRAKLION, CRETE, GREECE)	Fresh water, Oral (diet, drink, gavage), Food, 10 Male organisms	Unmeasured	0 ug/kg bdwt/d / 15 ug/kg bdwt/d / 1500 ug/kg bdwt/d	Cellular (Genetics-Fatty acid amide hydrolase mRNA, Response Site: Liver)	NOEC (1500 ug/kg bdwt/d)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Liver toxicology; Neurotoxicology	Medium	4829367

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28553-12-0	21 Day(s), (21 Day(s))	*Sparus aurata* (Gilthead Seabream), 2 Year(s), Male, Laboratory (AQUALABS FACILITIES OF THE INST. OF MARINE BIOLOGY, BIOTECHNOLOGY AND AQUACULTURE OF THE HELLENIC CENT. FOR MARINE RES., IRAKLION, CRETE, GREECE)	Fresh water, Oral (diet, drink, gavage), Food, 10 Male organisms	Unmeasured	0 ug/kg bdwt/d / 15 ug/kg bdwt/d / 1500 ug/kg bdwt/d	Cellular (Genetics-Fatty acid amide hydrolase mRNA, Response Site: Brain)	NOEC (1500 ug/kg bdwt/d)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Liver toxicology; Neurotoxicology	Medium	4829367
28553-12-0	21 Day(s), (21 Day(s))	*Sparus aurata* (Gilthead Seabream), 2 Year(s), Male, Laboratory (AQUALABS FACILITIES OF THE INST. OF MARINE BIOLOGY, BIOTECHNOLOGY AND AQUACULTURE OF THE HELLENIC CENT. FOR MARINE RES., IRAKLION, CRETE, GREECE)	Fresh water, Oral (diet, drink, gavage), Food, 10 Male organisms	Unmeasured	0 ug/kg bdwt/d / 15 ug/kg bdwt/d / 1500 ug/kg bdwt/d	Cellular (Genetics-Endocannabinoid receptor type 2 mRNA, Response Site: Brain)	NOEC (1500 ug/kg bdwt/d)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Liver toxicology; Neurotoxicology	Medium	4829367

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CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
28553-12-0	21 Day(s), (21 Day(s))	*Sparus aurata* (Gilthead Seabream), 2 Year(s), Male, Laboratory (AQUALABS FACILITIES OF THE INST. OF MARINE BIOLOGY, BIOTECHNOLOGY AND AQUACULTURE OF THE HELLENIC CENT. FOR MARINE RES., IRAKLION, CRETE, GREECE)	Fresh water, Oral (diet, drink, gavage), Food, 10 Male organisms	Unmeasured	0 ug/kg bdwt/d / 15 ug/kg bdwt/d / 1500 ug/kg bdwt/d	Cellular (Genetics-Leptin receptor mRNA, Response Site: Liver)	NOEC (1500 ug/kg bdwt/d)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Liver toxicology; Neurotoxicology	Medium	4829367
28553-12-0	21 Day(s), (21 Day(s))	*Sparus aurata* (Gilthead Seabream), 2 Year(s), Male, Laboratory (AQUALABS FACILITIES OF THE INST. OF MARINE BIOLOGY, BIOTECHNOLOGY AND AQUACULTURE OF THE HELLENIC CENT. FOR MARINE RES., IRAKLION, CRETE, GREECE)	Fresh water, Oral (diet, drink, gavage), Food, 10 Male organisms	Unmeasured	0 ug/kg bdwt/d / 15 ug/kg bdwt/d / 1500 ug/kg bdwt/d	Cellular (Genetics-N-acyl phosphatidylethanolamine phospholipase D mRNA, Response Site: Brain)	NOEC (1500 ug/kg bdwt/d)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Liver toxicology; Neurotoxicology	Medium	4829367

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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
28553-12-0	21 Day(s), (21 Day(s))	*Sparus aurata* (Gilthead Seabream), 2 Year(s), Male, Laboratory (AQUALABS FACILITIES OF THE INST. OF MARINE BIOLOGY, BIOTECHNOLOGY AND AQUACULTURE OF THE HELLENIC CENT. FOR MARINE RES., IRAKLION, CRETE, GREECE)	Fresh water, Oral (diet, drink, gavage), Food, 10 Male organisms	Unmeasured	0 ug/kg bdwt/d / 15 ug/kg bdwt/d / 1500 ug/kg bdwt/d	Cellular (Genetics-Nuclear receptor subfamily 1, group H, member 3 mRNA, Response Site: Liver)	NOEC (1500 ug/kg bdwt/d)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Liver toxicology; Neurotoxicology	Medium	4829367
28553-12-0	21 Day(s), (21 Day(s))	*Sparus aurata* (Gilthead Seabream), 2 Year(s), Male, Laboratory (AQUALABS FACILITIES OF THE INST. OF MARINE BIOLOGY, BIOTECHNOLOGY AND AQUACULTURE OF THE HELLENIC CENT. FOR MARINE RES., IRAKLION, CRETE, GREECE)	Fresh water, Oral (diet, drink, gavage), Food, 10 Male organisms	Unmeasured	0 ug/kg bdwt/d / 15 ug/kg bdwt/d / 1500 ug/kg bdwt/d	Cellular (Genetics-Nucleobindin-1 mRNA, Response Site: Brain)	NOEC (1500 ug/kg bdwt/d)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Liver toxicology; Neurotoxicology	Medium	4829367

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CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
28553-12-0	21 Day(s), (21 Day(s))	*Sparus aurata* (Gilthead Seabream), 2 Year(s), Male, Laboratory (AQUALABS FACILITIES OF THE INST. OF MARINE BIOLOGY, BIOTECHNOLOGY AND AQUACULTURE OF THE HELLENIC CENT. FOR MARINE RES., IRAKLION, CRETE, GREECE)	Fresh water, Oral (diet, drink, gavage), Food, 10 Male organisms	Unmeasured	0 ug/kg bdwt/d / 15 ug/kg bdwt/d / 1500 ug/kg bdwt/d	Cellular (Genetics-Nucleobindin-2-like mRNA, Response Site: Brain)	NOEC (1500 ug/kg bdwt/d)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Liver toxicology; Neurotoxicology	Medium	4829367
28553-12-0	21 Day(s), (21 Day(s))	*Sparus aurata* (Gilthead Seabream), 2 Year(s), Male, Laboratory (AQUALABS FACILITIES OF THE INST. OF MARINE BIOLOGY, BIOTECHNOLOGY AND AQUACULTURE OF THE HELLENIC CENT. FOR MARINE RES., IRAKLION, CRETE, GREECE)	Fresh water, Oral (diet, drink, gavage), Food, 10 Male organisms	Unmeasured	0 ug/kg bdwt/d / 15 ug/kg bdwt/d / 1500 ug/kg bdwt/d	Cellular (Genetics-Peroxisome proliferator-activated receptor alpha mRNA, Response Site: Brain)	NOEC (1500 ug/kg bdwt/d)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Liver toxicology; Neurotoxicology	Medium	4829367

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CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
28553-12-0	21 Day(s), (21 Day(s))	*Sparus aurata* (Gilthead Seabream), 2 Year(s), Male, Laboratory (AQUALABS FACILITIES OF THE INST. OF MARINE BIOLOGY, BIOTECHNOLOGY AND AQUACULTURE OF THE HELLENIC CENT. FOR MARINE RES., IRAKLION, CRETE, GREECE)	Fresh water, Oral (diet, drink, gavage), Food, 10 Male organisms	Unmeasured	0 ug/kg bdwt/d / 15 ug/kg bdwt/d / 1500 ug/kg bdwt/d	Cellular (Genetics-Peroxisome proliferator-activated receptor beta mRNA, Response Site: Liver)	NOEC (1500 ug/kg bdwt/d)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Liver toxicology; Neurotoxicology	Medium	4829367
28553-12-0	21 Day(s), (21 Day(s))	*Sparus aurata* (Gilthead Seabream), 2 Year(s), Male, Laboratory (AQUALABS FACILITIES OF THE INST. OF MARINE BIOLOGY, BIOTECHNOLOGY AND AQUACULTURE OF THE HELLENIC CENT. FOR MARINE RES., IRAKLION, CRETE, GREECE)	Fresh water, Oral (diet, drink, gavage), Food, 10 Male organisms	Unmeasured	0 ug/kg bdwt/d / 15 ug/kg bdwt/d / 1500 ug/kg bdwt/d	Cellular (Genetics-Sterol regulatory element binding protein 1 mRNA, Response Site: Liver)	LOEC (15 ug/kg bdwt/d)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Liver toxicology; Neurotoxicology	Medium	4829367

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CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
28553-12-0	21 Day(s), (21 Day(s))	*Sparus aurata* (Gilthead Seabream), 2 Year(s), Male, Laboratory (AQUALABS FACILITIES OF THE INST. OF MARINE BIOLOGY, BIOTECHNOLOGY AND AQUACULTURE OF THE HELLENIC CENT. FOR MARINE RES., IRAKLION, CRETE, GREECE)	Fresh water, Oral (diet, drink, gavage), Food, 10 Male organisms	Unmeasured	0 ug/kg bdwt/d / 15 ug/kg bdwt/d / 1500 ug/kg bdwt/d	Cellular (Genetics-Leptin mRNA, Response Site: Liver)	LOEC (1500 ug/kg bdwt/d)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Liver toxicology; Neurotoxicology	Medium	4829367
28553-12-0	21 Day(s), (21 Day(s))	*Sparus aurata* (Gilthead Seabream), 2 Year(s), Male, Laboratory (AQUALABS FACILITIES OF THE INST. OF MARINE BIOLOGY, BIOTECHNOLOGY AND AQUACULTURE OF THE HELLENIC CENT. FOR MARINE RES., IRAKLION, CRETE, GREECE)	Fresh water, Oral (diet, drink, gavage), Food, 10 Male organisms	Unmeasured	0 ug/kg bdwt/d / 15 ug/kg bdwt/d / 1500 ug/kg bdwt/d	Growth (Growth-Weight, Response Site: Whole organism)	NOEC (1500 ug/kg bdwt/d)	Development/Growth	Medium	4829367

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CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
28553-12-0	21 Day(s), (21 Day(s))	*Sparus aurata* (Gilthead Seabream), 2 Year(s), Male, Laboratory (AQUALABS FACILITIES OF THE INST. OF MARINE BIOLOGY, BIOTECHNOLOGY AND AQUACULTURE OF THE HELLENIC CENT. FOR MARINE RES., IRAKLION, CRETE, GREECE)	Fresh water, Oral (diet, drink, gavage), Food, 10 Male organisms	Unmeasured	0 ug/kg bdwt/d / 15 ug/kg bdwt/d / 1500 ug/kg bdwt/d	Cellular (Genetics-Phospholipase A2 mRNA, Response Site: Liver)	NOEC (1500 ug/kg bdwt/d)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Liver toxicology; Neurotoxicology	Medium	4829367
28553-12-0	21 Day(s), (21 Day(s))	*Sparus aurata* (Gilthead Seabream), 2 Year(s), Male, Laboratory (AQUALABS FACILITIES OF THE INST. OF MARINE BIOLOGY, BIOTECHNOLOGY AND AQUACULTURE OF THE HELLENIC CENT. FOR MARINE RES., IRAKLION, CRETE, GREECE)	Fresh water, Oral (diet, drink, gavage), Food, 10 Male organisms	Unmeasured	0 ug/kg bdwt/d / 15 ug/kg bdwt/d / 1500 ug/kg bdwt/d	Biochemical (Biochemistry-Oleoylethanolamine, Response Site: Brain)	NR (15-1500 ug/kg bdwt/d)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Liver toxicology; Neurotoxicology	Medium	4829367

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CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
28553-12-0	21 Day(s), (21 Day(s))	*Sparus aurata* (Gilthead Seabream), 2 Year(s), Male, Laboratory (AQUALABS FACILITIES OF THE INST. OF MARINE BIOLOGY, BIOTECHNOLOGY AND AQUACULTURE OF THE HELLENIC CENT. FOR MARINE RES., IRAKLION, CRETE, GREECE)	Fresh water, Oral (diet, drink, gavage), Food, 10 Male organisms	Unmeasured	0 ug/kg bdwt/d / 15 ug/kg bdwt/d / 1500 ug/kg bdwt/d	Cellular (Histology-Vacuolization, Response Site: Liver)	LOEC (1500 ug/kg bdwt/d)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Liver toxicology; Neurotoxicology	Medium	4829367
28553-12-0	21 Day(s), (21 Day(s))	*Sparus aurata* (Gilthead Seabream), 2 Year(s), Male, Laboratory (AQUALABS FACILITIES OF THE INST. OF MARINE BIOLOGY, BIOTECHNOLOGY AND AQUACULTURE OF THE HELLENIC CENT. FOR MARINE RES., IRAKLION, CRETE, GREECE)	Fresh water, Oral (diet, drink, gavage), Food, 10 Male organisms	Unmeasured	0 ug/kg bdwt/d / 15 ug/kg bdwt/d / 1500 ug/kg bdwt/d	Cellular (Genetics-Diacylglycerol O-acyltransferase 1 mRNA, Response Site: Liver)	NOEC (1500 ug/kg bdwt/d)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Liver toxicology; Neurotoxicology	Medium	4829367

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CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
28553-12-0	21 Day(s), (21 Day(s))	*Sparus aurata* (Gilthead Seabream), 2 Year(s), Male, Laboratory (AQUALABS FACILITIES OF THE INST. OF MARINE BIOLOGY, BIOTECHNOLOGY AND AQUACULTURE OF THE HELLENIC CENT. FOR MARINE RES., IRAKLION, CRETE, GREECE)	Fresh water, Oral (diet, drink, gavage), Food, 10 Male organisms	Unmeasured	0 ug/kg bdwt/d / 15 ug/kg bdwt/d / 1500 ug/kg bdwt/d	Cellular (Genetics-Monoacylglycerol lipase abhd6A mRNA, Response Site: Liver)	LOEC (1500 ug/kg bdwt/d)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Liver toxicology; Neurotoxicology	Medium	4829367
28553-12-0	21 Day(s), (21 Day(s))	*Sparus aurata* (Gilthead Seabream), 2 Year(s), Male, Laboratory (AQUALABS FACILITIES OF THE INST. OF MARINE BIOLOGY, BIOTECHNOLOGY AND AQUACULTURE OF THE HELLENIC CENT. FOR MARINE RES., IRAKLION, CRETE, GREECE)	Fresh water, Oral (diet, drink, gavage), Food, 10 Male organisms	Unmeasured	0 ug/kg bdwt/d / 15 ug/kg bdwt/d / 1500 ug/kg bdwt/d	Biochemical (Biochemistry-Anandamide, Response Site: Liver)	NOEC (15 ug/kg bdwt/d)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Liver toxicology; Neurotoxicology	Medium	4829367

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CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
28553-12-0	21 Day(s), (21 Day(s))	*Sparus aurata* (Gilthead Seabream), 2 Year(s), Male, Laboratory (AQUALABS FACILITIES OF THE INST. OF MARINE BIOLOGY, BIOTECHNOLOGY AND AQUACULTURE OF THE HELLENIC CENT. FOR MARINE RES., IRAKLION, CRETE, GREECE)	Fresh water, Oral (diet, drink, gavage), Food, 10 Male organisms	Unmeasured	0 ug/kg bdwt/d / 15 ug/kg bdwt/d / 1500 ug/kg bdwt/d	Cellular (Genetics-Leptin mRNA, Response Site: Liver)	NOEC (15 ug/kg bdwt/d)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Liver toxicology; Neurotoxicology	Medium	4829367
28553-12-0	21 Day(s), (21 Day(s))	*Sparus aurata* (Gilthead Seabream), 2 Year(s), Male, Laboratory (AQUALABS FACILITIES OF THE INST. OF MARINE BIOLOGY, BIOTECHNOLOGY AND AQUACULTURE OF THE HELLENIC CENT. FOR MARINE RES., IRAKLION, CRETE, GREECE)	Fresh water, Oral (diet, drink, gavage), Food, 10 Male organisms	Unmeasured	0 ug/kg bdwt/d / 15 ug/kg bdwt/d / 1500 ug/kg bdwt/d	Cellular (Genetics-Monoacylglycerol lipase abhd6A mRNA, Response Site: Liver)	NOEC (15 ug/kg bdwt/d)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Liver toxicology; Neurotoxicology	Medium	4829367

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CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
28553-12-0	21 Day(s), (21 Day(s))	*Sparus aurata* (Gilthead Seabream), 2 Year(s), Male, Laboratory (AQUALABS FACILITIES OF THE INST. OF MARINE BIOLOGY, BIOTECHNOLOGY AND AQUACULTURE OF THE HELLENIC CENT. FOR MARINE RES., IRAKLION, CRETE, GREECE)	Fresh water, Oral (diet, drink, gavage), Food, 10 Male organisms	Unmeasured	0 ug/kg bdwt/d / 15 ug/kg bdwt/d / 1500 ug/kg bdwt/d	Cellular (Histology-Vacuolization, Response Site: Liver)	NOEC (15 ug/kg bdwt/d)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Liver toxicology; Neurotoxicology	Medium	4829367
28553-12-0	21 Day(s), (21 Day(s))	*Sparus aurata* (Gilthead Seabream), 2 Year(s), Male, Laboratory (AQUALABS FACILITIES OF THE INST. OF MARINE BIOLOGY, BIOTECHNOLOGY AND AQUACULTURE OF THE HELLENIC CENT. FOR MARINE RES., IRAKLION, CRETE, GREECE)	Fresh water, Oral (diet, drink, gavage), Food, 10 Male organisms	Unmeasured	0 ug/kg bdwt/d / 15 ug/kg bdwt/d / 1500 ug/kg bdwt/d	Biochemical (Biochemistry-2-Arachidonoylglycerol, Response Site: Liver)	NOEC (1500 ug/kg bdwt/d)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Liver toxicology; Neurotoxicology	Medium	4829367

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CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
28553-12-0	21 Day(s), (21 Day(s))	*Sparus aurata* (Gilthead Seabream), 2 Year(s), Male, Laboratory (AQUALABS FACILITIES OF THE INST. OF MARINE BIOLOGY, BIOTECHNOLOGY AND AQUACULTURE OF THE HELLENIC CENT. FOR MARINE RES., IRAKLION, CRETE, GREECE)	Fresh water, Oral (diet, drink, gavage), Food, 10 Male organisms	Unmeasured	0 ug/kg bdwt/d / 15 ug/kg bdwt/d / 1500 ug/kg bdwt/d	Biochemical (Biochemistry-Total phospholipid content, Response Site: Liver)	NOEC (1500 ug/kg bdwt/d)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Liver toxicology; Neurotoxicology	Medium	4829367
28553-12-0	21 Day(s), (21 Day(s))	*Sparus aurata* (Gilthead Seabream), 2 Year(s), Male, Laboratory (AQUALABS FACILITIES OF THE INST. OF MARINE BIOLOGY, BIOTECHNOLOGY AND AQUACULTURE OF THE HELLENIC CENT. FOR MARINE RES., IRAKLION, CRETE, GREECE)	Fresh water, Oral (diet, drink, gavage), Food, 10 Male organisms	Unmeasured	0 ug/kg bdwt/d / 15 ug/kg bdwt/d / 1500 ug/kg bdwt/d	Biochemical (Enzyme(s)-Fatty acid amide hydrolase, Response Site: Liver)	NOEC (1500 ug/kg bdwt/d)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Liver toxicology; Neurotoxicology	Medium	4829367

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CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
28553-12-0	21 Day(s), (21 Day(s))	*Sparus aurata* (Gilthead Seabream), 2 Year(s), Male, Laboratory (AQUALABS FACILITIES OF THE INST. OF MARINE BIOLOGY, BIOTECHNOLOGY AND AQUACULTURE OF THE HELLENIC CENT. FOR MARINE RES., IRAKLION, CRETE, GREECE)	Fresh water, Oral (diet, drink, gavage), Food, 10 Male organisms	Unmeasured	0 ug/kg bdwt/d / 15 ug/kg bdwt/d / 1500 ug/kg bdwt/d	Cellular (Genetics-Abhydrolase domain containing 4 mRNA, Response Site: Brain)	NOEC (1500 ug/kg bdwt/d)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Liver toxicology; Neurotoxicology	Medium	4829367
28553-12-0	21 Day(s), (21 Day(s))	*Sparus aurata* (Gilthead Seabream), 2 Year(s), Male, Laboratory (AQUALABS FACILITIES OF THE INST. OF MARINE BIOLOGY, BIOTECHNOLOGY AND AQUACULTURE OF THE HELLENIC CENT. FOR MARINE RES., IRAKLION, CRETE, GREECE)	Fresh water, Oral (diet, drink, gavage), Food, 10 Male organisms	Unmeasured	0 ug/kg bdwt/d / 15 ug/kg bdwt/d / 1500 ug/kg bdwt/d	Cellular (Genetics-Abhydrolase domain containing 4 mRNA, Response Site: Liver)	NOEC (1500 ug/kg bdwt/d)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Liver toxicology; Neurotoxicology	Medium	4829367

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28553-12-0	21 Day(s), (21 Day(s))	*Sparus aurata* (Gilthead Seabream), 2 Year(s), Male, Laboratory (AQUALABS FACILITIES OF THE INST. OF MARINE BIOLOGY, BIOTECHNOLOGY AND AQUACULTURE OF THE HELLENIC CENT. FOR MARINE RES., IRAKLION, CRETE, GREECE)	Fresh water, Oral (diet, drink, gavage), Food, 10 Male organisms	Unmeasured	0 ug/kg bdwt/d / 15 ug/kg bdwt/d / 1500 ug/kg bdwt/d	Cellular (Genetics-Acyl-Coenzyme A oxidase 3, pristanoyl mRNA, Response Site: Liver)	NOEC (1500 ug/kg bdwt/d)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Liver toxicology; Neurotoxicology	Medium	4829367
28553-12-0	21 Day(s), (21 Day(s))	*Sparus aurata* (Gilthead Seabream), 2 Year(s), Male, Laboratory (AQUALABS FACILITIES OF THE INST. OF MARINE BIOLOGY, BIOTECHNOLOGY AND AQUACULTURE OF THE HELLENIC CENT. FOR MARINE RES., IRAKLION, CRETE, GREECE)	Fresh water, Oral (diet, drink, gavage), Food, 10 Male organisms	Unmeasured	0 ug/kg bdwt/d / 15 ug/kg bdwt/d / 1500 ug/kg bdwt/d	Cellular (Genetics-Agouti-related protein mRNA, Response Site: Brain)	NOEC (1500 ug/kg bdwt/d)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Liver toxicology; Neurotoxicology	Medium	4829367

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28553-12-0	21 Day(s), (21 Day(s))	*Sparus aurata* (Gilthead Seabream), 2 Year(s), Male, Laboratory (AQUALABS FACILITIES OF THE INST. OF MARINE BIOLOGY, BIOTECHNOLOGY AND AQUACULTURE OF THE HELLENIC CENT. FOR MARINE RES., IRAKLION, CRETE, GREECE)	Fresh water, Oral (diet, drink, gavage), Food, 10 Male organisms	Unmeasured	0 ug/kg bdwt/d / 15 ug/kg bdwt/d / 1500 ug/kg bdwt/d	Cellular (Genetics-COX2 mRNA, Response Site: Brain)	NOEC (1500 ug/kg bdwt/d)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Liver toxicology; Neurotoxicology	Medium	4829367
28553-12-0	21 Day(s), (21 Day(s))	*Sparus aurata* (Gilthead Seabream), 2 Year(s), Male, Laboratory (AQUALABS FACILITIES OF THE INST. OF MARINE BIOLOGY, BIOTECHNOLOGY AND AQUACULTURE OF THE HELLENIC CENT. FOR MARINE RES., IRAKLION, CRETE, GREECE)	Fresh water, Oral (diet, drink, gavage), Food, 10 Male organisms	Unmeasured	0 ug/kg bdwt/d / 15 ug/kg bdwt/d / 1500 ug/kg bdwt/d	Cellular (Genetics-COX2 mRNA, Response Site: Liver)	NOEC (1500 ug/kg bdwt/d)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Liver toxicology; Neurotoxicology	Medium	4829367

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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
28553-12-0	21 Day(s), (21 Day(s))	*Sparus aurata* (Gilthead Seabream), 2 Year(s), Male, Laboratory (AQUALABS FACILITIES OF THE INST. OF MARINE BIOLOGY, BIOTECHNOLOGY AND AQUACULTURE OF THE HELLENIC CENT. FOR MARINE RES., IRAKLION, CRETE, GREECE)	Fresh water, Oral (diet, drink, gavage), Food, 10 Male organisms	Unmeasured	0 ug/kg bdwt/d / 15 ug/kg bdwt/d / 1500 ug/kg bdwt/d	Cellular (Genetics-Pro-opiomelanocortin mRNA, Response Site: Brain)	NOEC (1500 ug/kg bdwt/d)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Liver toxicology; Neurotoxicology	Medium	4829367
28553-12-0	21 Day(s), (21 Day(s))	*Sparus aurata* (Gilthead Seabream), 2 Year(s), Male, Laboratory (AQUALABS FACILITIES OF THE INSTITUTE OF MARINE BIOLOGY, BIOTECHNOLOGY, AND AQUACULTURE OF THE HELLENIC CENTRE FOR MARINE RESEARCH, HERAKLION, CRETE, GREECE)	Salt water, Oral (diet, drink, gavage), Food, Not Reported	Unmeasured	0 ug/kg bdwt/d / 15 ug/kg bdwt/d / 1500 ug/kg bdwt/d	Growth (Morphology-Organ weight in relationship to body weight, Response Site: Gonad(s))	NOEC (15 ug/kg bdwt/d)	Reproductive/Teratogenic	Medium	5534689

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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
28553-12-0	21 Day(s), (21 Day(s))	*Sparus aurata* (Gilthead Seabream), 2 Year(s), Male, Laboratory (AQUALABS FACILITIES OF THE INSTITUTE OF MARINE BIOLOGY, BIOTECHNOLOGY, AND AQUACULTURE OF THE HELLENIC CENTRE FOR MARINE RESEARCH, HERAKLION, CRETE, GREECE)	Salt water, Oral (diet, drink, gavage), Food, Not Reported	Unmeasured	0 ug/kg bdwt/d / 15 ug/kg bdwt/d / 1500 ug/kg bdwt/d	Reproduction (Reproduction-Motility, Response Site: Sperm)	NOEC (15 ug/kg bdwt/d)	Reproductive/Teratogenic	Medium	5534689
28553-12-0	21 Day(s), (21 Day(s))	*Sparus aurata* (Gilthead Seabream), 2 Year(s), Male, Laboratory (AQUALABS FACILITIES OF THE INSTITUTE OF MARINE BIOLOGY, BIOTECHNOLOGY, AND AQUACULTURE OF THE HELLENIC CENTRE FOR MARINE RESEARCH, HERAKLION, CRETE, GREECE)	Salt water, Oral (diet, drink, gavage), Food, Not Reported	Unmeasured	0 ug/kg bdwt/d / 15 ug/kg bdwt/d / 1500 ug/kg bdwt/d	Cellular (Genetics-17 beta-hydroxysteroid dehydrogenase mRNA, Response Site: Testes)	NOEC (1500 ug/kg bdwt/d)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Liver toxicology; Reproductive/Teratogenic	Medium	5534689

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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
28553-12-0	21 Day(s), (21 Day(s))	*Sparus aurata* (Gilthead Seabream), 2 Year(s), Male, Laboratory (AQUALABS FACILITIES OF THE INSTITUTE OF MARINE BIOLOGY, BIOTECHNOLOGY, AND AQUACULTURE OF THE HELLENIC CENTRE FOR MARINE RESEARCH, HERAKLION, CRETE, GREECE)	Salt water, Oral (diet, drink, gavage), Food, Not Reported	Unmeasured	0 ug/kg bdwt/d / 15 ug/kg bdwt/d / 1500 ug/kg bdwt/d	Cellular (Genetics-3B-Hydroxysteroid dehydrogenase mRNA, Response Site: Testes)	NOEC (1500 ug/kg bdwt/d)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Liver toxicology; Reproductive/Teratogenic	Medium	5534689
28553-12-0	21 Day(s), (21 Day(s))	*Sparus aurata* (Gilthead Seabream), 2 Year(s), Male, Laboratory (AQUALABS FACILITIES OF THE INSTITUTE OF MARINE BIOLOGY, BIOTECHNOLOGY, AND AQUACULTURE OF THE HELLENIC CENTRE FOR MARINE RESEARCH, HERAKLION, CRETE, GREECE)	Salt water, Oral (diet, drink, gavage), Food, Not Reported	Unmeasured	0 ug/kg bdwt/d / 15 ug/kg bdwt/d / 1500 ug/kg bdwt/d	Cellular (Genetics-COX2 mRNA, Response Site: Testes)	NOEC (1500 ug/kg bdwt/d)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Liver toxicology; Reproductive/Teratogenic	Medium	5534689

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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
28553-12-0	21 Day(s), (21 Day(s))	*Sparus aurata* (Gilthead Seabream), 2 Year(s), Male, Laboratory (AQUALABS FACILITIES OF THE INSTITUTE OF MARINE BIOLOGY, BIOTECHNOLOGY, AND AQUACULTURE OF THE HELLENIC CENTRE FOR MARINE RESEARCH, HERAKLION, CRETE, GREECE)	Salt water, Oral (diet, drink, gavage), Food, Not Reported	Unmeasured	0 ug/kg bdwt/d / 15 ug/kg bdwt/d / 1500 ug/kg bdwt/d	Cellular (Genetics-Endocannabinoid receptor type 2 mRNA, Response Site: Testes)	NOEC (15 ug/kg bdwt/d)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Liver toxicology; Reproductive/Teratogenic	Medium	5534689
28553-12-0	21 Day(s), (21 Day(s))	*Sparus aurata* (Gilthead Seabream), 2 Year(s), Male, Laboratory (AQUALABS FACILITIES OF THE INSTITUTE OF MARINE BIOLOGY, BIOTECHNOLOGY, AND AQUACULTURE OF THE HELLENIC CENTRE FOR MARINE RESEARCH, HERAKLION, CRETE, GREECE)	Salt water, Oral (diet, drink, gavage), Food, Not Reported	Unmeasured	0 ug/kg bdwt/d / 15 ug/kg bdwt/d / 1500 ug/kg bdwt/d	Cellular (Genetics-Endocannabinoid receptor type 1 mRNA, Response Site: Testes)	LOEC (1500 ug/kg bdwt/d)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Liver toxicology; Reproductive/Teratogenic	Medium	5534689

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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
28553-12-0	21 Day(s), (21 Day(s))	*Sparus aurata* (Gilthead Seabream), 2 Year(s), Male, Laboratory (AQUALABS FACILITIES OF THE INSTITUTE OF MARINE BIOLOGY, BIOTECHNOLOGY, AND AQUACULTURE OF THE HELLENIC CENTRE FOR MARINE RESEARCH, HERAKLION, CRETE, GREECE)	Salt water, Oral (diet, drink, gavage), Food, Not Reported	Unmeasured	0 ug/kg bdwt/d / 15 ug/kg bdwt/d / 1500 ug/kg bdwt/d	Cellular (Genetics-Diacylglycerol lipase, alpha mRNA, Response Site: Testes)	LOEC (1500 ug/kg bdwt/d)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Liver toxicology; Reproductive/Teratogenic	Medium	5534689
28553-12-0	21 Day(s), (21 Day(s))	*Sparus aurata* (Gilthead Seabream), 2 Year(s), Male, Laboratory (AQUALABS FACILITIES OF THE INSTITUTE OF MARINE BIOLOGY, BIOTECHNOLOGY, AND AQUACULTURE OF THE HELLENIC CENTRE FOR MARINE RESEARCH, HERAKLION, CRETE, GREECE)	Salt water, Oral (diet, drink, gavage), Food, Not Reported	Unmeasured	0 ug/kg bdwt/d / 15 ug/kg bdwt/d / 1500 ug/kg bdwt/d	Cellular (Genetics-Androgen receptor mRNA, Response Site: Testes)	LOEC (1500 ug/kg bdwt/d)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Liver toxicology; Reproductive/Teratogenic	Medium	5534689

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CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
28553-12-0	21 Day(s), (21 Day(s))	*Sparus aurata* (Gilthead Seabream), 2 Year(s), Male, Laboratory (AQUALABS FACILITIES OF THE INSTITUTE OF MARINE BIOLOGY, BIOTECHNOLOGY, AND AQUACULTURE OF THE HELLENIC CENTRE FOR MARINE RESEARCH, HERAKLION, CRETE, GREECE)	Salt water, Oral (diet, drink, gavage), Food, Not Reported	Unmeasured	0 ug/kg bdwt/d / 15 ug/kg bdwt/d / 1500 ug/kg bdwt/d	Cellular (Genetics-Zona pellucida protein 1 mRNA, Response Site: Liver)	NOEC (15 ug/kg bdwt/d)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Liver toxicology; Reproductive/Teratogenic	Medium	5534689
28553-12-0	21 Day(s), (21 Day(s))	*Sparus aurata* (Gilthead Seabream), 2 Year(s), Male, Laboratory (AQUALABS FACILITIES OF THE INSTITUTE OF MARINE BIOLOGY, BIOTECHNOLOGY, AND AQUACULTURE OF THE HELLENIC CENTRE FOR MARINE RESEARCH, HERAKLION, CRETE, GREECE)	Salt water, Oral (diet, drink, gavage), Food, Not Reported	Unmeasured	0 ug/kg bdwt/d / 15 ug/kg bdwt/d / 1500 ug/kg bdwt/d	Cellular (Genetics-Zona pellucida glycoprotein3 mRNA, Response Site: Liver)	NOEC (15 ug/kg bdwt/d)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Liver toxicology; Reproductive/Teratogenic	Medium	5534689

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CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
28553-12-0	21 Day(s), (21 Day(s))	*Sparus aurata* (Gilthead Seabream), 2 Year(s), Male, Laboratory (AQUALABS FACILITIES OF THE INSTITUTE OF MARINE BIOLOGY, BIOTECHNOLOGY, AND AQUACULTURE OF THE HELLENIC CENTRE FOR MARINE RESEARCH, HERAKLION, CRETE, GREECE)	Salt water, Oral (diet, drink, gavage), Food, Not Reported	Unmeasured	0 ug/kg bdwt/d / 15 ug/kg bdwt/d / 1500 ug/kg bdwt/d	Cellular (Genetics-Monoacylglycerol lipase abhd12A mRNA, Response Site: Testes)	NOEC (15 ug/kg bdwt/d)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Liver toxicology; Reproductive/Teratogenic	Medium	5534689
28553-12-0	21 Day(s), (21 Day(s))	*Sparus aurata* (Gilthead Seabream), 2 Year(s), Male, Laboratory (AQUALABS FACILITIES OF THE INSTITUTE OF MARINE BIOLOGY, BIOTECHNOLOGY, AND AQUACULTURE OF THE HELLENIC CENTRE FOR MARINE RESEARCH, HERAKLION, CRETE, GREECE)	Salt water, Oral (diet, drink, gavage), Food, Not Reported	Unmeasured	0 ug/kg bdwt/d / 15 ug/kg bdwt/d / 1500 ug/kg bdwt/d	Cellular (Genetics-Monoacylglycerol lipase abhd6A mRNA, Response Site: Testes)	NOEC (1500 ug/kg bdwt/d)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Liver toxicology; Reproductive/Teratogenic	Medium	5534689

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CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
28553-12-0	21 Day(s), (21 Day(s))	*Sparus aurata* (Gilthead Seabream), 2 Year(s), Male, Laboratory (AQUALABS FACILITIES OF THE INSTITUTE OF MARINE BIOLOGY, BIOTECHNOLOGY, AND AQUACULTURE OF THE HELLENIC CENTRE FOR MARINE RESEARCH, HERAKLION, CRETE, GREECE)	Salt water, Oral (diet, drink, gavage), Food, Not Reported	Unmeasured	0 ug/kg bdwt/d / 15 ug/kg bdwt/d / 1500 ug/kg bdwt/d	Cellular (Genetics-Follicle-stimulating hormone receptor mRNA, Response Site: Testes)	NOEC (1500 ug/kg bdwt/d)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Liver toxicology; Reproductive/Teratogenic	Medium	5534689
28553-12-0	21 Day(s), (21 Day(s))	*Sparus aurata* (Gilthead Seabream), 2 Year(s), Male, Laboratory (AQUALABS FACILITIES OF THE INSTITUTE OF MARINE BIOLOGY, BIOTECHNOLOGY, AND AQUACULTURE OF THE HELLENIC CENTRE FOR MARINE RESEARCH, HERAKLION, CRETE, GREECE)	Salt water, Oral (diet, drink, gavage), Food, Not Reported	Unmeasured	0 ug/kg bdwt/d / 15 ug/kg bdwt/d / 1500 ug/kg bdwt/d	Cellular (Genetics-Estrogen receptor beta mRNA, Response Site: Testes)	NOEC (1500 ug/kg bdwt/d)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Liver toxicology; Reproductive/Teratogenic	Medium	5534689

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CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
28553-12-0	21 Day(s), (21 Day(s))	*Sparus aurata* (Gilthead Seabream), 2 Year(s), Male, Laboratory (AQUALABS FACILITIES OF THE INSTITUTE OF MARINE BIOLOGY, BIOTECHNOLOGY, AND AQUACULTURE OF THE HELLENIC CENTRE FOR MARINE RESEARCH, HERAKLION, CRETE, GREECE)	Salt water, Oral (diet, drink, gavage), Food, Not Reported	Unmeasured	0 ug/kg bdwt/d / 15 ug/kg bdwt/d / 1500 ug/kg bdwt/d	Cellular (Genetics-Estrogen receptor alpha mRNA, Response Site: Testes)	NOEC (1500 ug/kg bdwt/d)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Liver toxicology; Reproductive/Teratogenic	Medium	5534689
28553-12-0	21 Day(s), (21 Day(s))	*Sparus aurata* (Gilthead Seabream), 2 Year(s), Male, Laboratory (AQUALABS FACILITIES OF THE INSTITUTE OF MARINE BIOLOGY, BIOTECHNOLOGY, AND AQUACULTURE OF THE HELLENIC CENTRE FOR MARINE RESEARCH, HERAKLION, CRETE, GREECE)	Salt water, Oral (diet, drink, gavage), Food, Not Reported	Unmeasured	0 ug/kg bdwt/d / 15 ug/kg bdwt/d / 1500 ug/kg bdwt/d	Cellular (Genetics-Zona pellucida protein 1 mRNA, Response Site: Liver)	LOEC (1500 ug/kg bdwt/d)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Liver toxicology; Reproductive/Teratogenic	Medium	5534689

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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
28553-12-0	21 Day(s), (21 Day(s))	*Sparus aurata* (Gilthead Seabream), 2 Year(s), Male, Laboratory (AQUALABS FACILITIES OF THE INSTITUTE OF MARINE BIOLOGY, BIOTECHNOLOGY, AND AQUACULTURE OF THE HELLENIC CENTRE FOR MARINE RESEARCH, HERAKLION, CRETE, GREECE)	Salt water, Oral (diet, drink, gavage), Food, Not Reported	Unmeasured	0 ug/kg bdwt/d / 15 ug/kg bdwt/d / 1500 ug/kg bdwt/d	Growth (Morphology-Organ weight in relationship to body weight, Response Site: Gonad(s))	LOEC (1500 ug/kg bdwt/d)	Reproductive/Teratogenic	Medium	5534689
28553-12-0	21 Day(s), (21 Day(s))	*Sparus aurata* (Gilthead Seabream), 2 Year(s), Male, Laboratory (AQUALABS FACILITIES OF THE INSTITUTE OF MARINE BIOLOGY, BIOTECHNOLOGY, AND AQUACULTURE OF THE HELLENIC CENTRE FOR MARINE RESEARCH, HERAKLION, CRETE, GREECE)	Salt water, Oral (diet, drink, gavage), Food, Not Reported	Unmeasured	0 ug/kg bdwt/d / 15 ug/kg bdwt/d / 1500 ug/kg bdwt/d	Reproduction (Reproduction-Motility, Response Site: Sperm)	LOEC (1500 ug/kg bdwt/d)	Reproductive/Teratogenic	Medium	5534689

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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
28553-12-0	21 Day(s), (21 Day(s))	*Sparus aurata* (Gilthead Seabream), 2 Year(s), Male, Laboratory (AQUALABS FACILITIES OF THE INSTITUTE OF MARINE BIOLOGY, BIOTECHNOLOGY, AND AQUACULTURE OF THE HELLENIC CENTRE FOR MARINE RESEARCH, HERAKLION, CRETE, GREECE)	Salt water, Oral (diet, drink, gavage), Food, Not Reported	Unmeasured	0 ug/kg bdwt/d / 15 ug/kg bdwt/d / 1500 ug/kg bdwt/d	Biochemical (Biochemistry-Anandamide, Response Site: Gonad(s))	NOEC (15 ug/kg bdwt/d)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Liver toxicology; Reproductive/Teratogenic	Medium	5534689
28553-12-0	21 Day(s), (21 Day(s))	*Sparus aurata* (Gilthead Seabream), 2 Year(s), Male, Laboratory (AQUALABS FACILITIES OF THE INSTITUTE OF MARINE BIOLOGY, BIOTECHNOLOGY, AND AQUACULTURE OF THE HELLENIC CENTRE FOR MARINE RESEARCH, HERAKLION, CRETE, GREECE)	Salt water, Oral (diet, drink, gavage), Food, Not Reported	Unmeasured	0 ug/kg bdwt/d / 15 ug/kg bdwt/d / 1500 ug/kg bdwt/d	Biochemical (Biochemistry-Oleoylethanolamine, Response Site: Gonad(s))	NOEC (15 ug/kg bdwt/d)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Liver toxicology; Reproductive/Teratogenic	Medium	5534689

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CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
28553-12-0	21 Day(s), (21 Day(s))	*Sparus aurata* (Gilthead Seabream), 2 Year(s), Male, Laboratory (AQUALABS FACILITIES OF THE INSTITUTE OF MARINE BIOLOGY, BIOTECHNOLOGY, AND AQUACULTURE OF THE HELLENIC CENTRE FOR MARINE RESEARCH, HERAKLION, CRETE, GREECE)	Salt water, Oral (diet, drink, gavage), Food, Not Reported	Unmeasured	0 ug/kg bdwt/d / 15 ug/kg bdwt/d / 1500 ug/kg bdwt/d	Biochemical (Biochemistry-Palmitoylethanolamide, Response Site: Gonad(s))	NOEC (15 ug/kg bdwt/d)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Liver toxicology; Reproductive/Teratogenic	Medium	5534689
28553-12-0	21 Day(s), (21 Day(s))	*Sparus aurata* (Gilthead Seabream), 2 Year(s), Male, Laboratory (AQUALABS FACILITIES OF THE INSTITUTE OF MARINE BIOLOGY, BIOTECHNOLOGY, AND AQUACULTURE OF THE HELLENIC CENTRE FOR MARINE RESEARCH, HERAKLION, CRETE, GREECE)	Salt water, Oral (diet, drink, gavage), Food, Not Reported	Unmeasured	0 ug/kg bdwt/d / 15 ug/kg bdwt/d / 1500 ug/kg bdwt/d	Biochemical (Hormone(s)-11-Ketotestosterone, Response Site: Gonad(s))	NOEC (15 ug/kg bdwt/d)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Liver toxicology; Reproductive/Teratogenic	Medium	5534689

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CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
28553-12-0	21 Day(s), (21 Day(s))	*Sparus aurata* (Gilthead Seabream), 2 Year(s), Male, Laboratory (AQUALABS FACILITIES OF THE INSTITUTE OF MARINE BIOLOGY, BIOTECHNOLOGY, AND AQUACULTURE OF THE HELLENIC CENTRE FOR MARINE RESEARCH, HERAKLION, CRETE, GREECE)	Salt water, Oral (diet, drink, gavage), Food, Not Reported	Unmeasured	0 ug/kg bdwt/d / 15 ug/kg bdwt/d / 1500 ug/kg bdwt/d	Cellular (Genetics-Androgen receptor mRNA, Response Site: Testes)	NOEC (15 ug/kg bdwt/d)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Liver toxicology; Reproductive/Teratogenic	Medium	5534689
28553-12-0	21 Day(s), (21 Day(s))	*Sparus aurata* (Gilthead Seabream), 2 Year(s), Male, Laboratory (AQUALABS FACILITIES OF THE INSTITUTE OF MARINE BIOLOGY, BIOTECHNOLOGY, AND AQUACULTURE OF THE HELLENIC CENTRE FOR MARINE RESEARCH, HERAKLION, CRETE, GREECE)	Salt water, Oral (diet, drink, gavage), Food, Not Reported	Unmeasured	0 ug/kg bdwt/d / 15 ug/kg bdwt/d / 1500 ug/kg bdwt/d	Cellular (Genetics-Diacylglycerol lipase, alpha mRNA, Response Site: Testes)	NOEC (15 ug/kg bdwt/d)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Liver toxicology; Reproductive/Teratogenic	Medium	5534689

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CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
28553-12-0	21 Day(s), (21 Day(s))	*Sparus aurata* (Gilthead Seabream), 2 Year(s), Male, Laboratory (AQUALABS FACILITIES OF THE INSTITUTE OF MARINE BIOLOGY, BIOTECHNOLOGY, AND AQUACULTURE OF THE HELLENIC CENTRE FOR MARINE RESEARCH, HERAKLION, CRETE, GREECE)	Salt water, Oral (diet, drink, gavage), Food, Not Reported	Unmeasured	0 ug/kg bdwt/d / 15 ug/kg bdwt/d / 1500 ug/kg bdwt/d	Cellular (Genetics-Endocannabinoid receptor type 2 mRNA, Response Site: Testes)	LOEC (1500 ug/kg bdwt/d)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Liver toxicology; Reproductive/Teratogenic	Medium	5534689
28553-12-0	21 Day(s), (21 Day(s))	*Sparus aurata* (Gilthead Seabream), 2 Year(s), Male, Laboratory (AQUALABS FACILITIES OF THE INSTITUTE OF MARINE BIOLOGY, BIOTECHNOLOGY, AND AQUACULTURE OF THE HELLENIC CENTRE FOR MARINE RESEARCH, HERAKLION, CRETE, GREECE)	Salt water, Oral (diet, drink, gavage), Food, Not Reported	Unmeasured	0 ug/kg bdwt/d / 15 ug/kg bdwt/d / 1500 ug/kg bdwt/d	Cellular (Genetics-Endocannabinoid receptor type 1 mRNA, Response Site: Testes)	NOEC (15 ug/kg bdwt/d)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Liver toxicology; Reproductive/Teratogenic	Medium	5534689

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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
28553-12-0	21 Day(s), (21 Day(s))	*Sparus aurata* (Gilthead Seabream), 2 Year(s), Male, Laboratory (AQUALABS FACILITIES OF THE INSTITUTE OF MARINE BIOLOGY, BIOTECHNOLOGY, AND AQUACULTURE OF THE HELLENIC CENTRE FOR MARINE RESEARCH, HERAKLION, CRETE, GREECE)	Salt water, Oral (diet, drink, gavage), Food, Not Reported	Unmeasured	0 ug/kg bdwt/d / 15 ug/kg bdwt/d / 1500 ug/kg bdwt/d	Cellular (Genetics-Progesterone receptor mRNA, Response Site: Testes)	NOEC (15 ug/kg bdwt/d)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Liver toxicology; Reproductive/Teratogenic	Medium	5534689
28553-12-0	21 Day(s), (21 Day(s))	*Sparus aurata* (Gilthead Seabream), 2 Year(s), Male, Laboratory (AQUALABS FACILITIES OF THE INSTITUTE OF MARINE BIOLOGY, BIOTECHNOLOGY, AND AQUACULTURE OF THE HELLENIC CENTRE FOR MARINE RESEARCH, HERAKLION, CRETE, GREECE)	Salt water, Oral (diet, drink, gavage), Food, Not Reported	Unmeasured	0 ug/kg bdwt/d / 15 ug/kg bdwt/d / 1500 ug/kg bdwt/d	Cellular (Genetics-Monoacylglycerol lipase abhd12A mRNA, Response Site: Testes)	LOEC (1500 ug/kg bdwt/d)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Liver toxicology; Reproductive/Teratogenic	Medium	5534689

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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
28553-12-0	21 Day(s), (21 Day(s))	*Sparus aurata* (Gilthead Seabream), 2 Year(s), Male, Laboratory (AQUALABS FACILITIES OF THE INSTITUTE OF MARINE BIOLOGY, BIOTECHNOLOGY, AND AQUACULTURE OF THE HELLENIC CENTRE FOR MARINE RESEARCH, HERAKLION, CRETE, GREECE)	Salt water, Oral (diet, drink, gavage), Food, Not Reported	Unmeasured	0 ug/kg bdwt/d / 15 ug/kg bdwt/d / 1500 ug/kg bdwt/d	Cellular (Genetics-Luteinizing hormone receptor mRNA, Response Site: Testes)	LOEC (15 ug/kg bdwt/d)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Liver toxicology; Reproductive/Teratogenic	Medium	5534689
28553-12-0	21 Day(s), (21 Day(s))	*Sparus aurata* (Gilthead Seabream), 2 Year(s), Male, Laboratory (AQUALABS FACILITIES OF THE INSTITUTE OF MARINE BIOLOGY, BIOTECHNOLOGY, AND AQUACULTURE OF THE HELLENIC CENTRE FOR MARINE RESEARCH, HERAKLION, CRETE, GREECE)	Salt water, Oral (diet, drink, gavage), Food, Not Reported	Unmeasured	0 ug/kg bdwt/d / 15 ug/kg bdwt/d / 1500 ug/kg bdwt/d	Cellular (Genetics-Leptin receptor mRNA, Response Site: Testes)	LOEC (15 ug/kg bdwt/d)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Liver toxicology; Reproductive/Teratogenic	Medium	5534689

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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
28553-12-0	21 Day(s), (21 Day(s))	*Sparus aurata* (Gilthead Seabream), 2 Year(s), Male, Laboratory (AQUALABS FACILITIES OF THE INSTITUTE OF MARINE BIOLOGY, BIOTECHNOLOGY, AND AQUACULTURE OF THE HELLENIC CENTRE FOR MARINE RESEARCH, HERAKLION, CRETE, GREECE)	Salt water, Oral (diet, drink, gavage), Food, Not Reported	Unmeasured	0 ug/kg bdwt/d / 15 ug/kg bdwt/d / 1500 ug/kg bdwt/d	Biochemical (Hormone(s)-17-beta Estradiol, Response Site: Gonad(s))	LOEC (15 ug/kg bdwt/d)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Liver toxicology; Reproductive/Teratogenic	Medium	5534689
28553-12-0	21 Day(s), (21 Day(s))	*Sparus aurata* (Gilthead Seabream), 2 Year(s), Male, Laboratory (AQUALABS FACILITIES OF THE INSTITUTE OF MARINE BIOLOGY, BIOTECHNOLOGY, AND AQUACULTURE OF THE HELLENIC CENTRE FOR MARINE RESEARCH, HERAKLION, CRETE, GREECE)	Salt water, Oral (diet, drink, gavage), Food, Not Reported	Unmeasured	0 ug/kg bdwt/d / 15 ug/kg bdwt/d / 1500 ug/kg bdwt/d	Biochemical (Enzyme(s)-Fatty acid amide hydrolase, Response Site: Gonad(s))	LOEC (15 ug/kg bdwt/d)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Liver toxicology; Reproductive/Teratogenic	Medium	5534689

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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
28553-12-0	21 Day(s), (21 Day(s))	*Sparus aurata* (Gilthead Seabream), 2 Year(s), Male, Laboratory (AQUALABS FACILITIES OF THE INSTITUTE OF MARINE BIOLOGY, BIOTECHNOLOGY, AND AQUACULTURE OF THE HELLENIC CENTRE FOR MARINE RESEARCH, HERAKLION, CRETE, GREECE)	Salt water, Oral (diet, drink, gavage), Food, Not Reported	Unmeasured	0 ug/kg bdwt/d / 15 ug/kg bdwt/d / 1500 ug/kg bdwt/d	Biochemical (Biochemistry-2-Arachidonoylglycerol, Response Site: Gonad(s))	LOEC (15 ug/kg bdwt/d)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Liver toxicology; Reproductive/Teratogenic	Medium	5534689
28553-12-0	21 Day(s), (21 Day(s))	*Sparus aurata* (Gilthead Seabream), 2 Year(s), Male, Laboratory (AQUALABS FACILITIES OF THE INSTITUTE OF MARINE BIOLOGY, BIOTECHNOLOGY, AND AQUACULTURE OF THE HELLENIC CENTRE FOR MARINE RESEARCH, HERAKLION, CRETE, GREECE)	Salt water, Oral (diet, drink, gavage), Food, Not Reported	Unmeasured	0 ug/kg bdwt/d / 15 ug/kg bdwt/d / 1500 ug/kg bdwt/d	Cellular (Genetics-Transient receptor potential cation channel subfamily V member 1 mRNA, Response Site: Testes)	LOEC (15 ug/kg bdwt/d)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Liver toxicology; Reproductive/Teratogenic	Medium	5534689

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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
28553-12-0	21 Day(s), (21 Day(s))	*Sparus aurata* (Gilthead Seabream), 2 Year(s), Male, Laboratory (AQUALABS FACILITIES OF THE INSTITUTE OF MARINE BIOLOGY, BIOTECHNOLOGY, AND AQUACULTURE OF THE HELLENIC CENTRE FOR MARINE RESEARCH, HERAKLION, CRETE, GREECE)	Salt water, Oral (diet, drink, gavage), Food, Not Reported	Unmeasured	0 ug/kg bdwt/d / 15 ug/kg bdwt/d / 1500 ug/kg bdwt/d	Biochemical (Biochemistry-Anandamide, Response Site: Gonad(s))	LOEC (1500 ug/kg bdwt/d)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Liver toxicology; Reproductive/Teratogenic	Medium	5534689
28553-12-0	21 Day(s), (21 Day(s))	*Sparus aurata* (Gilthead Seabream), 2 Year(s), Male, Laboratory (AQUALABS FACILITIES OF THE INSTITUTE OF MARINE BIOLOGY, BIOTECHNOLOGY, AND AQUACULTURE OF THE HELLENIC CENTRE FOR MARINE RESEARCH, HERAKLION, CRETE, GREECE)	Salt water, Oral (diet, drink, gavage), Food, Not Reported	Unmeasured	0 ug/kg bdwt/d / 15 ug/kg bdwt/d / 1500 ug/kg bdwt/d	Biochemical (Biochemistry-Palmitoylethanolamide, Response Site: Gonad(s))	LOEC (1500 ug/kg bdwt/d)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Liver toxicology; Reproductive/Teratogenic	Medium	5534689

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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
28553-12-0	21 Day(s), (21 Day(s))	*Sparus aurata* (Gilthead Seabream), 2 Year(s), Male, Laboratory (AQUALABS FACILITIES OF THE INSTITUTE OF MARINE BIOLOGY, BIOTECHNOLOGY, AND AQUACULTURE OF THE HELLENIC CENTRE FOR MARINE RESEARCH, HERAKLION, CRETE, GREECE)	Salt water, Oral (diet, drink, gavage), Food, Not Reported	Unmeasured	0 ug/kg bdwt/d / 15 ug/kg bdwt/d / 1500 ug/kg bdwt/d	Cellular (Genetics-Progesterone receptor mRNA, Response Site: Testes)	LOEC (1500 ug/kg bdwt/d)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Liver toxicology; Reproductive/Teratogenic	Medium	5534689
28553-12-0	21 Day(s), (21 Day(s))	*Sparus aurata* (Gilthead Seabream), 2 Year(s), Male, Laboratory (AQUALABS FACILITIES OF THE INSTITUTE OF MARINE BIOLOGY, BIOTECHNOLOGY, AND AQUACULTURE OF THE HELLENIC CENTRE FOR MARINE RESEARCH, HERAKLION, CRETE, GREECE)	Salt water, Oral (diet, drink, gavage), Food, Not Reported	Unmeasured	0 ug/kg bdwt/d / 15 ug/kg bdwt/d / 1500 ug/kg bdwt/d	Biochemical (Hormone(s)-11-Ketotestosterone, Response Site: Gonad(s))	LOEC (1500 ug/kg bdwt/d)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Liver toxicology; Reproductive/Teratogenic	Medium	5534689

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CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
28553-12-0	21 Day(s), (21 Day(s))	*Sparus aurata* (Gilthead Seabream), 2 Year(s), Male, Laboratory (AQUALABS FACILITIES OF THE INSTITUTE OF MARINE BIOLOGY, BIOTECHNOLOGY, AND AQUACULTURE OF THE HELLENIC CENTRE FOR MARINE RESEARCH, HERAKLION, CRETE, GREECE)	Salt water, Oral (diet, drink, gavage), Food, Not Reported	Unmeasured	0 ug/kg bdwt/d / 15 ug/kg bdwt/d / 1500 ug/kg bdwt/d	Biochemical (Biochemistry-Oleoylethanolamine, Response Site: Gonad(s))	LOEC (1500 ug/kg bdwt/d)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Liver toxicology; Reproductive/Teratogenic	Medium	5534689
28553-12-0	21 Day(s), (21 Day(s))	*Sparus aurata* (Gilthead Seabream), 2 Year(s), Male, Laboratory (AQUALABS FACILITIES OF THE INSTITUTE OF MARINE BIOLOGY, BIOTECHNOLOGY, AND AQUACULTURE OF THE HELLENIC CENTRE FOR MARINE RESEARCH, HERAKLION, CRETE, GREECE)	Salt water, Oral (diet, drink, gavage), Food, Not Reported	Unmeasured	0 ug/kg bdwt/d / 15 ug/kg bdwt/d / 1500 ug/kg bdwt/d	Cellular (Histology-Percent cell type, Response Site: Gonad(s),Ovaries,Sperm,Testes)	NR (15-1500 ug/kg bdwt/d)	Reproductive/Teratogenic	Medium	5534689

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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
28553-12-0	21 Day(s), (21 Day(s))	*Sparus aurata* (Gilthead Seabream), 2 Year(s), Male, Laboratory (AQUALABS FACILITIES OF THE INSTITUTE OF MARINE BIOLOGY, BIOTECHNOLOGY, AND AQUACULTURE OF THE HELLENIC CENTRE FOR MARINE RESEARCH, HERAKLION, CRETE, GREECE)	Salt water, Oral (diet, drink, gavage), Food, Not Reported	Unmeasured	0 ug/kg bdwt/d / 15 ug/kg bdwt/d / 1500 ug/kg bdwt/d	Cellular (Genetics-Peroxisome proliferator-activated receptor beta mRNA, Response Site: Testes)	NR (15-1500 ug/kg bdwt/d)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Liver toxicology; Reproductive/Teratogenic	Medium	5534689
28553-12-0	21 Day(s), (21 Day(s))	*Sparus aurata* (Gilthead Seabream), 2 Year(s), Male, Laboratory (AQUALABS FACILITIES OF THE INSTITUTE OF MARINE BIOLOGY, BIOTECHNOLOGY, AND AQUACULTURE OF THE HELLENIC CENTRE FOR MARINE RESEARCH, HERAKLION, CRETE, GREECE)	Salt water, Oral (diet, drink, gavage), Food, Not Reported	Unmeasured	0 ug/kg bdwt/d / 15 ug/kg bdwt/d / 1500 ug/kg bdwt/d	Cellular (Genetics-Zona pellucida glycoprotein3 mRNA, Response Site: Liver)	LOEC (1500 ug/kg bdwt/d)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Liver toxicology; Reproductive/Teratogenic	Medium	5534689

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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
28553-12-0	21 Day(s), (21 Day(s))	*Sparus aurata* (Gilthead Seabream), 2 Year(s), Male, Laboratory (AQUALABS FACILITIES OF THE INSTITUTE OF MARINE BIOLOGY, BIOTECHNOLOGY, AND AQUACULTURE OF THE HELLENIC CENTRE FOR MARINE RESEARCH, HERAKLION, CRETE, GREECE)	Salt water, Oral (diet, drink, gavage), Food, Not Reported	Unmeasured	0 ug/kg bdwt/d / 15 ug/kg bdwt/d / 1500 ug/kg bdwt/d	Cellular (Genetics-Peroxisome proliferator-activated receptor gamma mRNA, Response Site: Testes)	NR (15-1500 ug/kg bdwt/d)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Liver toxicology; Reproductive/Teratogenic	Medium	5534689
28553-12-0	21 Day(s), (21 Day(s))	*Sparus aurata* (Gilthead Seabream), 2 Year(s), Male, Laboratory (AQUALABS FACILITIES OF THE INSTITUTE OF MARINE BIOLOGY, BIOTECHNOLOGY, AND AQUACULTURE OF THE HELLENIC CENTRE FOR MARINE RESEARCH, HERAKLION, CRETE, GREECE)	Salt water, Oral (diet, drink, gavage), Food, Not Reported	Unmeasured	0 ug/kg bdwt/d / 15 ug/kg bdwt/d / 1500 ug/kg bdwt/d	Cellular (Genetics-N-acyl phosphatidylethanolamine phospholipase D mRNA, Response Site: Testes)	NOEC (1500 ug/kg bdwt/d)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Liver toxicology; Reproductive/Teratogenic	Medium	5534689

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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
28553-12-0	21 Day(s), (21 Day(s))	*Sparus aurata* (Gilthead Seabream), 2 Year(s), Male, Laboratory (AQUALABS FACILITIES OF THE INSTITUTE OF MARINE BIOLOGY, BIOTECHNOLOGY, AND AQUACULTURE OF THE HELLENIC CENTRE FOR MARINE RESEARCH, HERAKLION, CRETE, GREECE)	Salt water, Oral (diet, drink, gavage), Food, Not Reported	Unmeasured	0 ug/kg bdwt/d / 15 ug/kg bdwt/d / 1500 ug/kg bdwt/d	Cellular (Genetics-Peroxisome proliferator-activated receptor alpha mRNA, Response Site: Testes)	NOEC (1500 ug/kg bdwt/d)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Liver toxicology; Reproductive/Teratogenic	Medium	5534689
28553-12-0	21 Day(s), (21 Day(s))	*Sparus aurata* (Gilthead Seabream), 2 Year(s), Male, Laboratory (AQUALABS FACILITIES OF THE INSTITUTE OF MARINE BIOLOGY, BIOTECHNOLOGY, AND AQUACULTURE OF THE HELLENIC CENTRE FOR MARINE RESEARCH, HERAKLION, CRETE, GREECE)	Salt water, Oral (diet, drink, gavage), Food, Not Reported	Unmeasured	0 ug/kg bdwt/d / 15 ug/kg bdwt/d / 1500 ug/kg bdwt/d	Cellular (Genetics-Phospholipase A2 mRNA, Response Site: Testes)	NOEC (1500 ug/kg bdwt/d)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Liver toxicology; Reproductive/Teratogenic	Medium	5534689

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CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
28553-12-0	21 Day(s), (21 Day(s))	*Sparus aurata* (Gilthead Seabream), 2 Year(s), Male, Laboratory (AQUALABS FACILITIES OF THE INSTITUTE OF MARINE BIOLOGY, BIOTECHNOLOGY, AND AQUACULTURE OF THE HELLENIC CENTRE FOR MARINE RESEARCH, HERAKLION, CRETE, GREECE)	Salt water, Oral (diet, drink, gavage), Food, Not Reported	Unmeasured	0 ug/kg bdwt/d / 15 ug/kg bdwt/d / 1500 ug/kg bdwt/d	Cellular (Genetics-Vitellogenin A mRNA, Response Site: Liver)	NOEC (1500 ug/kg bdwt/d)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Liver toxicology; Reproductive/Teratogenic	Medium	5534689
28553-12-0	21 Day(s), (21 Day(s))	*Sparus aurata* (Gilthead Seabream), 2 Year(s), Male, Laboratory (AQUALABS FACILITIES OF THE INSTITUTE OF MARINE BIOLOGY, BIOTECHNOLOGY, AND AQUACULTURE OF THE HELLENIC CENTRE FOR MARINE RESEARCH, HERAKLION, CRETE, GREECE)	Salt water, Oral (diet, drink, gavage), Food, Not Reported	Unmeasured	0 ug/kg bdwt/d / 15 ug/kg bdwt/d / 1500 ug/kg bdwt/d	Cellular (Genetics-gonadotrophin releasing hormone (GnRH) receptor mRNA, Response Site: Testes)	NOEC (1500 ug/kg bdwt/d)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Liver toxicology; Reproductive/Teratogenic	Medium	5534689

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28553-12-0	21 Day(s), (21 Day(s))	*Sparus aurata* (Gilthead Seabream), 2 Year(s), Male, Laboratory (AQUALABS FACILITIES OF THE INSTITUTE OF MARINE BIOLOGY, BIOTECHNOLOGY, AND AQUACULTURE OF THE HELLENIC CENTRE FOR MARINE RESEARCH, HERAKLION, CRETE, GREECE)	Salt water, Oral (diet, drink, gavage), Food, Not Reported	Unmeasured	0 ug/kg bdwt/d / 15 ug/kg bdwt/d / 1500 ug/kg bdwt/d	Reproduction (Reproduction-Linearity, Response Site: Sperm)	NOEC (1500 ug/kg bdwt/d)	Reproductive/Teratogenic	Medium	5534689
28553-12-0	21 Day(s), (21 Day(s))	*Sparus aurata* (Gilthead Seabream), 2 Year(s), Male, Laboratory (AQUALABS FACILITIES OF THE INSTITUTE OF MARINE BIOLOGY, BIOTECHNOLOGY, AND AQUACULTURE OF THE HELLENIC CENTRE FOR MARINE RESEARCH, HERAKLION, CRETE, GREECE)	Salt water, Oral (diet, drink, gavage), Food, Not Reported	Unmeasured	0 ug/kg bdwt/d / 15 ug/kg bdwt/d / 1500 ug/kg bdwt/d	Reproduction (Reproduction-Motility, Response Site: Sperm)	NOEC (1500 ug/kg bdwt/d)	Reproductive/Teratogenic	Medium	5534689

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CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
28553-12-0	21 Day(s), (21 Day(s))	*Sparus aurata* (Gilthead Seabream), 2 Year(s), Male, Laboratory (AQUALABS FACILITIES OF THE INSTITUTE OF MARINE BIOLOGY, BIOTECHNOLOGY, AND AQUACULTURE OF THE HELLENIC CENTRE FOR MARINE RESEARCH, HERAKLION, CRETE, GREECE)	Salt water, Oral (diet, drink, gavage), Food, Not Reported	Unmeasured	0 ug/kg bdwt/d / 15 ug/kg bdwt/d / 1500 ug/kg bdwt/d	Reproduction (Reproduction-Sperm cell counts, Response Site: Not reported)	NOEC (1500 ug/kg bdwt/d)	Reproductive/Teratogenic	Medium	5534689
28553-12-0	21 Day(s), (21 Day(s))	*Sparus aurata* (Gilthead Seabream), 2 Year(s), Male, Laboratory (AQUALABS FACILITIES OF THE INSTITUTE OF MARINE BIOLOGY, BIOTECHNOLOGY, AND AQUACULTURE OF THE HELLENIC CENTRE FOR MARINE RESEARCH, HERAKLION, CRETE, GREECE)	Salt water, Oral (diet, drink, gavage), Food, Not Reported	Unmeasured	0 ug/kg bdwt/d / 15 ug/kg bdwt/d / 1500 ug/kg bdwt/d	Reproduction (Reproduction-Velocity, Response Site: Sperm)	NOEC (1500 ug/kg bdwt/d)	Reproductive/Teratogenic	Medium	5534689

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CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
28553-12-0	21 Day(s), (21 Day(s))	*Sparus aurata* (Gilthead Seabream), 2 Year(s), Male, Laboratory (AQUALABS FACILITIES OF THE INSTITUTE OF MARINE BIOLOGY, BIOTECHNOLOGY, AND AQUACULTURE OF THE HELLENIC CENTRE FOR MARINE RESEARCH, HERAKLION, CRETE, GREECE)	Salt water, Oral (diet, drink, gavage), Food, Not Reported	Unmeasured	0 ug/kg bdwt/d / 15 ug/kg bdwt/d / 1500 ug/kg bdwt/d	Reproduction (Reproduction-Viability, Response Site: Sperm)	NOEC (1500 ug/kg bdwt/d)	Reproductive/Teratogenic	Medium	5534689
28553-12-0	21 Day(s), (21 Day(s))	*Sparus aurata* (Gilthead Seabream), 2 Year(s), Male, Laboratory (AQUALABS FACILITIES OF THE INSTITUTE OF MARINE BIOLOGY, BIOTECHNOLOGY, AND AQUACULTURE OF THE HELLENIC CENTRE FOR MARINE RESEARCH, HERAKLION, CRETE, GREECE)	Salt water, Oral (diet, drink, gavage), Food, Not Reported	Unmeasured	0 ug/kg bdwt/d / 15 ug/kg bdwt/d / 1500 ug/kg bdwt/d	Biochemical (Hormone(s)-17,20beta-Dihydroxy-4-pregnen-3-one, Response Site: Gonad(s))	NR (15-1500 ug/kg bdwt/d)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Liver toxicology; Reproductive/Teratogenic	Medium	5534689

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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
28553-12-0	21 Day(s), (21 Day(s))	*Sparus aurata* (Gilthead Seabream), 2 Year(s), Male, Laboratory (AQUALABS FACILITIES OF THE INSTITUTE OF MARINE BIOLOGY, BIOTECHNOLOGY, AND AQUACULTURE OF THE HELLENIC CENTRE FOR MARINE RESEARCH, HERAKLION, CRETE, GREECE)	Salt water, Oral (diet, drink, gavage), Food, Not Reported	Unmeasured	0 ug/kg bdwt/d / 15 ug/kg bdwt/d / 1500 ug/kg bdwt/d	Biochemical (Hormone(s)-Testosterone, Response Site: Gonad(s))	NR (15-1500 ug/kg bdwt/d)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Liver toxicology; Reproductive/Teratogenic	Medium	5534689
28553-12-0	21 Day(s), (21 Day(s))	*Sparus aurata* (Gilthead Seabream), 2 Year(s), Male, Laboratory (AQUALABS FACILITIES OF THE INSTITUTE OF MARINE BIOLOGY, BIOTECHNOLOGY, AND AQUACULTURE OF THE HELLENIC CENTRE FOR MARINE RESEARCH, HERAKLION, CRETE, GREECE)	Salt water, Oral (diet, drink, gavage), Food, Not Reported	Unmeasured	0 ug/kg bdwt/d / 15 ug/kg bdwt/d / 1500 ug/kg bdwt/d	Cellular (Genetics-Abhydrolase domain containing 4 mRNA, Response Site: Testes)	NR (15-1500 ug/kg bdwt/d)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Liver toxicology; Reproductive/Teratogenic	Medium	5534689

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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
28553-12-0	21 Day(s), (21 Day(s))	*Sparus aurata* (Gilthead Seabream), 2 Year(s), Male, Laboratory (AQUALABS FACILITIES OF THE INSTITUTE OF MARINE BIOLOGY, BIOTECHNOLOGY, AND AQUACULTURE OF THE HELLENIC CENTRE FOR MARINE RESEARCH, HERAKLION, CRETE, GREECE)	Salt water, Oral (diet, drink, gavage), Food, Not Reported	Unmeasured	0 ug/kg bdwt/d / 15 ug/kg bdwt/d / 1500 ug/kg bdwt/d	Cellular (Genetics-Fatty acid amide hydrolase mRNA, Response Site: Testes)	NR (15-1500 ug/kg bdwt/d)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Liver toxicology; Reproductive/Teratogenic	Medium	5534689
28553-12-0	21 Day(s), (21 Day(s))	*Sparus aurata* (Gilthead Seabream), 2 Year(s), Male, Laboratory (AQUALABS FACILITIES OF THE INSTITUTE OF MARINE BIOLOGY, BIOTECHNOLOGY, AND AQUACULTURE OF THE HELLENIC CENTRE FOR MARINE RESEARCH, HERAKLION, CRETE, GREECE)	Salt water, Oral (diet, drink, gavage), Food, Not Reported	Unmeasured	0 ug/kg bdwt/d / 15 ug/kg bdwt/d / 1500 ug/kg bdwt/d	Cellular (Genetics-Leptin mRNA, Response Site: Testes)	NR (15-1500 ug/kg bdwt/d)	Mechanistic: Biomarkers (exposure and effect); Cell signaling/function; Liver toxicology; Reproductive/Teratogenic	Medium	5534689

* 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
28553-12-0	24-168 Hour(s), (168 Hour(s))	*Karenia brevis* (Dinoflagellate), Exponential growth phase (log), Not Reported, Laboratory (INSTITUTE OF OCEANOGRAPHY, CHINESE ACADEMY OF SCIENCES)	Salt water, Aqueous (aquatic habitat), Not reported, Not Reported	Unmeasured	0 ml/L / 0 ml/L / 1 ml/L / 5 ml/L / 10 ml/L / 20 ml/L / 30 ml/L / 50 ml/L / 100 ml/L / 150 ml/L / 200 ml/L	Population (Population-Abundance, Response Site: Not reported)	NR (1-200 ml/L)	Development/Growth	Low	3230225
28553-12-0	96 Hour(s), (96 Hour(s))	*Selenastrum capricornutum* (Green Algae), Not reported, Not Reported, Not reported (NR)	Fresh water, Aqueous (aquatic habitat), Static, Not Reported	Measured	NR / NR	Population (Population-Abundance, Response Site: Not reported)	EC50 (>1.80 mg/L)	Development/Growth	High	1321996
28553-12-0	5 Day(s), (5 Day(s))	*Selenastrum capricornutum* (Green Algae), Not reported, Not Reported, Laboratory (FROM UNIVERSITY OF TEXAS AT AUSTIN, MAINTAINED AT SPRINGBORN BIONOMIC, INC)	Culture, Aqueous (aquatic habitat), Static, Not Reported	Measured	<0.1 mg/L / <0.1-2.9 mg/L	Population (Population-Chlorophyll, Response Site: Not reported)	EC50 (>2.8 mg/L)	Development/Growth	High	1316196

* 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
28553-12-0	21 Day(s), (26 Day(s))	*Rana arvalis* (Moorfrog), Egg, Not Reported, Wild (POND ON SMALL ISLAND IN UMEALVENS DELTA, NORTH OF UMEA, SWEDEN)	Fresh water, Aqueous (aquatic habitat), Static, NA Egg	Measured	<0.20 ug/L / <0.20 ug/L / <0.20 ug/L / <0.20-1.29 ug/L / 0.40-5.67 ug/L	Mortality (Mortality-Hatch, Response Site: Not reported)	NOEC (0.40-5.67 ug/L)	Mortality	High	7328184
28553-12-0	21 Day(s), (26 Day(s))	*Rana arvalis* (Moorfrog), Egg, Not Reported, Wild (POND ON SMALL ISLAND IN UMEALVENS DELTA, NORTH OF UMEA, SWEDEN)	Fresh water, Aqueous (aquatic habitat), Static, NA Egg	Measured	<0.20 ug/L / <0.20 ug/L / <0.20 ug/L / <0.20-2.65 ug/L / 3.13-5.66 ug/L	Mortality (Mortality-Hatch, Response Site: Not reported)	NOEC (3.13-5.66 ug/L)	Mortality	High	7328184
28553-12-0	26 Day(s), (26 Day(s))	*Rana arvalis* (Moorfrog), Egg (Measured in: Tadpole), Not Reported, Wild (POND ON SMALL ISLAND IN UMEALVENS DELTA, NORTH OF UMEA, SWEDEN)	Fresh water, Aqueous (aquatic habitat), Static, NA Tadpole	Measured	<0.20 ug/L / <0.20 ug/L / <0.20 ug/L / <0.20-1.29 ug/L / 0.40-5.67 ug/L	Growth (Development-Deformation, Response Site: Not reported)	NOEC (0.40-5.67 ug/L)	Development/Growth	High	7328184
28553-12-0	26 Day(s), (26 Day(s))	*Rana arvalis* (Moorfrog), Egg (Measured in: Tadpole), Not Reported, Wild (POND ON SMALL ISLAND IN UMEALVENS DELTA, NORTH OF UMEA, SWEDEN)	Fresh water, Aqueous (aquatic habitat), Static, NA Tadpole	Measured	<0.20 ug/L / <0.20 ug/L / <0.20 ug/L / <0.20-1.29 ug/L / 0.40-5.67 ug/L	Growth (Growth-Weight, Response Site: Whole organism)	NOEC (0.40-5.67 ug/L)	Development/Growth	High	7328184

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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
28553-12-0	26 Day(s), (26 Day(s))	*Rana arvalis* (Moorfrog), Egg (Measured in: Tadpole), Not Reported, Wild (POND ON SMALL ISLAND IN UMEALVENS DELTA, NORTH OF UMEA, SWEDEN)	Fresh water, Aqueous (aquatic habitat), Static, NA Tadpole	Measured	<0.20 ug/L / <0.20 ug/L / <0.20 ug/L / <0.20-1.29 ug/L / 0.40-5.67 ug/L	Mortality (Mortality-Mortality, Response Site: Not reported)	NOEC (0.40-5.67 ug/L)	Mortality	High	7328184
28553-12-0	26 Day(s), (26 Day(s))	*Rana arvalis* (Moorfrog), Egg (Measured in: Tadpole), Not Reported, Wild (POND ON SMALL ISLAND IN UMEALVENS DELTA, NORTH OF UMEA, SWEDEN)	Fresh water, Aqueous (aquatic habitat), Static, NA Tadpole	Measured	<0.20 ug/L / <0.20 ug/L / <0.20 ug/L / <0.20-2.65 ug/L / 3.13-5.66 ug/L	Growth (Development-Deformation, Response Site: Not reported)	NOEC (3.13-5.66 ug/L)	Development/Growth	High	7328184
28553-12-0	26 Day(s), (26 Day(s))	*Rana arvalis* (Moorfrog), Egg (Measured in: Tadpole), Not Reported, Wild (POND ON SMALL ISLAND IN UMEALVENS DELTA, NORTH OF UMEA, SWEDEN)	Fresh water, Aqueous (aquatic habitat), Static, NA Tadpole	Measured	<0.20 ug/L / <0.20 ug/L / <0.20 ug/L / <0.20-2.65 ug/L / 3.13-5.66 ug/L	Growth (Growth-Weight, Response Site: Whole organism)	NOEC (3.13-5.66 ug/L)	Development/Growth	High	7328184
28553-12-0	26 Day(s), (26 Day(s))	*Rana arvalis* (Moorfrog), Egg (Measured in: Tadpole), Not Reported, Wild (POND ON SMALL ISLAND IN UMEALVENS DELTA, NORTH OF UMEA, SWEDEN)	Fresh water, Aqueous (aquatic habitat), Static, NA Tadpole	Measured	<0.20 ug/L / <0.20 ug/L / <0.20 ug/L / <0.20-2.65 ug/L / 3.13-5.66 ug/L	Mortality (Mortality-Mortality, Response Site: Not reported)	NOEC (3.13-5.66 ug/L)	Mortality	High	7328184

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

Terrestrial: Arthropods Extraction Table

CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
28553-12-0	NA Lifetime;no associated numeric value, (NA Lifetime;no associated numeric value)	*Drosophila melanogaster* (Fruit Fly), Not reported, Both (Measured in: Male organisms), Laboratory (PROVIDED BY TSINGHUA UNIVERSITY)	No substrate, Oral (diet, drink, gavage), Diet, unspecified, NA Male organisms	Unmeasured	0 uM diet / 10 uM diet	Cellular (Genetics-Autophagy related 3 mRNA, Response Site: Not reported)	NOEL (10 uM diet)	Mechanistic: Cell signaling/function	Uninformative	11784619
28553-12-0	NA Lifetime;no associated numeric value, (NA Lifetime;no associated numeric value)	*Drosophila melanogaster* (Fruit Fly), Not reported, Both (Measured in: Male organisms), Laboratory (PROVIDED BY TSINGHUA UNIVERSITY)	No substrate, Oral (diet, drink, gavage), Diet, unspecified, NA Male organisms	Unmeasured	0 uM diet / 10 uM diet	Cellular (Genetics-p53 mRNA, Response Site: Not reported)	NOEL (10 uM diet)	Mechanistic: Cell signaling/function	Uninformative	11784619
28553-12-0	NA Lifetime;no associated numeric value, (NA Lifetime;no associated numeric value)	*Drosophila melanogaster* (Fruit Fly), Not reported, Both (Measured in: Female organisms), Laboratory (PROVIDED BY TSINGHUA UNIVERSITY)	No substrate, Oral (diet, drink, gavage), Diet, unspecified, NA Female organisms	Unmeasured	0 uM diet / 10 uM diet	Cellular (Genetics-p53 mRNA, Response Site: Not reported)	NOEL (10 uM diet)	Mechanistic: Cell signaling/function	Uninformative	11784619
28553-12-0	NA Lifetime;no associated numeric value, (NA Lifetime;no associated numeric value)	*Drosophila melanogaster* (Fruit Fly), Not reported, Both (Measured in: Male organisms), Laboratory (PROVIDED BY TSINGHUA UNIVERSITY)	No substrate, Oral (diet, drink, gavage), Diet, unspecified, NA Male organisms	Unmeasured	0 uM diet / 10 uM diet	Cellular (Genetics-Sirtuin 1 mRNA, Response Site: Not reported)	NOEL (10 uM diet)	Mechanistic: Cell signaling/function	Uninformative	11784619

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Terrestrial: Arthropods Extraction Table

CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
28553-12-0	NA Lifetime;no associated numeric value, (NA Lifetime;no associated numeric value)	*Drosophila melanogaster* (Fruit Fly), Not reported, Both (Measured in: Female organisms), Laboratory (PROVIDED BY TSINGHUA UNIVERSITY)	No substrate, Oral (diet, drink, gavage), Diet, unspecified, NA Female organisms	Unmeasured	0 uM diet / 10 uM diet	Cellular (Genetics-Sirtuin 1 mRNA, Response Site: Not reported)	NOEL (10 uM diet)	Mechanistic: Cell signaling/function	Uninformative	11784619
28553-12-0	NA Lifetime;no associated numeric value, (NA Lifetime;no associated numeric value)	*Drosophila melanogaster* (Fruit Fly), Not reported, Both (Measured in: Male organisms), Laboratory (PROVIDED BY TSINGHUA UNIVERSITY)	No substrate, Oral (diet, drink, gavage), Diet, unspecified, NA Male organisms	Unmeasured	0 uM diet / 10 uM diet	Cellular (Genetics-Mechanistic target of rapamycin kinase mRNA, Response Site: Not reported)	NOEL (10 uM diet)	Mechanistic: Cell signaling/function	Uninformative	11784619
28553-12-0	NA Lifetime;no associated numeric value, (NA Lifetime;no associated numeric value)	*Drosophila melanogaster* (Fruit Fly), Not reported, Both (Measured in: Female organisms), Laboratory (PROVIDED BY TSINGHUA UNIVERSITY)	No substrate, Oral (diet, drink, gavage), Diet, unspecified, NA Female organisms	Unmeasured	0 uM diet / 10 uM diet	Cellular (Genetics-Mechanistic target of rapamycin kinase mRNA, Response Site: Not reported)	NOEL (10 uM diet)	Mechanistic: Cell signaling/function	Uninformative	11784619
28553-12-0	NA Lifetime;no associated numeric value, (NA Lifetime;no associated numeric value)	*Drosophila melanogaster* (Fruit Fly), Not reported, Both (Measured in: Female organisms), Laboratory (PROVIDED BY TSINGHUA UNIVERSITY)	No substrate, Oral (diet, drink, gavage), Diet, unspecified, NA Female organisms	Unmeasured	0 uM diet / 10 uM diet	Cellular (Genetics-Autophagy related 3 mRNA, Response Site: Not reported)	NOEL (10 uM diet)	Mechanistic: Cell signaling/function	Uninformative	11784619

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Terrestrial: Arthropods Extraction Table

CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
28553-12-0	NA Lifetime;no associated numeric value, (NA Lifetime;no associated numeric value)	*Drosophila melanogaster* (Fruit Fly), Not reported, Both (Measured in: Female organisms), Laboratory (PROVIDED BY TSINGHUA UNIVERSITY)	No substrate, Oral (diet, drink, gavage), Diet, unspecified, NA Female organisms	Unmeasured	0 uM diet / 10 uM diet	Cellular (Genetics-Protein kinase b mRNA, Response Site: Not reported)	LOEL (10 uM diet)	Mechanistic: Cell signaling/function	Uninformative	11784619
28553-12-0	NA Lifetime;no associated numeric value, (NA Lifetime;no associated numeric value)	*Drosophila melanogaster* (Fruit Fly), Not reported, Both (Measured in: Male organisms), Laboratory (PROVIDED BY TSINGHUA UNIVERSITY)	No substrate, Oral (diet, drink, gavage), Diet, unspecified, NA Male organisms	Unmeasured	0 uM diet / 10 uM diet	Cellular (Genetics-Forkhead box O1 mRNA , Response Site: Not reported)	LOEL (10 uM diet)	Mechanistic: Cell signaling/function	Uninformative	11784619
28553-12-0	NA Lifetime;no associated numeric value, (NA Lifetime;no associated numeric value)	*Drosophila melanogaster* (Fruit Fly), Not reported, Both (Measured in: Female organisms), Laboratory (PROVIDED BY TSINGHUA UNIVERSITY)	No substrate, Oral (diet, drink, gavage), Diet, unspecified, NA Female organisms	Unmeasured	0 uM diet / 10 uM diet	Cellular (Genetics-Forkhead box O1 mRNA , Response Site: Not reported)	LOEL (10 uM diet)	Mechanistic: Cell signaling/function	Uninformative	11784619
28553-12-0	NA Lifetime;no associated numeric value, (NA Lifetime;no associated numeric value)	*Drosophila melanogaster* (Fruit Fly), Not reported, Both (Measured in: Male organisms), Laboratory (PROVIDED BY TSINGHUA UNIVERSITY)	No substrate, Oral (diet, drink, gavage), Diet, unspecified, NA Male organisms	Unmeasured	0 uM diet / 10 uM diet	Cellular (Genetics-Protein kinase b mRNA, Response Site: Not reported)	LOEL (10 uM diet)	Mechanistic: Cell signaling/function	Uninformative	11784619

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Terrestrial: Arthropods Extraction Table

CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
28553-12-0	3 Day(s), (3 Day(s))	*Drosophila melanogaster* (Fruit Fly), Not reported, Both, Laboratory (THE CORE FACILITY OF DROSOPHILA RESOURCE AND TECHNOLOGY AT THE CAS CENTER FOR EXCELLENCE IN MOLECULAR CELL SCIENCE)	No substrate, Oral (diet, drink, gavage), Diet, unspecified, <=20 Both male and female	Unmeasured	0 uM diet / 1 uM diet / 10 uM diet	Reproduction (Reproduction-Progeny counts/numbers, Response Site: Not reported)	LOEL (1 uM diet)	Reproductive/Teratogenic	Medium	11784619
28553-12-0	17.63 Day(s), (80 Day(s))	*Drosophila melanogaster* (Fruit Fly), 3 Day(s), Both (Measured in: Male organisms), Laboratory (THE CORE FACILITY OF DROSOPHILA RESOURCE AND TECHNOLOGY AT THE CAS CENTER FOR EXCELLENCE IN MOLECULAR CELL SCIENCE)	No substrate, Oral (diet, drink, gavage), Diet, unspecified, 80 Male organisms	Unmeasured	0 uM diet / 1 uM diet / 10 uM diet	Mortality (Mortality-Lifespan, Response Site: Not reported)	LOEL (1 uM diet)	Mortality	Medium	11784619

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Terrestrial: Arthropods Extraction Table

CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
28553-12-0	20 Day(s), (20 Day(s))	*Drosophila melanogaster* (Fruit Fly), 3 Day(s), Both (Measured in: Male organisms), Laboratory (THE CORE FACILITY OF DROSOPHILA RESOURCE AND TECHNOLOGY AT THE CAS CENTER FOR EXCELLENCE IN MOLECULAR CELL SCIENCE)	No substrate, Oral (diet, drink, gavage), Diet, unspecified, 100 Male organisms	Unmeasured	0 uM diet / 1 uM diet / 10 uM diet	Behavior (Behavior-Distance moved, change in direct movement, Response Site: Not reported)	NOEL (1 uM diet)	Behavioral	Medium	11784619
28553-12-0	20 Day(s), (20 Day(s))	*Drosophila melanogaster* (Fruit Fly), 3 Day(s), Both (Measured in: Female organisms), Laboratory (THE CORE FACILITY OF DROSOPHILA RESOURCE AND TECHNOLOGY AT THE CAS CENTER FOR EXCELLENCE IN MOLECULAR CELL SCIENCE)	No substrate, Oral (diet, drink, gavage), Diet, unspecified, 100 Female organisms	Unmeasured	0 uM diet / 1 uM diet / 10 uM diet	Behavior (Behavior-Distance moved, change in direct movement, Response Site: Not reported)	NOEL (1 uM diet)	Behavioral	Medium	11784619

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Terrestrial: Arthropods Extraction Table

CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
28553-12-0	20 Day(s), (20 Day(s))	*Drosophila melanogaster* (Fruit Fly), 3 Day(s), Both (Measured in: Male organisms), Laboratory (THE CORE FACILITY OF DROSOPHILA RESOURCE AND TECHNOLOGY AT THE CAS CENTER FOR EXCELLENCE IN MOLECULAR CELL SCIENCE)	No substrate, Oral (diet, drink, gavage), Diet, unspecified, 100 Male organisms	Unmeasured	0 uM diet / 1 uM diet / 10 uM diet	Behavior (Behavior-Distance moved, change in direct movement, Response Site: Not reported)	LOEL (10 uM diet)	Behavioral	Medium	11784619
28553-12-0	20 Day(s), (20 Day(s))	*Drosophila melanogaster* (Fruit Fly), 3 Day(s), Both (Measured in: Female organisms), Laboratory (THE CORE FACILITY OF DROSOPHILA RESOURCE AND TECHNOLOGY AT THE CAS CENTER FOR EXCELLENCE IN MOLECULAR CELL SCIENCE)	No substrate, Oral (diet, drink, gavage), Diet, unspecified, 100 Female organisms	Unmeasured	0 uM diet / 1 uM diet / 10 uM diet	Behavior (Behavior-Distance moved, change in direct movement, Response Site: Not reported)	LOEL (10 uM diet)	Behavioral	Medium	11784619

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Terrestrial: Arthropods Extraction Table

CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
28553-12-0	20.95 Day(s), (80 Day(s))	*Drosophila melanogaster* (Fruit Fly), 3 Day(s), Both (Measured in: Female organisms), Laboratory (THE CORE FACILITY OF DROSOPHILA RESOURCE AND TECHNOLOGY AT THE CAS CENTER FOR EXCELLENCE IN MOLECULAR CELL SCIENCE)	No substrate, Oral (diet, drink, gavage), Diet, unspecified, 80 Female organisms	Unmeasured	0 uM diet / 1 uM diet / 10 uM diet	Mortality (Mortality-Lifespan, Response Site: Not reported)	LOEL (1 uM diet)	Mortality	Medium	11784619
28553-12-0	13-44 Day(s), (80 Day(s))	*Drosophila melanogaster* (Fruit Fly), 3 Day(s), Both, Laboratory (THE CORE FACILITY OF DROSOPHILA RESOURCE AND TECHNOLOGY AT THE CAS CENTER FOR EXCELLENCE IN MOLECULAR CELL SCIENCE)	No substrate, Oral (diet, drink, gavage), Diet, unspecified, 80 Both male and female	Unmeasured	0 uM diet / 1 uM diet / 10 uM diet	Mortality (Mortality-Lifespan, Response Site: Not reported)	NR (1-10 uM diet)	Mortality	Medium	11784619

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Terrestrial: Arthropods Extraction Table

CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
28553-12-0	48.35 Day(s), (80 Day(s))	*Drosophila melanogaster* (Fruit Fly), 3 Day(s), Both (Measured in: Male organisms), Laboratory (THE CORE FACILITY OF DROSOPHILA RESOURCE AND TECHNOLOGY AT THE CAS CENTER FOR EXCELLENCE IN MOLECULAR CELL SCIENCE)	No substrate, Oral (diet, drink, gavage), Diet, unspecified, 100 Male organisms	Unmeasured	0 uM diet / 1 uM diet / 10 uM diet	Mortality (Mortality-Lifespan, Response Site: Not reported)	LOEL (1 uM diet)	Mortality	Medium	11784619
28553-12-0	0-<50 Day(s), (80 Day(s))	*Drosophila melanogaster* (Fruit Fly), 3 Day(s), Both, Laboratory (THE CORE FACILITY OF DROSOPHILA RESOURCE AND TECHNOLOGY AT THE CAS CENTER FOR EXCELLENCE IN MOLECULAR CELL SCIENCE)	No substrate, Oral (diet, drink, gavage), Diet, unspecified, 80 Both male and female	Unmeasured	0 uM diet / 1 uM diet / 10 uM diet	Mortality (Mortality-Survival, Response Site: Not reported)	NR (1-10 uM diet)	Mortality	Medium	11784619

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Terrestrial: Arthropods Extraction Table

CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
28553-12-0	52.85 Day(s), (80 Day(s))	*Drosophila melanogaster* (Fruit Fly), 3 Day(s), Both (Measured in: Female organisms), Laboratory (THE CORE FACILITY OF DROSOPHILA RESOURCE AND TECHNOLOGY AT THE CAS CENTER FOR EXCELLENCE IN MOLECULAR CELL SCIENCE)	No substrate, Oral (diet, drink, gavage), Diet, unspecified, 100 Female organisms	Unmeasured	0 uM diet / 1 uM diet / 10 uM diet	Mortality (Mortality-Lifespan, Response Site: Not reported)	LOEL (10 uM diet)	Mortality	Medium	11784619
28553-12-0	57 Day(s), (80 Day(s))	*Drosophila melanogaster* (Fruit Fly), 3 Day(s), Both (Measured in: Female organisms), Laboratory (THE CORE FACILITY OF DROSOPHILA RESOURCE AND TECHNOLOGY AT THE CAS CENTER FOR EXCELLENCE IN MOLECULAR CELL SCIENCE)	No substrate, Oral (diet, drink, gavage), Diet, unspecified, 100 Female organisms	Unmeasured	0 uM diet / 1 uM diet / 10 uM diet	Mortality (Mortality-Lifespan, Response Site: Not reported)	NOEL (1 uM diet)	Mortality	Medium	11784619

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Terrestrial: Arthropods Extraction Table

CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
28553-12-0	>40-<60 Day(s), (100 Day(s))	*Drosophila melanogaster* (Fruit Fly), Not reported, Both (Measured in: Male organisms), Laboratory (PROVIDED BY TSINGHUA UNIVERSITY)	No substrate, Oral (diet, drink, gavage), Diet, unspecified, 100 Male organisms	Unmeasured	0 uM diet / 10 uM diet	Mortality (Mortality-Lifespan, Response Site: Not reported)	LOEL (10 uM diet)	Mortality	Medium	11784619
28553-12-0	>40-<60 Day(s), (100 Day(s))	*Drosophila melanogaster* (Fruit Fly), Not reported, Both (Measured in: Female organisms), Laboratory (PROVIDED BY TSINGHUA UNIVERSITY)	No substrate, Oral (diet, drink, gavage), Diet, unspecified, 100 Female organisms	Unmeasured	0 uM diet / 10 uM diet	Mortality (Mortality-Lifespan, Response Site: Not reported)	LOEL (10 uM diet)	Mortality	Medium	11784619
28553-12-0	~60 Day(s), (100 Day(s))	*Drosophila melanogaster* (Fruit Fly), Not reported, Both (Measured in: Female organisms), Laboratory (PROVIDED BY TSINGHUA UNIVERSITY)	No substrate, Oral (diet, drink, gavage), Diet, unspecified, 100 Female organisms	Unmeasured	0 uM diet / 10 uM diet	Mortality (Mortality-Lifespan, Response Site: Not reported)	NOEL (10 uM diet)	Mortality	Medium	11784619
28553-12-0	<60 Day(s), (100 Day(s))	*Drosophila melanogaster* (Fruit Fly), Not reported, Both, Laboratory (PROVIDED BY TSINGHUA UNIVERSITY)	No substrate, Oral (diet, drink, gavage), Diet, unspecified, 100 Both male and female	Unmeasured	0 uM diet / 10 uM diet	Mortality (Mortality-Survival, Response Site: Not reported)	NR (10 uM diet)	Mortality	Medium	11784619

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Terrestrial: Arthropods Extraction Table

CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
28553-12-0	>40-<60 Day(s), (100 Day(s))	*Drosophila melanogaster* (Fruit Fly), Not reported, Both (Measured in: Male organisms), Laboratory (PROVIDED BY TSINGHUA UNIVERSITY)	No substrate, Oral (diet, drink, gavage), Diet, unspecified, 100 Male organisms	Unmeasured	0 uM diet / 10 uM diet	Mortality (Mortality-Lifespan, Response Site: Not reported)	NOEL (10 uM diet)	Mortality	Medium	11784619
28553-12-0	>60-<80 Day(s), (100 Day(s))	*Drosophila melanogaster* (Fruit Fly), Not reported, Both (Measured in: Female organisms), Laboratory (PROVIDED BY TSINGHUA UNIVERSITY)	No substrate, Oral (diet, drink, gavage), Diet, unspecified, 100 Female organisms	Unmeasured	0 uM diet / 10 uM diet	Mortality (Mortality-Lifespan, Response Site: Not reported)	NOEL (10 uM diet)	Mortality	Medium	11784619
28553-12-0	>60-<80 Day(s), (100 Day(s))	*Drosophila melanogaster* (Fruit Fly), Not reported, Both (Measured in: Male organisms), Laboratory (PROVIDED BY TSINGHUA UNIVERSITY)	No substrate, Oral (diet, drink, gavage), Diet, unspecified, 100 Male organisms	Unmeasured	0 uM diet / 10 uM diet	Mortality (Mortality-Lifespan, Response Site: Not reported)	LOEL (10 uM diet)	Mortality	Medium	11784619

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Terrestrial: Arthropods Extraction Table

CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
28553-12-0	46-80 Day(s), (80 Day(s))	*Drosophila melanogaster* (Fruit Fly), 3 Day(s), Both, Laboratory (THE CORE FACILITY OF DROSOPHILA RESOURCE AND TECHNOLOGY AT THE CAS CENTER FOR EXCELLENCE IN MOLECULAR CELL SCIENCE)	No substrate, Oral (diet, drink, gavage), Diet, unspecified, 100 Both male and female	Unmeasured	0 uM diet / 1 uM diet / 10 uM diet	Mortality (Mortality-Lifespan, Response Site: Not reported)	NR (1-10 uM diet)	Mortality	Medium	11784619
28553-12-0	<80 Day(s), (100 Day(s))	*Drosophila melanogaster* (Fruit Fly), Not reported, Both, Laboratory (PROVIDED BY TSINGHUA UNIVERSITY)	No substrate, Oral (diet, drink, gavage), Diet, unspecified, 100 Both male and female	Unmeasured	0 uM diet / 10 uM diet	Mortality (Mortality-Survival, Response Site: Not reported)	NR (10 uM diet)	Mortality	Medium	11784619
28553-12-0	>60-<80 Day(s), (100 Day(s))	*Drosophila melanogaster* (Fruit Fly), Not reported, Both (Measured in: Male organisms), Laboratory (PROVIDED BY TSINGHUA UNIVERSITY)	No substrate, Oral (diet, drink, gavage), Diet, unspecified, 100 Male organisms	Unmeasured	0 uM diet / 10 uM diet	Mortality (Mortality-Lifespan, Response Site: Not reported)	NOEL (10 uM diet)	Mortality	Medium	11784619

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Terrestrial: Arthropods Extraction Table

CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
28553-12-0	~80 Day(s), (100 Day(s))	*Drosophila melanogaster* (Fruit Fly), Not reported, Both (Measured in: Female organisms), Laboratory (PROVIDED BY TSINGHUA UNIVERSITY)	No substrate, Oral (diet, drink, gavage), Diet, unspecified, 100 Female organisms	Unmeasured	0 uM diet / 10 uM diet	Mortality (Mortality-Lifespan, Response Site: Not reported)	LOEL (10 uM diet)	Mortality	Medium	11784619
28553-12-0	>80-<100 Day(s), (100 Day(s))	*Drosophila melanogaster* (Fruit Fly), Not reported, Both (Measured in: Female organisms), Laboratory (PROVIDED BY TSINGHUA UNIVERSITY)	No substrate, Oral (diet, drink, gavage), Diet, unspecified, 100 Female organisms	Unmeasured	0 uM diet / 10 uM diet	Mortality (Mortality-Lifespan, Response Site: Not reported)	LOEL (10 uM diet)	Mortality	Medium	11784619
28553-12-0	>50-<100 Day(s), (100 Day(s))	*Drosophila melanogaster* (Fruit Fly), Not reported, Both (Measured in: Female organisms), Laboratory (PROVIDED BY TSINGHUA UNIVERSITY)	No substrate, Oral (diet, drink, gavage), Diet, unspecified, 100 Female organisms	Unmeasured	0 uM diet / 10 uM diet	Mortality (Mortality-Lifespan, Response Site: Not reported)	LOEL (10 uM diet)	Mortality	Medium	11784619
28553-12-0	<100 Day(s), (100 Day(s))	*Drosophila melanogaster* (Fruit Fly), Not reported, Both, Laboratory (PROVIDED BY TSINGHUA UNIVERSITY)	No substrate, Oral (diet, drink, gavage), Diet, unspecified, 100 Both male and female	Unmeasured	0 uM diet / 10 uM diet	Mortality (Mortality-Survival, Response Site: Not reported)	NR (10 uM diet)	Mortality	Medium	11784619

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Terrestrial: Arthropods Extraction Table

CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
28553-12-0	0-<100 Day(s), (80 Day(s))	*Drosophila melanogaster* (Fruit Fly), 3 Day(s), Both, Laboratory (THE CORE FACILITY OF DROSOPHILA RESOURCE AND TECHNOLOGY AT THE CAS CENTER FOR EXCELLENCE IN MOLECULAR CELL SCIENCE)	No substrate, Oral (diet, drink, gavage), Diet, unspecified, 100 Both male and female	Unmeasured	0 uM diet / 1 uM diet / 10 uM diet	Mortality (Mortality-Survival, Response Site: Not reported)	NR (1-10 uM diet)	Mortality	Medium	11784619
28553-12-0	NA Until larva, (NA Until larva)	*Drosophila melanogaster* (Fruit Fly), Adult, <=3 Hours post-emergence (Measured in: F1 generation), Not Reported, Laboratory (BLOOMINGTON STOCK CENTER, 3605)	No substrate, Oral (diet, drink, gavage), Food, NA F1 generation	Unmeasured	0 % diet / 0.1 % diet / 0.2 % diet / 0.5 % diet / 1.0 % diet	Behavior (Behavior-Distance moved, change in direct movement, Response Site: Not reported)	LOEL (0.1 % diet)	Behavioral	High	7978406
28553-12-0	NA Until larva, (NA Until larva)	*Drosophila melanogaster* (Fruit Fly), Adult, <=3 Hours post-emergence (Measured in: F1 generation), Not Reported, Laboratory (BLOOMINGTON STOCK CENTER, 3605)	No substrate, Oral (diet, drink, gavage), Food, NA F1 generation	Unmeasured	0 % diet / 0.1 % diet / 0.2 % diet / 0.5 % diet / 1.0 % diet	Behavior (Behavior-Distance moved, change in direct movement, Response Site: Not reported)	LOEL (1.0 % diet)	Behavioral	High	7978406

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Terrestrial: Arthropods Extraction Table

CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
28553-12-0	NA Until larva, (NA Until larva)	*Drosophila melanogaster* (Fruit Fly), Adult, <=3 Hours post-emergence (Measured in: F1 generation), Not Reported, Laboratory (BLOOMINGTON STOCK CENTER, 3605)	No substrate, Oral (diet, drink, gavage), Food, NA F1 generation	Unmeasured	0 % diet / 0.1 % diet / 0.2 % diet / 0.5 % diet / 1.0 % diet	Biochemical (Biochemistry-Reactive oxygen species, Response Site: Not reported)	LOEL (0.1 % diet)	Mechanistic: Oxidative stress (including redox biology)	High	7978406
28553-12-0	NA Until larva, (NA Until larva)	*Drosophila melanogaster* (Fruit Fly), Adult, <=3 Hours post-emergence (Measured in: F1 generation), Not Reported, Laboratory (BLOOMINGTON STOCK CENTER, 3605)	No substrate, Oral (diet, drink, gavage), Food, NA F1 generation	Unmeasured	0 % diet / 0.1 % diet / 0.2 % diet / 0.5 % diet / 1.0 % diet	Biochemical (Enzyme(s)-Superoxide dismutase (SOD) enzyme activity, Response Site: Not reported)	LOEL (0.1 % diet)	Mechanistic: Oxidative stress (including redox biology)	High	7978406
28553-12-0	NA Until larva, (NA Until larva)	*Drosophila melanogaster* (Fruit Fly), Adult, <=3 Hours post-emergence (Measured in: F1 generation), Not Reported, Laboratory (BLOOMINGTON STOCK CENTER, 3605)	No substrate, Oral (diet, drink, gavage), Food, NA F1 generation	Unmeasured	0 % diet / 0.1 % diet / 0.2 % diet / 0.5 % diet / 1.0 % diet	Behavior (Behavior-Distance moved, change in direct movement, Response Site: Not reported)	NOEL (0.5 % diet)	Behavioral	High	7978406
28553-12-0	NA Until larva, (NA Until larva)	*Drosophila melanogaster* (Fruit Fly), Adult, <=3 Hours post-emergence (Measured in: F1 generation), Not Reported, Laboratory (BLOOMINGTON STOCK CENTER, 3605)	No substrate, Oral (diet, drink, gavage), Food, NA F1 generation	Unmeasured	0 % diet / 0.1 % diet / 0.2 % diet / 0.5 % diet / 1.0 % diet	Behavior (Behavior-Distance moved, change in direct movement, Response Site: Not reported)	NOEL (1.0 % diet)	Behavioral	High	7978406

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Terrestrial: Arthropods Extraction Table

CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
28553-12-0	NA Until larva, (NA Until larva)	*Drosophila melanogaster* (Fruit Fly), Adult, <=3 Hours post-emergence (Measured in: F1 generation), Not Reported, Laboratory (BLOOMINGTON STOCK CENTER, 3605)	No substrate, Oral (diet, drink, gavage), Food, NA F1 generation	Unmeasured	0 % diet / 0.1 % diet / 0.2 % diet / 0.5 % diet / 1.0 % diet	Behavior (Behavior-Distance moved, change in direct movement, Response Site: Not reported)	NR (0.1-1.0 % diet)	Behavioral	High	7978406
28553-12-0	NA Until larva, (NA Until larva)	*Drosophila melanogaster* (Fruit Fly), Adult, <=3 Hours post-emergence (Measured in: F1 generation), Not Reported, Laboratory (BLOOMINGTON STOCK CENTER, 3605)	No substrate, Oral (diet, drink, gavage), Food, NA F1 generation	Unmeasured	0 % diet / 0.1 % diet / 0.2 % diet / 0.5 % diet / 1.0 % diet	Biochemical (Enzyme(s)-Catalase, Response Site: Not reported)	NR (0.1-1.0 % diet)	Mechanistic: Oxidative stress (including redox biology)	High	7978406
28553-12-0	12 Hour(s), (30 Hour(s))	*Drosophila melanogaster* (Fruit Fly), Larva, 3 Instar, Not Reported, Laboratory (BLOOMINGTON STOCK CENTER, 3605)	No substrate, Oral (diet, drink, gavage), Food, Not Reported	Unmeasured	0 % diet / 0.1 % diet / 0.2 % diet / 0.5 % diet / 1.0 % diet	Physiology (Injury-Damage, Response Site: Intestinal tract,Tissue)	LOEL (1.0 % diet)	Gastrointestinal	High	7978406
28553-12-0	12 Hour(s), (30 Hour(s))	*Drosophila melanogaster* (Fruit Fly), Larva, 3 Instar, Not Reported, Laboratory (BLOOMINGTON STOCK CENTER, 3605)	No substrate, Oral (diet, drink, gavage), Food, Not Reported	Unmeasured	0 % diet / 0.1 % diet / 0.2 % diet / 0.5 % diet / 1.0 % diet	Physiology (Injury-Damage, Response Site: Intestinal tract,Tissue)	NOEL (0.5 % diet)	Gastrointestinal	High	7978406

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Terrestrial: Arthropods Extraction Table

CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
28553-12-0	24 Hour(s), (24 Hour(s))	*Drosophila melanogaster* (Fruit Fly), Larva, 3 Instar, Not Reported, Laboratory (BLOOMINGTON STOCK CENTER, 3605)	No substrate, Oral (diet, drink, gavage), Food, Not Reported	Unmeasured	0 % diet / 0.1 % diet / 0.2 % diet / 0.5 % diet / 1.0 % diet	Biochemical (Biochemistry-Reactive oxygen species, Response Site: Not reported)	LOEL (0.1 % diet)	Mechanistic: Oxidative stress (including redox biology)	High	7978406
28553-12-0	24 Hour(s), (24 Hour(s))	*Drosophila melanogaster* (Fruit Fly), Larva, 3 Instar, Not Reported, Laboratory (BLOOMINGTON STOCK CENTER, 3605)	No substrate, Oral (diet, drink, gavage), Food, Not Reported	Unmeasured	0 % diet / 0.1 % diet / 0.2 % diet / 0.5 % diet / 1.0 % diet	Biochemical (Enzyme(s)-Catalase, Response Site: Not reported)	NR (0.1-1.0 % diet)	Mechanistic: Oxidative stress (including redox biology)	High	7978406
28553-12-0	24 Hour(s), (24 Hour(s))	*Drosophila melanogaster* (Fruit Fly), Larva, 3 Instar, Not Reported, Laboratory (BLOOMINGTON STOCK CENTER, 3605)	No substrate, Oral (diet, drink, gavage), Food, Not Reported	Unmeasured	0 % diet / 0.1 % diet / 0.2 % diet / 0.5 % diet / 1.0 % diet	Biochemical (Enzyme(s)-Superoxide dismutase (SOD) enzyme activity, Response Site: Not reported)	LOEL (0.1 % diet)	Mechanistic: Oxidative stress (including redox biology)	High	7978406
28553-12-0	30 Hour(s), (30 Hour(s))	*Drosophila melanogaster* (Fruit Fly), Larva, 3 Instar, Not Reported, Laboratory (BLOOMINGTON STOCK CENTER, 3605)	No substrate, Oral (diet, drink, gavage), Food, Not Reported	Unmeasured	0 % diet / 0.1 % diet / 0.2 % diet / 0.5 % diet / 1.0 % diet	Physiology (Injury-Damage, Response Site: Intestinal tract,Tissue)	NOEL (0.2 % diet)	Gastrointestinal	High	7978406
28553-12-0	30 Hour(s), (30 Hour(s))	*Drosophila melanogaster* (Fruit Fly), Larva, 3 Instar, Not Reported, Laboratory (BLOOMINGTON STOCK CENTER, 3605)	No substrate, Oral (diet, drink, gavage), Food, Not Reported	Unmeasured	0 % diet / 0.1 % diet / 0.2 % diet / 0.5 % diet / 1.0 % diet	Physiology (Injury-Damage, Response Site: Intestinal tract,Tissue)	LOEL (0.5 % diet)	Gastrointestinal	High	7978406

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Terrestrial: Arthropods Extraction Table

CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
28553-12-0	1 Week(s), (1 Week(s))	*Drosophila melanogaster* (Fruit Fly), Larva, 3 Instar, Not Reported, Laboratory (BLOOMINGTON STOCK CENTER, 3605)	No substrate, Oral (diet, drink, gavage), Food, Not Reported	Unmeasured	0 % diet / 0.1 % diet / 0.2 % diet / 0.5 % diet / 1.0 % diet	Growth (Development-Pupation, Response Site: Not reported)	NOEL (1.0 % diet)	Development/Growth	High	7978406
28553-12-0	1 Week(s), (1 Week(s))	*Drosophila melanogaster* (Fruit Fly), Larva, 3 Instar, Not Reported, Laboratory (BLOOMINGTON STOCK CENTER, 3605)	No substrate, Oral (diet, drink, gavage), Food, Not Reported	Unmeasured	0 % diet / 0.1 % diet / 0.2 % diet / 0.5 % diet / 1.0 % diet	Reproduction (Reproduction-Hatch, Response Site: Not reported)	NOEL (0.2 % diet)	Development/Growth	High	7978406
28553-12-0	1 Week(s), (1 Week(s))	*Drosophila melanogaster* (Fruit Fly), Larva, 3 Instar, Not Reported, Laboratory (BLOOMINGTON STOCK CENTER, 3605)	No substrate, Oral (diet, drink, gavage), Food, Not Reported	Unmeasured	0 % diet / 0.1 % diet / 0.2 % diet / 0.5 % diet / 1.0 % diet	Physiology (Physiology-Pigmentation, Response Site: Not reported)	NR (0.1-1.0 % diet)	Development/Growth	High	7978406
28553-12-0	1 Week(s), (1 Week(s))	*Drosophila melanogaster* (Fruit Fly), Larva, 3 Instar, Not Reported, Laboratory (BLOOMINGTON STOCK CENTER, 3605)	No substrate, Oral (diet, drink, gavage), Food, NA Male organisms	Unmeasured	0 % diet / 0.1 % diet / 0.2 % diet / 0.5 % diet / 1.0 % diet	Growth (Growth-Weight, Response Site: Whole organism)	NR (0.1-1.0 % diet)	Development/Growth	High	7978406
28553-12-0	1 Week(s), (1 Week(s))	*Drosophila melanogaster* (Fruit Fly), Larva, 3 Instar, Not Reported, Laboratory (BLOOMINGTON STOCK CENTER, 3605)	No substrate, Oral (diet, drink, gavage), Food, Not Reported	Unmeasured	0 % diet / 0.1 % diet / 0.2 % diet / 0.5 % diet / 1.0 % diet	Growth (Development-Deformation,Developmental changes, general, Response Site: Not reported)	NR (0.1-1.0 % diet)	Development/Growth	High	7978406

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Terrestrial: Arthropods Extraction Table

CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
28553-12-0	1 Week(s), (1 Week(s))	*Drosophila melanogaster* (Fruit Fly), Larva, 3 Instar, Not Reported, Laboratory (BLOOMINGTON STOCK CENTER, 3605)	No substrate, Oral (diet, drink, gavage), Food, Not Reported	Unmeasured	0 % diet / 0.1 % diet / 0.2 % diet / 0.5 % diet / 1.0 % diet	Reproduction (Reproduction-Hatch, Response Site: Not reported)	LOEL (0.5 % diet)	Development/Growth	High	7978406
28553-12-0	1 Week(s), (1 Week(s))	*Drosophila melanogaster* (Fruit Fly), Larva, 3 Instar, Not Reported, Laboratory (BLOOMINGTON STOCK CENTER, 3605)	No substrate, Oral (diet, drink, gavage), Food, Not Reported	Unmeasured	0 % diet / 0.1 % diet / 0.2 % diet / 0.5 % diet / 1.0 % diet	Growth (Development-Metamorphosis, Response Site: Not reported)	NOEL (0.5 % diet)	Development/Growth	High	7978406
28553-12-0	1 Week(s), (1 Week(s))	*Drosophila melanogaster* (Fruit Fly), Larva, 3 Instar, Not Reported, Laboratory (BLOOMINGTON STOCK CENTER, 3605)	No substrate, Oral (diet, drink, gavage), Food, NA Female organisms	Unmeasured	0 % diet / 0.1 % diet / 0.2 % diet / 0.5 % diet / 1.0 % diet	Growth (Growth-Weight, Response Site: Whole organism)	LOEL (0.5 % diet)	Development/Growth	High	7978406
28553-12-0	1 Week(s), (1 Week(s))	*Drosophila melanogaster* (Fruit Fly), Larva, 3 Instar, Not Reported, Laboratory (BLOOMINGTON STOCK CENTER, 3605)	No substrate, Oral (diet, drink, gavage), Food, Not Reported	Unmeasured	0 % diet / 0.1 % diet / 0.2 % diet / 0.5 % diet / 1.0 % diet	Growth (Development-Metamorphosis, Response Site: Not reported)	LOEL (1.0 % diet)	Development/Growth	High	7978406
28553-12-0	1 Week(s), (1 Week(s))	*Drosophila melanogaster* (Fruit Fly), Larva, 3 Instar, Not Reported, Laboratory (BLOOMINGTON STOCK CENTER, 3605)	No substrate, Oral (diet, drink, gavage), Food, NA Female organisms	Unmeasured	0 % diet / 0.1 % diet / 0.2 % diet / 0.5 % diet / 1.0 % diet	Growth (Growth-Weight, Response Site: Whole organism)	NOEL (0.2 % diet)	Development/Growth	High	7978406

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

Terrestrial: Worms Extraction Table

CASRN	Exposure and Overall Duration	Test Organism Species, Age, Sex, Source	Exposure Media, Route Grouping, Type, Sample Number	Test Analysis Exposure Parameters	Dose/ Concentration for Each Main Group of the Study	Health Effect as reported by the Study Author(s)	Effect Level as reported by the Study Author(s)*	Health Outcome Identified by the Assessor	Overall Quality Determination	HERO ID
28553-12-0	28 Day(s), (56 Day(s))	*Eisenia fetida* (Earthworm), Adult, Not Reported, Laboratory (CAROLINA BIOLOGICAL SUPPLY CO., 2700 YORK ROAD, BURLINGTON, NC 27215-3398)	Artificial soil, Environmental, Soil slurry, Not Reported	Measured	0 mg/kg dry soil / 389.6-1052 mg/kg dry soil	Mortality (Mortality-Mortality, Response Site: Not reported)	NOEL (651.4-1052 mg/kg dry soil)	Mortality	High	10748710
28553-12-0	28 Day(s), (56 Day(s))	*Eisenia fetida* (Earthworm), Adult, Not Reported, Laboratory (CAROLINA BIOLOGICAL SUPPLY CO., 2700 YORK ROAD, BURLINGTON, NC 27215-3398)	Artificial soil, Environmental, Soil slurry, Not Reported	Measured	0 mg/kg dry soil / 389.6-1052 mg/kg dry soil	Mortality (Mortality-Mortality, Response Site: Not reported)	NR-ZERO (651.4-1052 mg/kg dry soil)	Mortality	High	10748710
28553-12-0	29 Day(s), (56 Day(s))	*Eisenia fetida* (Earthworm), Adult, Not Reported, Laboratory (CAROLINA BIOLOGICAL SUPPLY CO., 2700 YORK ROAD, BURLINGTON, NC 27215-3398)	Artificial soil, Environmental, Soil slurry, Not Reported	Measured	0 mg/kg dry soil / 389.6-1052 mg/kg dry soil	Growth (Growth-Weight, Response Site: Whole organism)	NR (~651.4-~1052 mg/kg dry soil)	Development/Growth	High	10748710
28553-12-0	56 Day(s), (56 Day(s))	*Eisenia fetida* (Earthworm), Adult, Not Reported, Laboratory (CAROLINA BIOLOGICAL SUPPLY CO., 2700 YORK ROAD, BURLINGTON, NC 27215-3398)	Artificial soil, Environmental, Soil slurry, Not Reported	Measured	0 mg/kg dry soil / 389.6-1052 mg/kg dry soil	Reproduction (Reproduction-Progeny counts/numbers, Response Site: Not reported)	NOEL (389.6-1052 mg/kg dry soil)	Reproductive/Teratogenic	High	10748710

* 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
75-34-3	105 weeks, (105 weeks)	Rat (Rattus norvegicus), Sampling Age:juvenile Exposure Age: 6 weeksMale, Fischer 344 (CDF®(F-344)CrlBR)	food	nominal	0/29.2/88.3/358.7/733.2 mg/kg/d	88.3 mg/kg/d	NOAEL	Growth-body weight	high	680087
75-34-3	105 weeks, (105 weeks)	Rat (Rattus norvegicus), Sampling Age:juvenile Exposure Age: 6 weeksMale, Fischer 344 (CDF®(F-344)CrlBR)	food	nominal	0/29.2/88.3/358.7/733.2 mg/kg/d	358.7 mg/kg/d	LOAEL	Growth-body weight	high	680087
75-34-3	105 weeks, (105 weeks)	Rat (Rattus norvegicus), Sampling Age:juvenile Exposure Age: 6 weeksMale, Fischer 344 (CDF®(F-344)CrlBR)	food	nominal	0/29.2/88.3/358.7/733.2 mg/kg/d	358.7 mg/kg/d	NOAEL	Survival	high	680087
75-34-3	105 weeks, (105 weeks)	Rat (Rattus norvegicus), Sampling Age:juvenile Exposure Age: 6 weeksMale, Fischer 344 (CDF®(F-344)CrlBR)	food	nominal	0/29.2/88.3/358.7/733.2 mg/kg/d	733.2 mg/kg/d	LOAEL	Survival	high	680087

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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
75-34-3	21 days, (21 days)	Rat (Rattus norvegicus), Sampling Age:juvenile Exposure Age: 21 daysFemale, Fischer 344	food	measured	0/607/1193/2289 mg/kg/d	1193 mg/kg/d	NOAEL	Growth-body weight	high	1325511
75-34-3	21 days, (21 days)	Rat (Rattus norvegicus), Sampling Age:juvenile Exposure Age: 21 daysFemale, Fischer 344	food	measured	0/607/1193/2289 mg/kg/d	2289 mg/kg/d	LOAEL	Growth-body weight	high	1325511
75-34-3	2 years, (2 years)	Rat (Rattus norvegicus), Sampling Age:juvenile Exposure Age: 6 weeksFemale, Fischer 344	food	nominal	0/18/184/375 mg/kg/d	18 mg/kg/d	NOAEL	Survival	high	1065989
75-34-3	2 years, (2 years)	Rat (Rattus norvegicus), Sampling Age:juvenile Exposure Age: 6 weeksFemale, Fischer 344	food	nominal	0/18/184/375 mg/kg/d	184 mg/kg/d	LOAEL	Survival	high	1065989
75-34-3	2 years, (2 years)	Rat (Rattus norvegicus), Sampling Age:juvenile Exposure Age: 6 weeksMale, Fischer 344	food	nominal	0/15/152/307 mg/kg/d	15 mg/kg/d	NOAEL	Growth-body weight	high	1065989
75-34-3	2 years, (2 years)	Rat (Rattus norvegicus), Sampling Age:juvenile Exposure Age: 6 weeksMale, Fischer 344	food	nominal	0/15/152/307 mg/kg/d	152 mg/kg/d	LOAEL	Growth-body weight	high	1065989

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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
75-34-3	24 months, (24 months)	Rat (Rattus norvegicus), Sampling Age:juvenile Exposure Age: 6 weeksFemale, Sprague-Dawley CD	food	nominal	0/33/331/672 mg/kg/d	331 mg/kg/d	NOAEL	Growth-body weight	high	679889
75-34-3	24 months, (24 months)	Rat (Rattus norvegicus), Sampling Age:juvenile Exposure Age: 6 weeksFemale, Sprague-Dawley CD	food	nominal	0/33/331/672 mg/kg/d	672 mg/kg/d	LOAEL	Growth-body weight	high	679889
75-34-3	33 days, (33 days)	Rat (Rattus norvegicus), Sampling Age:not reported Exposure Age: LactationFemale, Wistar (Han-Tac:WH)	gavage	unmeasured	0/300/600/750/900 mg/kg/d	750 mg/kg/d	NOAEL	Reproduction-progeny weight-progeny	medium	806135
75-34-3	33 days, (33 days)	Rat (Rattus norvegicus), Sampling Age:not reported Exposure Age: LactationFemale, Wistar (Han-Tac:WH)	gavage	unmeasured	0/300/600/750/900 mg/kg/d	900 mg/kg/d	LOAEL	Reproduction-progeny weight-progeny	medium	806135
75-34-3	25 days, (25 days)	Rat (Rattus norvegicus), Sampling Age:11 weeks Exposure Age: LactationFemale, Sprague-Dawley (Crl:CD(SD))	food	nominal	0/56/288/720 mg/kg/d	56 mg/kg/d	NOAEL	Reproduction-progeny weight-progeny	medium	1325348

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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
75-34-3	25 days, (25 days)	Rat (Rattus norvegicus), Sampling Age:12 weeks Exposure Age: Lacta-tionFemale, Sprague-Dawley (Crl:CD(SD))	food	nominal	0/56/288/720 mg/kg/d	288 mg/kg/d	LOAEL	Reproduction-progeny weight-progeny	medium	1325348
75-34-3	25 days, (25 days)	Rat (Rattus norvegicus), Sampling Age:11 weeks Exposure Age: Lacta-tionFemale, Sprague-Dawley (Crl:CD(SD))	food	nominal	0/109/555/1513 mg/kg/d	555 mg/kg/d	NOAEL	Growth-body weight	medium	1325348
75-34-3	25 days, (25 days)	Rat (Rattus norvegicus), Sampling Age:11 weeks Exposure Age: Lacta-tionFemale, Sprague-Dawley (Crl:CD(SD))	food	nominal	0/109/555/1513 mg/kg/d	1513 mg/kg/d	LOAEL	Growth-body weight	medium	1325348
75-34-3	104 weeks, (104 weeks)	Mouse (Mus musculus), Sampling Age:juvenile Exposure Age: 6 weeksFemale, B6C3F1/Cr1Br	food	nominal	0/112/335.6/910.3/1887.6 mg/kg/d	335.6 mg/kg/d	NOAEL	Growth-body weight	high	1325481
75-34-3	104 weeks, (104 weeks)	Mouse (Mus musculus), Sampling Age:juvenile Exposure Age: 6 weeksFemale, B6C3F1/Cr1Br	food	nominal	0/112/335.6/910.3/1887.6 mg/kg/d	910.3 mg/kg/d	LOAEL	Growth-body weight	high	1325481

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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
75-34-3	104 weeks, (104 weeks)	Mouse (Mus musculus), Sampling Age:juvenile Exposure Age: 6 weeksMale, B6C3F1/Cr1Br	food	nominal	0/90.3/275.6/741.8/1560.2 mg/kg/d	275.6 mg/kg/d	NOAEL	Growth-body weight	high	1325481
75-34-3	104 weeks, (104 weeks)	Mouse (Mus musculus), Sampling Age:juvenile Exposure Age: 6 weeksMale, B6C3F1/Cr1Br	food	nominal	0/90.3/275.6/741.8/1560.2 mg/kg/d	741.8 mg/kg/d	LOAEL	Growth-body weight	high	1325481
75-34-3	104 weeks, (104 weeks)	Mouse (Mus musculus), Sampling Age:juvenile Exposure Age: 6 weeksMale, B6C3F1/Cr1Br	food	nominal	0/90.3/275.6/741.8/1560.2 mg/kg/d	741.8 mg/kg/d	NOAEL	Survival	high	1325481
75-34-3	104 weeks, (104 weeks)	Mouse (Mus musculus), Sampling Age:juvenile Exposure Age: 6 weeksMale, B6C3F1/Cr1Br	food	nominal	0/90.3/275.6/741.8/1560.2 mg/kg/d	1560.2 mg/kg/d	LOAEL	Survival	high	1325481
75-34-3	19 weeks, (19 weeks)	Rat (Rattus norvegicus), Sampling Age:not reported Exposure Age: GestationalFemale, Sprague-Dawley (CRL:CD BR)	food	nominal	0/377/741/1087 mg/kg/d	377 mg/kg/d	NOAEL	Reproduction	medium	1987588

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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
75-34-3	19 weeks, (19 weeks)	Rat (Rattus norvegicus), Sampling Age:not reported Exposure Age: GestationalFemale, Sprague-Dawley (CRL:CD BR)	food	nominal	0/377/741/1087 mg/kg/d	741 mg/kg/d	LOAEL	Reproduction	medium	1987588
75-34-3	19 weeks, (19 weeks)	Rat (Rattus norvegicus), Sampling Age:not reported Exposure Age: LactationFemale, Sprague-Dawley (CRL:CD BR)	food	nominal	0/363/734/1114 mg/kg/d	363 mg/kg/d	NOAEL	Growth-body weight	medium	1987588
75-34-3	19 weeks, (19 weeks)	Rat (Rattus norvegicus), Sampling Age:not reported Exposure Age: LactationFemale, Sprague-Dawley (CRL:CD BR)	food	nominal	0/363/734/1114 mg/kg/d	734 mg/kg/d	LOAEL	Growth-body weight	medium	1987588
75-34-3	10 weeks, (10 weeks)	Rat (Rattus norvegicus), Sampling Age:juvenile Exposure Age: not reportedMale, Sprague-Dawley (CRL:CD BR)	food	nominal	0/301/622/966 mg/kg/d	301 mg/kg/d	NOAEL	Growth-body weight	medium	1987588
75-34-3	10 weeks, (10 weeks)	Rat (Rattus norvegicus), Sampling Age:juvenile Exposure Age: not reportedMale, Sprague-Dawley (CRL:CD BR)	food	nominal	0/301/622/966 mg/kg/d	622 mg/kg/d	LOAEL	Growth-body weight	medium	1987588

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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
75-34-3	19 weeks, (19 weeks)	Rat (Rattus norvegicus), Sampling Age:not reported Exposure Age: GestationalFemale, Sprague-Dawley (CRL:CD BR)	food	nominal	0/146/287/555 mg/kg/d	287 mg/kg/d	NOAEL	Reproduction-progeny weight-whole organism	high	1987589
75-34-3	19 weeks, (19 weeks)	Rat (Rattus norvegicus), Sampling Age:not reported Exposure Age: GestationalFemale, Sprague-Dawley (CRL:CD BR)	food	nominal	0/146/287/555 mg/kg/d	555 mg/kg/d	LOAEL	Reproduction-progeny weight-whole organism	high	1987589
75-34-3	19 weeks, (19 weeks)	Rat (Rattus norvegicus), Sampling Age:not reported Exposure Age: GestationalFemale, Sprague-Dawley (CRL:CD BR)	food	nominal	0/143/288/560 mg/kg/d	143 mg/kg/d	NOAEL	Reproduction-progeny weight-progeny	high	1987589
75-34-3	19 weeks, (19 weeks)	Rat (Rattus norvegicus), Sampling Age:not reported Exposure Age: GestationalFemale, Sprague-Dawley (CRL:CD BR)	food	nominal	0/143/288/560 mg/kg/d	288 mg/kg/d	LOAEL	Reproduction-progeny weight-progeny	high	1987589
75-34-3	19 weeks, (19 weeks)	Rat (Rattus norvegicus), Sampling Age:not reported Exposure Age: LactationFemale, Sprague-Dawley (CRL:CD BR)	food	nominal	0/146/287/555 m/kg/d	287 mg/kg/d	NOAEL	Growth-body weight	high	1987589

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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
75-34-3	19 weeks, (19 weeks)	Rat (Rattus norvegicus), Sampling Age:not reported Exposure Age: LactationFemale, Sprague-Dawley (CRL:CD BR)	food	nominal	0/146/287/555 m/kg/d	555 mg/kg/d	LOAEL	Growth-body weight	high	1987589
75-34-3	19 weeks, (19 weeks)	Rat (Rattus norvegicus), Sampling Age:3 weeks Exposure Age: LactationFemale, Sprague-Dawley (CRL:CD BR)	food	nominal	0/143/288/560 mg/kg/d	288 mg/kg/d	NOAEL	Growth-body weight	high	1987589
75-34-3	19 weeks, (19 weeks)	Rat (Rattus norvegicus), Sampling Age:3 weeks Exposure Age: LactationFemale, Sprague-Dawley (CRL:CD BR)	food	nominal	0/143/288/560 mg/kg/d	560 mg/kg/d	LOAEL	Growth-body weight	high	1987589
75-34-3	10 days, (10 days)	Rat (Rattus norvegicus), Sampling Age:not reported Exposure Age: GestationalFemale, Wistar (Chbb/THOM)	gavage	unmeasured	0/40/200/1000 mg/kg/d	200 mg/kg/d	NOAEL	Reproduction	medium	674193
75-34-3	10 days, (10 days)	Rat (Rattus norvegicus), Sampling Age:not reported Exposure Age: GestationalFemale, Wistar (Chbb/THOM)	gavage	unmeasured	0/40/200/1000 mg/kg/d	1000 mg/kg/d	LOAEL	Reproduction	medium	674193

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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
75-34-3	18 days, (18 days)	Rat (Rattus norvegicus), Sampling Age:not reported Exposure Age: LactationFemale, Sprague-Dawley (CD(SD)IGS)	food	unmeasured	0/30.7/306.7/1164.5 mg/kg/d	30.7 mg/kg/d	NOAEL	Reproduction	medium	192872
75-34-3	18 days, (18 days)	Rat (Rattus norvegicus), Sampling Age:not reported Exposure Age: LactationFemale, Sprague-Dawley (CD(SD)IGS)	food	unmeasured	0/30.7/306.7/1164.5 mg/kg/d	306.7 mg/kg/d	LOAEL	Reproduction	medium	192872
75-34-3	18 days, (18 days)	Rat (Rattus norvegicus), Sampling Age:not reported Exposure Age: LactationFemale, Sprague-Dawley (CD(SD)IGS)	food	unmeasured	0/30.7/306.7/1164.5 mg/kg/d	306.7 mg/kg/d	NOAEL	Growth-body weight	medium	192872
75-34-3	18 days, (18 days)	Rat (Rattus norvegicus), Sampling Age:not reported Exposure Age: LactationFemale, Sprague-Dawley (CD(SD)IGS)	food	unmeasured	0/30.7/306.7/1164.5 mg/kg/d	1164.5 mg/kg/d	LOAEL	Growth-body weight	medium	192872
75-34-3	10 days, (10 days)	Rat (Rattus norvegicus), Sampling Age:not reported Exposure Age: GestationalFemale, Sprague-Dawley	gavage	unmeasured	0/100/500/1000 mg/kg/d	500 mg/kg/d	NOAEL	Reproduction	high	680201

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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
75-34-3	10 days, (10 days)	Rat (Rattus norvegicus), Sampling Age:not reported Exposure Age: GestationalFemale, Sprague-Dawley	gavage	unmeasured	0/100/500/1000 mg/kg/d	1000 mg/kg/d	LOAEL	Reproduction	high	680201

Diisononyl 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 study was GPL compliant. Rat-Fischer 344 - [rat]-Both	Oral-Diet-Duration: Short-term (>1-30 days)-7-24-21-day(s) 24 hours/day 7 days/week 21 day(s) Animals were fed diet containing test substance for 21 days	**POD: 639 mg/kg-bw/day (LOAEL) -Increased liver weight, decreased serum triglyceride and cholesterol levels** n= 5 Dose= 0, n= 5 Dose= 639, n= 5 Dose= 1192, n= 5 Dose= 2195, mg/kg-bw/day	See footnotes for full summary [1]	Purity of test substance was not reported. Food intake was significantly reduced (>20% difference from control).	Nutritional/Metabolic-Body weight and food intake-Hepatic/Liver-Liver weight and histology. Serum triglyceride and total cholesterol. Biochemical analysis of liver (cyanide-insensitive palmitoyl-CoA oxidation and protein concentration; microsomal fraction rate of lauric acid 11-hydroxylase and 12-hydroxylase activity) and ultrastructure of liver assessing peroxisome proliferation (TEM); High	1325511
The study was GPL compliant. Rat-Fischer 344 - [rat]-Both	Oral-Diet-Duration: Short-term (>1-30 days)-7-24-21-day(s) 24 hours/day 7 days/week 21 day(s) Animals were fed diet containing test substance for 21 days	**POD: 1149 mg/kg-bw/day (LOAEL) -Increased liver weight, decrease in serum triglyceride and total cholesterol, increased incidence of reduced cytoplasmic basophilia in the liver** n= 40 Dose= 0, n= 40 Dose= 1149, mg/kg-bw/day	See footnotes for full summary [2]	Purity of test substance was not reported. Food intake was significantly reduced (>20% difference from control).	Nutritional/Metabolic-Body weight and food intake-Hepatic/Liver-Liver weight and histology. Serum triglyceride and total cholesterol. Biochemical analysis of liver (cyanide-insensitive palmitoyl-CoA oxidation and protein concentration; microsomal fraction rate of lauric acid 11-hydroxylase and 12-hydroxylase activity) and ultrastructure of liver assessing peroxisome proliferation (TEM); Medium	1325511

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Diisononyl 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
Adherence to a guideline was not specified. Mouse-Other (Kunming)-Female	Oral-Gavage-Duration: Short-term (>1-30 days)-7-14-day(s) 7 days/week 14 day(s)	**POD: 2 mg/kg-bw/day (NOAEL) -Decreased serum estradiol and increased oxidative stress in ovaries** n= 6 Dose= 0, n= 6 Dose= 2, n= 6 Dose= 20, n= 6 Dose= 200, mg/kg-bw/day	In a short-term toxicity study, female Kunming mice (6/group) were administered 0, 2, 20, or 200 mg/kg-day of diisononyl phthalate (DINP; vehicle not reported) via gavage, daily for 14 days. Blood samples were collected for the measurement of estradiol in serum. Ovarian tissues were analyzed for histology, oxidative stress (levels of glutathione [GSH] and malondialdehyde [MDA], and activities of GSH-peroxidase [GSH-PX] and superoxide dismutase [SOD]), and apoptosis and autophagy-related protein levels (via Western blot). Serum estradiol levels were significantly decreased (~15%) at 20 and 200 mg/kg/day, compared with control. In the ovary, disordered arrangement of follicular granulosa cells was observed in exposed mice (representative photos shown, data not quantified). Increased oxidative stress was seen in the ovaries of exposed mice as evidence by a significant increase in MDA content at 200 mg/kg-day and decreased the levels of GSH, GSH-PX activity and SOD activity at 20 and 200 mg/kg-day. A significant dose-related increase in proteins associated with apoptosis (cleaved caspase 8 and 3, and Bax) and autophagy (Beclin1, Atg5, ratio of LC3-II/LC3-I) and decrease in anti-apoptotic proteins (Bcl-2) were seen at $\geq$ 2 mg/kg/day. No author-reported toxicity values were provided. Based on the available data, a NOAEL of 2 mg/kg/day and a LOAEL of 20 mg/kg-day, was identified based decreased serum estradiol and increased oxidative stress indicators in the ovary (decreased GSH levels, and GSH-PX and SOD activity).	Histological changes in the ovary were not adequately reported. Vehicle was not reported, and estrous cycle was not monitored.	Reproductive/Developmental- Serum estradiol, ovary histology, ovarian oxidative stress (levels of glutathione [GSH] and malondialdehyde [MDA], and activities of GSH-peroxidase [GSH-PX] and superoxide dismutase [SOD]), and apoptosis and autophagy-related protein levels in ovary via Western blot.; Low	11784564

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Diisononyl 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
All procedures involving animal handling were approved by the University of Illinois at Urbana-Champaign Institutional Animal Care and Use Committee (Protocol No.: 17079). Mouse-CD-1 - [mouse]-Female	Oral-Gavage-Duration: Short-term (>1-30 days)-7-10-day(s) 7 days/week 10 day(s) Female mice were dosed 10 consecutive days every morning at 2 h following the start of the light cycle.	**POD: 0.02 mg/kg-bw/day (LOAEL) -Decreased percentage of primary ovarian follicles** n= 12 Dose= 0, n= 4 Dose= 0.02, n= 4 Dose= .1, n= 4 Dose= 20, n= 4 Dose= 200, mg/kg-bw/day	The study doses female CD-1 mice orally via insertion of a pipette tip into the mouth, utilizes a control (corn oil vehicle), and includes a large range of doses: DEHP (20 μg/kg/day, 200 μg/kg/day, 20 mg/kg/day, and 200 mg/kg/day) and DINP 20 μg/kg/day, 100 μg/kg/day, 20 mg/kg/day, and 200 mg/kg/day). Dosing occurred at PND 39-40 for 10 days followed by various post-dosing assessments for ovarian follicle and sex hormone endpoints. For the 9-month post-dosing group used in histological analysis of ovarian follicle development and sex hormone assays: Histological analysis of ovarian follicle development occurred for DINP exposed adult female mice. A significant POD was found in the percentage of primary follicles in the 20 μg/kg/day group (n = 4–12 mice/group). No change in total follicle number was found between groups (data was not shown). Analysis of sex hormone levels in sera were measured for testosterone (n = 5-12 mice/group), progesterone (n = 5-12 mice/group), estradiol (n = 5-12 mice/group), and Inhibin B (n = 4-12 mice/group) using ELISAs and FSH (n = 5-12 mice/group) using a radioimmunoassay. No significant POD in sex hormone levels following DINP exposure.	Some major limitations include lack of clarity in different experimental metrics. This includes not giving the CASN or catalog number for the chemical of interest, not providing the exact number of animals per group, not listing the measure of variance per group (e.g., standard error, standard deviation, etc.), and not having sufficient sample sizes for some metrics.	Reproductive/Developmental-Following 10 days of exposure at various post-dosing time points (e.g., immediately post-dosing, 3-, 6-, and 9-months post-dosing depending on the experiments) histological analysis of the follicular development in ovarian tissue samples and the sex hormone present in sera (e.g., testosterone, progesterone, estradiol, FSH, and Inhibin B) from adult female mice were analyzed.; Medium	7978479

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Diisononyl 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
All animal handling procedures were approved by the University of Illinois at Urbana-Champaign Institutional Animal Care and Use Committee (Protocol No.: 17079). Mouse-CD-1 - [mouse]-Female	Oral-Gavage-Duration: Short-term (>1-30 days)-1-F0- premating (At PND 39-40 female mice were exposed for 10 days with a single oral dose/day) Female mice were dosed at age 39–40 days for 10 days with either vehicle control (corn oil), DEHP (20 μg/kg/day – 200 mg/kg/day), or DiNP (20 μg/ kg/day – 200 mg/kg/day)	**POD: 0.02 mg/kg-bw/day (LOAEL) -Number of antral follicles** n= 12 Dose= 0, n= 5 Dose= 0.02, n= 5 Dose= 0.2, n= 5 Dose= 20, n= 5 Dose= 200, mg/kg-bw/dayTotal # of generations: 1 Female Exposure: F0- premating, At PND 39-40 female mice were exposed for 10 days with a single oral dose/day	For the 18 months post-dosing group used in histological analysis and sex hormone assays: Histological analysis was done on ovarian tissue sections and follicle number/type were determined (control n = 12 mice/group, DiNP 20 μg/kg/day – 200 mg/kg/day n = 5–6 mice/group). A significant POD in the number of primordial (100 μg/kg/day group & 200 mg/kg/day group) and antral (20 μg/kg/day group) follicles were found. Analysis of sex hormone levels in sera were also measured for testosterone, progesterone, and estradiol* using commercially available using ELISAs (control n = 16 mice/group, DiNP 20 μg/kg/day – 200 mg/kg/day n = 7/8*–11 mice/group), and for FSH and Inhibin B using a radioimmunoassay (control n = 16 mice/group, DiNP 20 μg/kg/day –200 mg/kg/day n = 8–11 mice/group). A significant POD in testosterone and estradiol levels in sera were found in the 100 μg/kg/day group, and in Inhibin B in the 20 mg/kg/day group.	Some major limitations include lack of clarity in different experimental metrics. This includes not giving the CASN or catalog number for the chemical of interest, not providing the exact number of animals per group, not listing the measure of variance per group (e.g., standard error, standard deviation, etc.), and not having sufficient sample sizes for some metrics.	Reproductive/Developmental- Post-dosing (12, 15, and 18 months depending on the experiments) estrous cyclicity presented as percent time spent in each stage (e.g., proestrus, estrus, metestrus/diestrus), raw number and quality assessment of follicles in the ovaries of mice following varying number of months post-dosing, duration to begin mating and overall gestational period, fertility index, number of female mice that gave birth at various months post-dosing, live pup weights, litter sizes, sex ratio, sex hormone levels (e.g., testosterone, progesterone, estradiol, FSH, and Inhibin B) at various months post-dosing.; Medium	7978481
No guideline or compliance methods were reported. Mouse-CD-1 - [mouse]-Female	Oral-Duration: Short-term (>1-30 days)-7-10-day(s) 7 days/week 10 day(s) Animals were exposed for a minimum of 10 days and a maximum of 14. Animals were sacrificed when in diestrus.	**POD: 0.02 mg/kg-bw/day (Other) -Increase in proliferating cells in the colon (Ki67 positive cells)** n= 6 Dose= 0, n= 6 Dose= 0.02, n= 6 Dose= 0.2, n= 6 Dose= 2, n= 6 Dose= 20, n= 6 Dose= 200, mg/kg-bw/day	See footnotes for full summary [3]	This study was missing some details, including the test substance purity, and whether or not measures were taken to reduce exposures to other phthalates.	Gastrointestinal- Distal colon weight, immunohistochemistry for proliferation (Ki67).; Medium	11151638

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No guideline or compliance methods were reported. Mouse-CD-1 - [mouse]-Female	Oral-Duration: Short-term (>1-30 days)-7-10-day(s) 7 days/week 10 day(s) Animals were exposed for a minimum of 10 days and a maximum of 14. Animals were sacrificed when in diestrus.	**POD: 0.02 mg/kg-bw/day (Other) -Increase in proliferating cells in the colon (Ki67 positive cells)** n= 6 Dose= 0, n= 6 Dose= 0.02, n= 6 Dose= 0.2, n= 6 Dose= 2, n= 6 Dose= 20, n= 6 Dose= 200, mg/kg-bw/day	See footnotes for full summary [4]	This study was missing some details, including the test substance purity, and whether or not measures were taken to reduce exposures to other phthalates.	Gastrointestinal-Distal colon weight, immunohistochemistry for proliferation (Ki67).; Medium	11151638
No guideline or compliance methods were reported. Mouse-CD-1 - [mouse]-Female	Oral-Duration: Short-term (>1-30 days)-7-10-day(s) 7 days/week 10 day(s) Animals were exposed for a minimum of 10 days and a maximum of 14. Animals were sacrificed when in diestrus.	**POD: 0.02 mg/kg-bw/day (Other) -Increase in proliferating cells in the colon (Ki67 positive cells)** n= 6 Dose= 0, n= 6 Dose= 0.02, n= 6 Dose= 0.2, n= 6 Dose= 2, n= 6 Dose= 20, n= 6 Dose= 200, mg/kg-bw/day	See footnotes for full summary [5]	This study was missing some details, including the test substance purity, and whether or not measures were taken to reduce exposures to other phthalates.	Gastrointestinal-Distal colon weight, immunohistochemistry for proliferation (Ki67).; Medium	11151638
No guidance, but authors indicated the experiment was performed in an AAALAC (Association for Assessment and Accreditation of Laboratory Animal Care) Mouse-CD-1 - [mouse]-Female	Oral-Gavage-Duration: Short-term (>1-30 days)-7-14-day(s) 7 days/week 14 day(s) Female mice exposed to 0 (control), 0.02,0.2,2,20,200mg/kg DINP, oral daily for 10-14 days (no diestrus went for additional 4 days)	**POD: 0.02 mg/kg-bw/day (LOAEL) -Significantly increase colonic damage; cellular infiltration and aberrant colon walls, enterocyte sloughing. Marginally decreased testosterone levels. Increased the expression of interferon gamma (Ifng)** n= 6 Dose= 0, n= 6 Dose= 0.02, n= 6 Dose= 0.2, n= 6 Dose= 2, n= 6 Dose= 20, n= 6 Dose= 200, mg/kg-bw/day	See footnotes for full summary [6]	The authors acknowledged limitations in understanding how DINP exposure impacts the gut microbiome in female mice which was not fully addressed in this study.	Gastrointestinal-Gross measurements of the colon , Histological analysis , Colon Hormone level , Gene expression; High	7978425

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The study did not report any compliance methods adhered to. Rat-Sprague-Dawley - [rat]-Female	Oral-Gavage-Duration: Short-term (>1-30 days)-1-F0 - gestation (GD 12-19) Pregnant rats were dosed from GD 12-19	**POD: 50 mg/kg-bw/day (Other) -Developmental effects in fetus (reduced testis testosterone, increased multinucleated gonocytes** n= 34 Dose= 0, n= 32 Dose= 50, n= 32 Dose= 250, n= 32 Dose= 500, mg/kg-bw/dayTotal # of generations: 1 Female Exposure: F0 - gestation, GD 12-19	See footnotes for full summary [7]	No information was provided as to how animals were allocated into study groups.	Nutritional/Metabolic-Maternal body weight-Hepatic/Liver-Maternal liver weight-Reproductive/Developmental-Fetal weight, testis testosterone level, AGD, and histology on testis; High	1325350

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Diisononyl 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
None Rat-Sprague-Dawley - [rat]-Male	nan 1 days/week 4 week(s) Animals were treated 4 weeks, although it doesn't specifically say 7 days/week.	**POD: 500 mg/kg-bw/day (LOAEL) -Male reproductive effects (decreased sperm counts/motility)** n= 6 Dose= 0, n= 6 Dose= 500, mg/kg-bw/day	Male SD rats (5-6/group) were exposed by oral gavage to one of multiple phthalates, including BBP, DEHP, DBP, DIDP, and DINP. It is assumed that animals were exposed one time per day, 7 days per week for 4 weeks, although it is not explicitly stated. Negative controls were exposed to corn oil (vehicle) only. Animals were monitored for clinical signs and mortality, and body weights were measured every three days. Urinalysis was collected, and following euthanasian, blood was collected for hematology and serum chemistry parameters. Organ weights and sperm quality were also analyzed.No animals died during the exposure period, and the only clinical sign observed was salivation. Body weights were decreased starting at 2 weeks of exposure in animals exposed to BBP, DBP, and DINP, but not in animals exposed to DEHP or DIDP, and no differences in food consumption were measured in any group. Increased relative liver weights were observed in animals exposed to BBP, DBP, DEHP, DIDP, and DINP, while relative testis weights were decreased and relative thymus weights were increased in animals exposed to DEHP. No other organ weight changes were observed. Animals exposed to DBP and DIDP had altered hematology parameters, while animals exposed to DEHP, DBP, DINP, and DIDP had altered serum chemistry parameters. Urinalysis results were not shown, but text stated that animals exposed to DIDP add altered results. Sperm counts and motility were decreased in animals exposed to BBP, DEHP, DBP, DIDP, and DINP. The only dose examined (500 mg/kg/day) was the LOAEL for male reproductive effects.	The major limitation of this study is the lack of reporting. Very little information is provided on the exposure methods, test substance preparation, number of animals per group, and dosing frequency. The urinalysis information was also not reported.	Reproductive/Developmental-Testis and epididymis weights, sperm count and motility; Medium	697382

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Guideline and Animal Species, Strain, Sex	Exposure Route and Exposure Duration	Study-wide POD and Dose/ Concentration(s)	Summary	Major Limitations	Principal Target Organs/Systems and OQD*	HERO ID
OECD protocol for detecting endocrine disruptors (OECD, 2001). Rat-Sprague-Dawley - [rat]-Male	Oral-Gavage-Duration: Short-term (>1-30 days)-7-10-day(s) 7 days/week 10 day(s) Animals were treated for 10 days	**POD: mg/kg-bw/day (Dichotomous (P/N)) -Positive in Hershberger assay at 500 mg/kg/day** n= 6 Dose= 0, n= 6 Dose= 20, n= 6 Dose= 100, n= 6 Dose= 500, mg/kg-bw/day	Hershberger assay was performed in castrated Sprague-Dawley male rats. One week after surgery, animals were administered 0, 20, 100 or 500 mg/kg/day of di-isodecyl phthalate (DIDP) in corn oil via oral gavage along with 0.4 mg/kg/day testosterone propionate delivered subcutaneously for 10 days. Endpoints evaluated included lethality, clinical signs, body weight, serum testosterone and luteinizing hormone, organ weights (liver, kidneys, adrenal gland, testes, glans penis, ventral prostates, combined seminal vesicles and coagulating glands, levator ani/bulbocavernosus [LABC], and Cowper's glands).All animals survived the entirety of the experiment. No clinical signs of toxicity were seen. No significant differences in terminal body weights were seen compared to control. Significant increases in serum LH ~33% occurred at 100 and 500 mg/kg/day and significant decreases in testosterone (~27%) was seen in all dose groups compared to testosterone alone control. Absolute liver weight was significantly increased at 500 mg/kg/day (17%) compared to testosterone alone. At 500 mg/kg/day, significant decreases in absolute seminal vesicles weight (9%) and ventral prostate weight (21%) compared to testosterone alone. No significant differences in LAB, Cowper's glands or glans penis weight were seen compared to testosterone alone. A reduction in the weight of two out of the five androgen-dependent tissues occurred at 500 mg/kg/day, indicating a positive response.A positive control group for antiandrogenic effects (treated with flutamide) was included and gave expected results (data not shown).	No major limitation.	Nutritional/Metabolic-Body weight-Other (please specify below) (Clinical signs)-Clinical signs-Hepatic/Liver-Liver weight-Renal/Kidney-Kidney weight-Other (please specify below) (Endocrine)-Adrenal weight-Reproductive/Developmental-The following 5 tissues were weighed: testes, ventral prostates, combined seminal vesicles and coagulating glands, levator ani/bulbocavernosus (LABC), and Cowper's gland.Serum testosterone and luteinizing hormone; Medium	673292

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Guideline and Animal Species, Strain, Sex	Exposure Route and Exposure Duration	Study-wide POD and Dose/ Concentration(s)	Summary	Major Limitations	Principal Target Organs/Systems and OQD*	HERO ID
No guidance was reported, but the study followed procedures were approved by the Institutional Animal Care and Use Committee (IACUC), Office of Scientific Research Management, Hubei University of Science and Technology, with a certificate of Application for the Use of Animals (approval ID: HBUST-IACUC-2018-001). Mouse-Balb/c - [mouse]-Male	Dermal-Duration: Short-term (>1-30 days)-7-24-28-day(s) 24 hours/day 7 days/week 28 day(s) Mice were exposed to DINP (0.02, 0.2, 2, 20, and 200mg/kg) and saline control, for 28 days continuous dermal exposure	**POD: 20 mg/kg (LOAEL) - significant skin alteration, significant increase in organ coefficient for liver, increase liver weight, hepatic and renal damage, increased kidney DPC coefficient, increase kidney weight, increased hepatic and renal ROS, MDA level and decrease GSH level.** n= 7 Dose= 0, n= 7 Dose= 0.02, n= 7 Dose= 0.2, n= 7 Dose= 2, n= 7 Dose= 20, n= 7 Dose= 200, mg/kg	See footnotes for full summary [8]	No major limitations were identified.	Nutritional/Metabolic-body weight-Hepatic/Liver-organ weight, organ coefficient, ROS, MDA, GSH, DPC coefficient and histology-Renal/Kidney-organ weight, organ coefficient, ROS, MDA, GSH, DPC coefficient and histology-Skin/Connective Tissue-histology; Medium	7978423
No guidelines or adherence to GLP were reported. Mouse-CD-1 - [mouse]-Female	Oral-Diet-Duration: Short-term (>1-30 days)-7-1-month(s) 7 days/week 1 month(s) Mice were exposed via the diet ad libitum for 1 month	**POD: 240 mg/kg-bw/day (NOAEL) -No adverse dose-related effects.** n= 10 Dose= 0, n= 10 Dose= 0.024, n= 10 Dose= 0.24, n= 10 Dose= 240, mg/kg-bw/day	See footnotes for full summary [9]	This was a dietary study that did not report food intake or body weights; however, the reported doses in mg/kg-day are generally consistent with doses calculated using default body weight and food consumption values in female mice. There were other minor reporting deficiencies (test substance purity, animal husbandry, and number of animals per group).	nan; Medium	11784618

* Overall Quality Determination

[1] 1325511: Fisher 344 rats (5/sex/group) were provided a diet containing 0, 0.3, 1.2, 2.5% DINP for 21 days. Authors calculated mean DINP intake based on food intake and body weight as 639, 1192, and 2195 mg/kg/day in males and 607, 1193, 2289 mg/kg/day in females at 0, 0.3, 1.2, 2.5% DINP in diet, respectively. Endpoints evaluated included clinical signs (daily), body weight (days: -3, 0, 3, 7, 10, 14, 17, and 20), food intake (measured in intervals from days: -3 to 0; 0-3; 3-7; 7-10; 10-14; 14-17; and 17-20), serum concentrations of triglyceride and total cholesterol, gross necropsy, organ weights (liver, kidney, and testes), histopathology (liver, kidney, and testes), biochemical analysis of liver (cyanide-insensitive palmitoyl-CoA oxidation levels and protein concentration; microsomal fraction rate of lauric acid hydroxylation) and ultrastructure of liver to assess peroxisome proliferation (TEM; one negative control, 2 positive controls and 2 from high-dose groups). A positive control group was also included in which rats (n=5/sex) were fed 1.2% DEHP (1084 mg/kg/day for males and 896 mg/kg/day for females).The study did not report that any animals died, and all animals were accounted for in the results. Clinical signs were not reported. Body weights were significantly decreased in mid-dose males (6-12%) from days 7-20 and high-dose males (10-28%) from days 3-20; and in females in the mid-dose group (6-7%) on days 7-10 and high-dose group (9-14%) on days 3-20. Terminal body weights were significantly decreased in males (13% and 30%) in mid-and high-dose groups, respectively and in high-dose females (16%) compared to control. Food intake in males was decreased in (10-14%) on day 7-20 in the mid-dose groups. In the high-dose group, food intake was decreased the first 3 days 48% in males and 41% in females; food intake in males remained decreased (19-36%) for the remainder of the study in males but returned to control levels in females. Serum triglycerides were significantly decreased in males (24%, 42% and 48%) in the low-, mid-, and high-dose groups, respectively and in females (23% and 26%) in the mid- and high dose groups compared to control. Serum total cholesterol levels were significantly decreased in males (24%, 32%, and 9%) and females (24%, 15%, and 14%) in the low-, mid-, and high-dose groups, respectively. Significant increases in absolute liver weight were seen in males (36%, 50% and 65%) and females (24%, 64%, and 98%) and relative liver weight in males (36%, 73%, 132%) and females (31%, 75% and 137%) in the low-, mid- and high-dose groups, respectively compared to control. Absolute kidney weights in males were significantly increased 14% in the low-dose group and decreased in the high-dose group (13%) compared to control. No significant differences in absolute kidney weight were seen in females compared to control. Relative kidney weights were increased in males (15%, 22% and 24%) and females (7%, 8% and 14%) in the low-, mid-, and high-dose groups respectively compared to control. Relative (but not absolute) testis weight was significantly increased 35% in the high-dose group compared to control; this may be a reflection of the severe decrease in body weight in this group. In the liver cyanide-insensitive palmitoyl-CoA oxidation levels were significantly increased in males (5-fold and 10-fold) and females (4-fold and 11-fold) in mid- and high-dose groups, respectively compared to control. In males, significant increases in the activities of lauric acid 11-hydroxylase (2-fold, 3-fold, and 3-fold) and lauric acid 12-hydroxylase (5-fold, 8-fold, and 10-fold) in the low-, mid- and high-dose groups, respectively compared to control. In the high-dosed females, significant increases in the activities of lauric acid 11-hydroxylase (5-fold) and lauric acid 12-hydroxylase (8-fold) were seen in the liver compared to control. Total protein levels in the liver were significantly increased in males (8%, 10%, and 18%) and females (19%, 20%, and 23%) in the low-, mid, and high-dose group. Microsomal protein levels were significantly in females (17% and 17%) in the low- and mid-dose groups respectively compared to control. In the high-dose group, histological examination of liver showed increased incidences of reduction cytoplasmic basophilia and increased cytoplasmic eosinophilia in 5/5 males and 5/5 females compared 0/5 males and females in controls. In the mid-dose group, increased incidences of reduction cytoplasmic basophilia was seen in 5/5 males and 5/5 females compared to 0/5 in controls. Proliferation of centrilobular and periportal peroxisomes were very markedly increase in males and markedly increase in females compared to control.In the positive control DEHP group, expected effects on the liver were observed (increased liver weights, decreased serum triglycerides and total cholesterol increased liver PCoA levels and lauric acid 11 and 12 hydroxylase activities, reduction in cytoplasmic basophilia, marked increase in peroxisome proliferation.

[2] 1325511: Fisher 344 rats (5/sex/group) were provided a diet containing 0 or 1.2% DEHP for 21 days. The experiment was repeated 7 times, as rats receiving DEHP served as a positive control group for hepatic peroxisome proliferation experiments performed with different phthalic acid esters. Authors calculated mean DEHP intake for each experiment based on dietary intake. This reviewer averaged the intake for all eight experiments. The mean intake for males was 1149 +/- 64 mg/kg/day and in females as 1115 +/- 117 mg/kg/day for all experiments. Endpoints evaluated included clinical signs (daily), body weight (days-3, 0, 3, 7, 10, 14, 17, and 20), food intake (measured in intervals from days: -3 to 0; 0-3; 3-7; 7-10; 10-14; 14-17; and 17-20), serum concentrations of triglyceride and total cholesterol, gross necropsy, organ weights (liver, kidney, and testes), histopathology (liver, kidney, and testes), biochemical analysis of liver (cyanide-insensitive palmitoyl-CoA oxidation [PCoA] levels and protein concentration; microsomal fraction rate of lauric acid hydroxylation) and ultrastructure of liver to assess peroxisome proliferation).The study did not report that any animals died, and all animals were accounted for in the results. Clinical signs were not reported. Body weights were significantly decreased in males (in 6 out 8 experiments) and females (in 8 out of 8 experiments) compared to control. Food intake was significantly decreased in males (in 7/8 experiments and increased in 1/8 experiments) and females (6/8 experiments and no change in 2/8 experiments) compared to control. In males significant decreases in serum triglycerides (in 6/8 experiments) and total cholesterol (in 8/8 experiments) were seen. In females, no changes in serum triglycerides or total cholesterol were seen in 5/8 experiments; decreases in serum total cholesterol was observed in 3/8 experiments compared to control. A significant increase in absolute and relative liver weights were seen in males and females in all 8 experiments, compared to control. No changes in absolute kidney weights were seen but significant increases in relative kidney weights were observed (males 7/8 experiments; females (in 6/8 experiments) compared to control. These changes may be a reflection of the decreased body weight and not effect on the kidney itself. Changes in testis weights were not consistent between the eight experiments. Absolute and relative testis weights were significantly decreased in 1/8 experiments; increases in relative testis weight were reported in 2/8 experiments; decreases in relative testis weight was reported in 1/8 experiments; no change absolute or relative testis weights were seen in 4/8 experiments compared to control. Histologically, reduction of cytoplasmic basophilia in the liver was observed in 5/5 males and 5/5 females in all 8 experiments. No significant histological changes were seen in the kidneys or testis in male or females in all 8 experiments. Significant increases in liver PCoA levels and lauric acid 11 and 12 hydroxylase activities, and marked increase in peroxisome proliferation were observed in male and female rats after exposure.

[3] 11151638: Adult female CD-1 mice (6/group) were administered 0, 0.02, 0.2, 2, 20, or 200 mg/kg/day of DINP in corn oil by gently pipetting the test substance into the mouth. The mice were dosed daily for a minimum of 10 days and sacrificed during diestrus (determined by monitoring estrous cyclicity via vaginal lavage). Mice that were not in diestrus on day 10 continued to be dosed (up to day 14) until they were in diestrus. At sacrifice, blood was collected to determine estradiol levels. The distal colon was weighed and processed for either immunohistochemistry (Ki67 to determine proliferating cells or MUC2 as a marker of goblet cells), determination of cytokine levels (via array or ELISA [CXCL12 and IL-1RA]), or colon mRNA levels of immune and immune-related factors: mucins (Muc1, 2, 3a, and 4), toll-like receptors (Trl4and 5), and specialized epithelial cells (ChgA [mature enteroendocrine cells], Lgr5 [stem cells], Lyz1 [Paneth cell marker], Cd24a [epithelial cell marker for cells located at bottom of intestinal crypts], and Vil1 [epithelium border]). Serum estradiol levels were significantly increased at 20 mg/kg/day (~ 6-fold); however, at 200 mg/kg/day levels were non-significantly increased (~4.8-fold) compared to control. No significant difference in CXCL12 or IL-1RA levels in the colon was seen either by ELISA or immunoblot screening. The number of proliferating cells in the colon (Ki67 positive cells) was significantly increased at $\geq$ 0.02 mg/kg/day (~2.4-2.8 fold) over control levels. Protein levels of MUC2 (goblet cell marker) were significantly increased in the colon at $\geq$0.2 mg/kg/day; levels were also increased at 0.02 mg/kg/day; however, due to a large variation, the levels were not statistically significant. mRNA levels of Paneth cells marker (Lyz1) were significantly increased at 200 mg/kg/day. No other mRNA levels were significantly increased compared to controls.The study authors did not report NOAEL or LOAEL. A mechanistic LOEL of 0.02 mg/kg/day (lowest dose tested) was determined for increased cell proliferation in the colon. No apical POD was identified.

[4] 11151638: Adult female CD-1 mice (6/group) were administered 0, 0.02, 0.2, 2, 20, or 200 mg/kg/day of DINP in corn oil by gently pipetting the test substance into the mouth. The mice were dosed daily for a minimum of 10 days and sacrificed during diestrus (determined by monitoring estrous cyclicity via vaginal lavage). Mice that were not in diestrus on day 10 continued to be dosed (up to day 14) until they were in diestrus. At sacrifice, blood was collected to determine estradiol levels. The distal colon was weighed and processed for either immunohistochemistry (Ki67 to determine proliferating cells or MUC2 as a marker of goblet cells), determination of cytokine levels (via array or ELISA [CXCL12 and IL-1RA]), or colon mRNA levels of immune and immune-related factors: mucins (Muc1, 2, 3a, and 4), toll-like receptors (Trl4and 5), and specialized epithelial cells (ChgA [mature enteroendocrine cells], Lgr5 [stem cells], Lyz1 [Paneth cell marker], Cd24a [epithelial cell marker for cells located at bottom of intestinal crypts], and Vil1 [epithelium border]). Serum estradiol levels were significantly increased at 20 mg/kg/day (~ 6-fold); however, at 200 mg/kg/day levels were non-significantly increased (~4.8-fold) compared to control. No significant difference in CXCL12 or IL-1RA levels in the colon was seen either by ELISA or immunoblot screening. The number of proliferating cells in the colon (Ki67 positive cells) was significantly increased at $\geq$ 0.02 mg/kg/day (~2.4-2.8 fold) over control levels. Protein levels of MUC2 (goblet cell marker) were significantly increased in the colon at $\geq$0.2 mg/kg/day; levels were also increased at 0.02 mg/kg/day; however, due to a large variation, the levels were not statistically significant. mRNA levels of Paneth cells marker (Lyz1) were significantly increased at 200 mg/kg/day. No other mRNA levels were significantly increased compared to controls.The study authors did not report NOAEL or LOAEL. A mechanistic LOEL of 0.02 mg/kg/day (lowest dose tested) was determined for increased cell proliferation in the colon. No apical POD was identified.

[5] 11151638: Adult female CD-1 mice (6/group) were administered 0, 0.02, 0.2, 2, 20, or 200 mg/kg/day of DINP in corn oil by gently pipetting the test substance into the mouth. The mice were dosed daily for a minimum of 10 days and sacrificed during diestrus (determined by monitoring estrous cyclicity via vaginal lavage). Mice that were not in diestrus on day 10 continued to be dosed (up to day 14) until they were in diestrus. At sacrifice, blood was collected to determine estradiol levels. The distal colon was weighed and processed for either immunohistochemistry (Ki67 to determine proliferating cells or MUC2 as a marker of goblet cells), determination of cytokine levels (via array or ELISA [CXCL12 and IL-1RA]), or colon mRNA levels of immune and immune-related factors: mucins (Muc1, 2, 3a, and 4), toll-like receptors (Trl4and 5), and specialized epithelial cells (ChgA [mature enteroendocrine cells], Lgr5 [stem cells], Lyz1 [Paneth cell marker], Cd24a [epithelial cell marker for cells located at bottom of intestinal crypts], and Vil1 [epithelium border]). Serum estradiol levels were significantly increased at 20 mg/kg/day (~ 6-fold); however, at 200 mg/kg/day levels were non-significantly increased (~4.8-fold) compared to control. No significant difference in CXCL12 or IL-1RA levels in the colon was seen either by ELISA or immunoblot screening. The number of proliferating cells in the colon (Ki67 positive cells) was significantly increased at $\geq$ 0.02 mg/kg/day (~2.4-2.8 fold) over control levels. Protein levels of MUC2 (goblet cell marker) were significantly increased in the colon at $\geq$0.2 mg/kg/day; levels were also increased at 0.02 mg/kg/day; however, due to a large variation, the levels were not statistically significant. mRNA levels of Paneth cells marker (Lyz1) were significantly increased at 200 mg/kg/day. No other mRNA levels were significantly increased compared to controls.The study authors did not report NOAEL or LOAEL. A mechanistic LOEL of 0.02 mg/kg/day (lowest dose tested) was determined for increased cell proliferation in the colon. No apical POD was identified.

[6] 7978425: Female CD-1 mice aged 2 months were exposed to DINP (CASRN# 28553-12-0) at doses of 0 (control group received corn oil), 0.02, 0.2,2,20,200 mg/kg daily for 10-14 days to evaluate the subacute DINP exposure toxicity on the gastrointestinal tract (GIT). In all mice, the colon length ranged from 5.8 to 10.2 cm. DINP exposure at all doses did not significantly affect colon length, weight, or the weight-to-length ratio compared to the control. The study observed significant histological damage in the colon, including enterocyte sloughing, focal or cellular inflammation, edema, crypt damage, and aberrant colon walls (graded 0 to 3, with 0 being normal, 1 being minimal or mild, 2 being moderate, and 3 being severe; the grade were summed to give each tissue a total score). DINP doses of 0.02, 0.2, 2, and 200mg/kg showed increased colon damage compared to control. Notably, low doses (0.02, 0.2mg/kg/d) primarily caused cellular infiltration, changes in colon walls, and enterocyte sloughing. While the highest doses (2 and 200mg/kg) were associated with edema. The study also examined the effects of DINP on colon sex hormones, including testosterone and estradiol. At 0.02mg/kg/d slightly reduced testosterone levels, while doses (0.2, 20 and 200 mg/kg/day) significantly reduced estradiol levels compared to the control. Gene expression related to cell cycle regulation, such as cyclin (cyclinA2 (Ccna2), cyclin B1 (Ccnb1), cyclin D2 (Ccnd2), cyclin E2 (Ccne1)), and cyclin dependent kinase 4 (Cdk4), remained unaffected by DINP exposure, except at 200mg/kg, which significantly reduced Ccnb1 expression compared to control. Apoptosis and cell proliferation factors, including Aifm1 and Bcl2l10, were also analyzed. DINP environmentally

relevant dose (0.2 mg/kg/day) increased Aifm1 expression, while 20 mg/kg/day significantly increased Bcl2l10 expression. Despite these changes, TUNEL staining showed no significant DNA fragmentation caused by DINP exposure. Distal colon inflammation expression, such as expression of the following (Il4, Il5, Il6, Il13, Il17a, Tnf, and Ifng, was measured. DINP did not significantly alter most markers, though environmentally relevant doses 0.02, and 0.2mg/kg/day slightly increased interferon gamma (Ifng), and (0.2 mg/kg/day) of DINP exposure significantly increased Tnf expression compared to control. However, these changes did not result in altered TNF protein levels. sICAM-1 level showed a dose -dependent response, with slight increases at low doses and significant decreases at high doses. Tight junction proteins playing a role in mediating immune responses were also examined (Zo-1, Zo-2, Zo-3, Cldn1, Cldn4, and Ocln), with significantly reduction of Zo-3 expression was seen at 200mg/kg DINP compared to control.

[7] 1325350: Timed-pregnant Sprague-Dawley rats were administered 0, 50, 250, or 500 mg/kg/day of diisononyl phthalate (DiNP) in corn oil via gavage from GD 12-19. Animals were sacrificed 0.5, 1, 6 and 12 hours after last dose (4 litters/group/time point) or 2 and 24 hours (8-9 litters/group/timepoint). At the 2-hour time-point the following were evaluated: maternal weight, maternal liver weight, fetal weight, and testis testosterone levels. At 24-hour time-point the following were evaluated: fetal weight, anogenital distance (AGD), testis testosterone, and histology on testis was examined. AGD was measured in fetuses from 24-hour time point. One pair of fetal testes from control (n=9) and DiNP treated rats (n=8) from the 24-hour time point were collected for histopathological examination (seminiferous tubule morphology and organization, presence of multinucleated gonocytes (MNG), and morphology and relative size of interstitial Leydig cell aggregates). Morphological changes were scored from minimal (grade 1) to severe (grade 5). The following tissues were collected and analyzed for DiNP metabolites (MCiOP, MiNP, MHiNP, MOiNP, and MiNP-G) over the time course: maternal plasma, maternal liver, placenta, maternal urine (measured at 7 and 24 hours after final dose), amniotic fluid, fetal plasma, and fetal testes. No significant difference in maternal weight gain or terminal maternal weight were seen compared to control. Maternal liver weight was significantly increased at 250 mg/kg/day (17% and 15%) at 250 and 750 mg/kg/day, respectively. DiNP did not induce spontaneous abortion or increased incidence of fetal resorption. No significant differences in AGD or AGD/BW were seen compared to control. Fetal weights 2 hours and 24 hours after last dose were similar to control. A significant increase in the number of animals with MNGs (6/7) and LC aggregates (7/7) was seen at 750 mg/kg/day (6/7) compared control (MNGs: 0/27 and LC: 2/27). The number of MNGs per testis section and MNGs per ST cross-section were significantly increased at $\geq$250 mg/kg/day. Testis testosterone levels were significantly decreased at 250 mg/kg/day (50%) and 750 mg/kg/day (65%) 2 hours after dosing compared to control. Twenty-four hours after dosing, testosterone levels appeared to be increased at $\geq$250 mg/kg/day, however the increase was not statistically significant compared to control. The study authors determine a NOEL of 50 mg/kg/day based on increased MNGs and reduced testes testosterone in fetal rat. None of the DiNP metabolites were detected in the control samples. All metabolites were detected in all tissues examined from dosed rats. MCiOP was the major metabolite, followed by MiNP, MHiNP, MOiNP and MiNP-G.

[8] 7978423: 5-week-old SPF Male Balb/c mice were exposed via dermal to DINP at five concentration levels (low and middle doses: (0.02,0.2,2mg/kg, and high doses: 20,200mg/kg), and saline control group continuously for 28 days to evaluate the hepatic and renal toxicity. Skin appearance after exposure to low (0.02-and 0.2mg/kg) and middle dose group ((2mg/kg) resulted in slightly changes of skin appearance, while significant alterations, including wrinkles and white protuberance vesicles, were observed in the high dose groups (20, and 200mg/kg). The epidermal thickness did not increase notably in the low and medium dose groups, and hair follicle structures remained clear. However, in (20 mg/kg) and the higher dose group (200 mg/kg), the epidermis thickened, and the hair follicle contours became larger. Body Weight and Organ Effects: Body weigh decreased in lower and middle (0.02,0.2,2mg/kg) doses but increased at (20,200mg/kg). Liver weight also increased at 20 and 200 mg/kg from 1.74g in the control to 2.02g. The liver organ coefficient increased from 0.051g in the control to 0.055g at 20 mg/kg. Higher DINP doses caused pronounced hepatic damage, including enlarged hepatocytes, burden liver cords broadened, and central veins expanded in the 20 and 200 mg/kg DINP groups, particularly at 200mg/kg, liver tissue appeared edematous, cytoplasm loosened, and slices became indistinct. Reactive oxygen species (ROS) levels showed no significant change in the low and medium dose groups but increased significantly at 200 gm/kg. Malondialdehyde (MDA) levels in the liver were significantly elevated in 200mg/kg group compared to control. Conversely, glutathione (GSH) levels in liver tissue were significantly reduced at higher doses. The DPC coefficient in the liver also increased significantly in the high dose group. Kidney weight decreased at low and medium doses but increased at 20 and 200 mg/kg (from 0.52g in controls to 0.640g at 200mg/kg). The kidney organ coefficient increased from 0.015g in control to 0.018g at 200mg/kg. Higher doses of DINP caused substantial kidney damage with reduced tubular space and sever edema in epithelial cells of the glomeruli at 20 and 200mg/kg. ROS and MDA levels in renal tissue increased significantly at higher doses, while GSH level decreased. The renal DPC coefficient in increased significantly at 200mg/kg. In summary, the author concluded increased DINP doses led to grater hepatic and renal toxicity in male Balb/c mice, evidenced by biochemical changes and histopathological damage in both organs.

[9] 11784618: In a short-term dietary study, adult female CD-1 mice (number per group not specified, sample sizes suggest up to 10/group) were administered diisononylphthalate (DiNP, purity not reported) at doses of 0, 0.15, 1.5, or 1500 ppm in rodent chow ad libitum for 1 month. The doses were roughly equivalent to 0.024, 0.24, and 240 mg phthalate/kg/day. Doses were selected based on published rationale. After the treatment period, mice were euthanized during diestrus and ovaries, pituitary glands, and blood were collected. One ovary per mouse was fixed, embedded, and stained; the other was frozen for RNA extraction. Slides were used to assess follicle populations by counting numbers of primordial, primary, preantral, antral, and atretic follicles and then calculating the follicle type percentage. Human counters were blinded to treatments. Blood samples were centrifuged and sera were collected for the analysis of the sex hormones progesterone, testosterone, estradiol, follicle-stimulating hormone (FSH) and luteinizing hormone (LH). Ovary tissues were used to analyze the expression of the Star, Hsd3b1, Hsd17b1, and Cyp19a1 steroidogenic genes and ovarian expression of the FSH (fshr) and LH/choriogonadotropin (Lhcgr) receptors. Pituitary tissues from these animals were presumably frozen to measure mRNA levels of genes that regulate the FSH and LH gonadotropin hormones (Nr5a1, Lhb, Fshb, and Cga), but these data were not reported and may have only been evaluated in the longer duration study (evaluated separately).Short-term exposure did not affect the number of ovarian follicles and the percentage of follicles was comparable to controls. There was no significant effect on serum progesterone, testosterone, or estradiol levels, compared to controls. There were no effects on ovarian expression of genes that regulate steroidogenesis (Star, Hsd3b1, Hsd17b1, and Cyp19a1). Treatment also did not affect the expression of the FSH receptor in the ovary. An increase in the expression of Lhcgr was borderline significant at the high dose. Serum FSH levels were significantly decreased in the mice administered 24 mg/kg-day, but not 240 mg/kg-day. No effects on serum LH levels were observed. Pituitary expression of Cga and Nr5a1 were slightly, but significantly increased at 0.024 mg/kg-day, the lowest dose, only. The authors concluded that short-term exposure to phthalates decreases FSH levels. No author-reported toxicity values were reported. Based on the data provided, a NOAEL of 0.024 mg/kg-day was determined for the lack of dose-related effects on a limited number of endpoints.

Diisononyl Phthalate- Parent compound - Subchronic (>30-91 days)

Guideline and Animal Species, Strain, Sex	Exposure Route and Exposure Duration	Study-wide POD and Dose/ Concentration(s)	Summary	Major Limitations	Principal Target Organs/Systems and OQD*	HERO ID
American Physiology Society's "Guides for the Care and Use of Laboratory Animals" published by the National Institutes of Health Mouse-ICR - [mouse]-Male	Oral-Gavage-Duration: Subchronic (>30-90 days)-7-5-week(s) 7 days/week 5 week(s) Mice were administered DINP or DEHP (0.05 and 4.8 mg/kg bw), corn oil vehicle control group daily via gavage for 5 weeks.	**POD: 0.05 mg/kg-bw/day (LOAEL) -Significant increase of body weight in mice and increased oxidative stress, reduced GSH and MDA** n= 8 Dose= 0, n= 8 Dose= 0.05, n= 8 Dose= 4.8, mg/kg-bw/day	See footnotes for full summary [1]	Limitation of this study was the lack of data on food intake and changes of adipose tissue which are useful in interpreting the body weight changes observed in the low dose groups	Nutritional/Metabolic-Body weight-Renal/Kidney-organ weight, renal biomarkers for oxidative stress (ROS, MDA, GSH), inflammatory cytokines (TNF-a and IL-6); Medium	7978408

* Overall Quality Determination

[1] 7978408: Male ICR mice were exposed to DINP or DEHP of 0.05 (low dose) and 4.8 mg/kg bw (high dose), and corn oil vehicle (control group) daily via gavage for 5 weeks to evaluate the renal toxicity. Mice administered a low dose (0.05 mg/kg bw) showed a significant increase in body weight, while those given a high dose (4.8 mg/kg bw) exhibited a decrease, compared to the control group. Despite changes in body weight, no differences in kidney organ weight were observed between the control and treatment groups. Urinary metabolites revealed that the major metabolites of DEHP (MEHP, MEOHP, MEHHP, and MECPP) and DINP (MINP and MCOP) were approximately two-fold higher in the high dose group compared to the control in DINP/DEHP treated groups. The study revealed that phthalates induced oxidative stress and disrupted metabolic responses. Notably, there was an increase in renal ROS and MDA levels and decrease in GSH levels at higher doses of DINP/DEHP. Additionally, elevated levels of inflammatory cytokines (TNF-a and IL-6) were observed following higher exposure. 246 lipids were quantifiable, including ceramides (Cer), sphingomyelin (SM), phosphatidylcholine (PC), PC alkyl ether [PC-(O)], PC plasmalogen [PC-(P)], lyso PC (LPC), di-acylglyceride (DG), tri-acylglyceride (TG), and cholesterol esters (CE), as well as other groups. Lipidomic alterations induced by high doses were significant, particularly in phospholipids and diacylglycerides, which accumulated and contributed to inflammation and metabolic disruption. Additionally, a heatmap analysis indicated marginal changes in the lipidomic profile, with a notable reduction in certain lipids, including specific sphingolipids and glycolipids (Cer, SM, PC, LPC) identified in the higher dose group. On the contrary, DG and some CE were found to be substantially elevated in DINP/DEHP high doses treated mice compared to the control mice. Variable importance in projection (VIP) scores calculated using the PLS-DA model identified differential lipid molecules induced by phthalate exposure, included DG (DG 16:0_20:3, DG 16:0_18:2, DG 16:0_18:0, DG 18:1_18:2, DG 18:1_18:3, and DG 16:0_16:0), all which VIP scores exceeding 4, suggesting high predictability for phthalate induced disruptions in lipid metabolism.

Diisononyl Phthalate- Parent compound - Chronic (>91 days)

Guideline and Animal Species, Strain, Sex	Exposure Route and Exposure Duration	Study-wide POD and Dose/ Concentration(s)	Summary	Major Limitations	Principal Target Organs/Systems and OQD*	HERO ID
No specific guidance document was cited, other than the authors specifying that the study was conducted for Monsanto, so it may adhere to Monsanto's internal guidelines. Rat-Other (Sprague-Dawley CD)-Both	Oral-Diet-Duration: Chronic (>90 days)-2-year(s) 2 year(s)	**POD: 27 ppm (in air, water, or food) (LOAEL) -Increased absolute and relative thyroid weights and blood serum chemistry parameter changes (increased serum glutamic oxaloacetic transaminase, serum glutamic pyruvic transaminase and alkaline phosphatase in males)** n= 70 Dose= 0, n= 70 Dose= 27, n= 70 Dose= 271, n= 70 Dose= 553, ppm (in air, water, or food)	See footnotes for full summary [1]	There are some minor concerns regarding potential palatability issues and lacking detail on statistical methods. Methods to reduce observational bias were also not stated.	Hepatic/Liver-Blood serum chemistry (total protein, triglycerides, blood urea nitrogen, albumin, fasting glucose, globulin, glutamic pyruvic transaminase, A/G Ratio, Glutamic oxaloacetic transaminase, sodium, alkaline phosphatase, potassium, cholesterol, calcium), organ weights: liver, gross pathology and histopathology: liver-Other (please specify below) (Endocrine)-Organ weights: adrenals, pituitary, thyroid/parathyroids, gross pathology and histopathology: adrenals, pancreas, pituitary, thymus, thyroid/parathyroids-Cancer/Carcinogenesis-Neoplastic lesions; High	679889

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Diisononyl Phthalate- Parent compound - Chronic (>91 days)

Guideline and Animal Species, Strain, Sex	Exposure Route and Exposure Duration	Study-wide POD and Dose/ Concentration(s)	Summary	Major Limitations	Principal Target Organs/Systems and OQD*	HERO ID
No specific guidance document was cited, other than the authors specifying that the study was conducted for Monsanto, so it may adhere to Monsanto's internal guidelines. Rat-Other (Sprague-Dawley CD)-Both	Oral-Diet-Duration: Chronic (>90 days)-2-year(s) 2 year(s)	**POD: 27 ppm (in air, water, or food) (LOAEL) -Increased absolute and relative thyroid weights and blood serum chemistry parameter changes (increased serum glutamic oxaloacetic transaminase, serum glutamic pyruvic transaminase and alkaline phosphatase in males)** n= 70 Dose= 0, n= 70 Dose= 27, n= 70 Dose= 271, n= 70 Dose= 553, ppm (in air, water, or food)	See footnotes for full summary [2]	There are some minor concerns regarding potential palatability issues and lacking detail on statistical methods. Methods to reduce observational bias were also not stated.	Hepatic/Liver-Blood serum chemistry (total protein, triglycerides, blood urea nitrogen, albumin, fasting glucose, globulin, glutamic pyruvic transaminase, A/G Ratio, Glutamic oxaloacetic transaminase, sodium, alkaline phosphatase, potassium, cholesterol, calcium), organ weights: liver, gross pathology and histopathology: liver-Other (please specify below) (Endocrine)-Organ weights: adrenals, pituitary, thyroid/parathyroids, gross pathology and histopathology: adrenals, pancreas, pituitary, thymus, thyroid/parathyroids-Cancer/Carcinogenesis-Neoplastic lesions; Medium	679889

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Diisononyl Phthalate- Parent compound - Chronic (>91 days)

Guideline and Animal Species, Strain, Sex	Exposure Route and Exposure Duration	Study-wide POD and Dose/ Concentration(s)	Summary	Major Limitations	Principal Target Organs/Systems and OQD*	HERO ID
No specific guidance document was cited, other than the authors specifying that the study was conducted for Monsanto, so it may adhere to Monsanto's internal guidelines. Rat-Other (Sprague-Dawley CD)-Both	Oral-Diet-Duration: Chronic (>90 days)-2-year(s) 2 year(s)	**POD: 27 ppm (in air, water, or food) (LOAEL) -Increased absolute and relative thyroid weights and blood serum chemistry parameter changes (increased serum glutamic oxaloacetic transaminase, serum glutamic pyruvic transaminase and alkaline phosphatase in males)** n= 70 Dose= 0, n= 70 Dose= 27, n= 70 Dose= 271, n= 70 Dose= 553, ppm (in air, water, or food)	See footnotes for full summary [3]	There are some minor concerns regarding potential palatability issues and lacking detail on statistical methods. Methods to reduce observational bias were also not stated.	Hepatic/Liver-Blood serum chemistry (total protein, triglycerides, blood urea nitrogen, albumin, fasting glucose, globulin, glutamic pyruvic transaminase, A/G Ratio, Glutamic oxaloacetic transaminase, sodium, alkaline phosphatase, potassium, cholesterol, calcium), organ weights: liver, gross pathology and histopathology: liver-Other (please specify below) (Endocrine)-Organ weights: adrenals, pituitary, thyroid/parathyroids, gross pathology and histopathology: adrenals, pancreas, pituitary, thymus, thyroid/parathyroids-Cancer/Carcinogenesis-Neoplastic lesions; High	679889
U.S. Environmental Protection Agency (Toxic Substances Control Act, 40 CFR Part 798.3300); the study was GLP compliant. Mouse-B6C3F1 - [mouse]-Both	Oral-Diet-Duration: Chronic (>90 days)-7-104-week(s) 7 days/week 104 week(s) Animals were exposed for at least 104 weeks via the diet. A recovery group was exposed for 78 weeks (followed by a 26-week recovery); interim sacrifice at 79 weeks.	**POD: 112 mg/kg-bw/day (Dichotomous (P/N)) - positive for carcinogenicity (combined incidence of hepatocellular adenomas and carcinomas in females)** n= 140 Dose= 0, n= 140 Dose= 112.0, n= 140 Dose= 335.6, n= 140 Dose= 910.3, n= 140 Dose= 1887.6, mg/kg-bw/day	See footnotes for full summary [4]	No major limitations were identified.	Mortality; Nutritional/Metabolic; Renal/Kidney; Hepatic/Liver; Cancer/Carcinogenesis; High	1325481

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Diisononyl Phthalate- Parent compound - Chronic (>91 days)

Guideline and Animal Species, Strain, Sex	Exposure Route and Exposure Duration	Study-wide POD and Dose/ Concentration(s)	Summary	Major Limitations	Principal Target Organs/Systems and OQD*	HERO ID
U.S. Environmental Protection Agency (Toxic Substances Control Act, 40 CFR Part 798.3300); the study was GLP compliant. Mouse-B6C3F1 - [mouse]-Both	Oral-Diet-Duration: Chronic (>90 days)-7-104-week(s) 7 days/week 104 week(s) Animals were exposed for at least 104 weeks via the diet. A recovery group was exposed for 78 weeks (followed by a 26-week recovery); interim sacrifice at 79 weeks.	**POD: 112 mg/kg-bw/day (Dichotomous (P/N)) - positive for carcinogenicity (combined incidence of hepatocellular adenomas and carcinomas in females)** n= 140 Dose= 0, n= 140 Dose= 112.0, n= 140 Dose= 335.6, n= 140 Dose= 910.3, n= 140 Dose= 1887.6, mg/kg-bw/day	See footnotes for full summary [5]	No major limitations were identified.	Mortality; Nutritional/Metabolic; Renal/Kidney; Hepatic/Liver; Cancer/Carcinogenesis; High	1325481
U.S. Environmental Protection Agency (Toxic Substances Control Act, 40 CFR Part 798.3300); the study was GLP compliant. Mouse-B6C3F1 - [mouse]-Both	Oral-Diet-Duration: Chronic (>90 days)-7-104-week(s) 7 days/week 104 week(s) Animals were exposed for at least 104 weeks via the diet. A recovery group was exposed for 78 weeks (followed by a 26-week recovery); interim sacrifice at 79 weeks.	**POD: 112 mg/kg-bw/day (Dichotomous (P/N)) - positive for carcinogenicity (combined incidence of hepatocellular adenomas and carcinomas in females)** n= 140 Dose= 0, n= 140 Dose= 112.0, n= 140 Dose= 335.6, n= 140 Dose= 910.3, n= 140 Dose= 1887.6, mg/kg-bw/day	See footnotes for full summary [6]	No major limitations were identified.	Mortality; Nutritional/Metabolic; Renal/Kidney; Hepatic/Liver; Cancer/Carcinogenesis; High	1325481
U.S. Environmental Protection Agency (Toxic Substances Control Act, 40 CFR Part 798.3300); the study was GLP compliant. Rat-Other (CDF (F-344) CrlBR)-Both	Oral-Diet-Duration: Chronic (>90 days)-7-104-week(s) 7 days/week 104 week(s) Animals were exposed up to 104 weeks via the diet. A recovery group was exposed for 78 weeks; interim sacrifices at 1, 2, 13, and 78 weeks.	**POD: 358.7 mg/kg-bw/day (Dichotomous (P/N)) - Positive for carcinogenicity (mononuclear cell leukemia)** n= 170 Dose= 0, n= 140 Dose= 29.2, n= 140 Dose= 88.3, n= 170 Dose= 358.7, n= 170 Dose= 733.2, mg/kg-bw/day	See footnotes for full summary [7]	No major limitations were identified.	Mortality; Nutritional/Metabolic; Hepatic/Liver; Renal/Kidney; Cancer/Carcinogenesis-Microscopic examinations for tumors; High	680087

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Diisononyl Phthalate- Parent compound - Chronic (>91 days)

Guideline and Animal Species, Strain, Sex	Exposure Route and Exposure Duration	Study-wide POD and Dose/ Concentration(s)	Summary	Major Limitations	Principal Target Organs/Systems and OQD*	HERO ID
U.S. Environmental Protection Agency (Toxic Substances Control Act, 40 CFR Part 798.3300); the study was GLP compliant. Rat-Other (CDF (F-344) CrlBR)-Both	Oral-Diet-Duration: Chronic (>90 days)-7-104-week(s) 7 days/week 104 week(s) Animals were exposed up to 104 weeks via the diet. A recovery group was exposed for 78 weeks; interim sacrifices at 1, 2, 13, and 78 weeks.	**POD: 358.7 mg/kg-bw/day (Dichotomous (P/N)) - Positive for carcinogenicity (mononuclear cell leukemia)** n= 170 Dose= 0, n= 140 Dose= 29.2, n= 140 Dose= 88.3, n= 170 Dose= 358.7, n= 170 Dose= 733.2, mg/kg-bw/day	See footnotes for full summary [8]	No major limitations were identified.	Nutritional/Metabolic; Renal/Kidney; Hepatic/Liver; Cancer/Carcinogenesis; High	680087
U.S. Environmental Protection Agency (Toxic Substances Control Act, 40 CFR Part 798.3300); the study was GLP compliant. Rat-Other (CDF (F-344) CrlBR)-Both	Oral-Diet-Duration: Chronic (>90 days)-7-104-week(s) 7 days/week 104 week(s) Animals were exposed up to 104 weeks via the diet. A recovery group was exposed for 78 weeks; interim sacrifices at 1, 2, 13, and 78 weeks.	**POD: 358.7 mg/kg-bw/day (Dichotomous (P/N)) - Positive for carcinogenicity (mononuclear cell leukemia)** n= 170 Dose= 0, n= 140 Dose= 29.2, n= 140 Dose= 88.3, n= 170 Dose= 358.7, n= 170 Dose= 733.2, mg/kg-bw/day	See footnotes for full summary [9]	No major limitations were identified.	Nutritional/Metabolic; Renal/Kidney; Hepatic/Liver; Cancer/Carcinogenesis; High	680087
No compliance methods or guidelines were reported. Mouse-CD-1 - [mouse]-Female	Oral-Diet-Duration: Chronic (>90 days)-7-11-month(s) 7 days/week 11 month(s)	**POD: 1500 ppm (in air, water, or food) (NOAEL) -No dose-related adverse effect** n= 12 Dose= 0, n= 12 Dose= 0.15, n= 12 Dose= 1.5, n= 12 Dose= 1500, ppm (in air, water, or food)	See footnotes for full summary [10]	Phthalate concentration in the diet was not verified. Authors estimate daily intake but do not base it on measured food intake or body weight.	Reproductive/Developmental- Estrous cycle; Fertility indices (mating index, gestational index, pregnancy, birth rate, dystocia and fertility index); Low	11784622
No compliance methods or guidelines were reported. Mouse-CD-1 - [mouse]-Female	Oral-Diet-Duration: Chronic (>90 days)-7-11-month(s) 7 days/week 11 month(s)	**POD: 1.5 ppm (in air, water, or food) (NOAEL) -Decreased gestational index and birth rate** n= 12 Dose= 0, n= 12 Dose= 0.15, n= 12 Dose= 1.5, n= 12 Dose= 1500, ppm (in air, water, or food)	See footnotes for full summary [11]	Phthalate concentration in the diet was not verified. Authors estimate daily intake but do not base it on measured food intake or body weight. The reproductive endpoints used to calculate the reproductive indices were not reported.	Reproductive/Developmental- Estrous cycle; Fertility indices (mating index, gestational index, pregnancy, birth rate, dystocia and fertility index); Medium	11784622

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Diisononyl Phthalate- Parent compound - Chronic (>91 days)

Guideline and Animal Species, Strain, Sex	Exposure Route and Exposure Duration	Study-wide POD and Dose/ Concentration(s)	Summary	Major Limitations	Principal Target Organs/Systems and OQD*	HERO ID
No guidelines or adherence to GLP were reported. Mouse-CD-1 - [mouse]-Female	Oral-Diet-Duration: Chronic (>90 days)-7-6-month(s) 7 days/week 6 month(s) Mice were exposed via the diet ad libitum for 6 months	**POD: 0.024 mg/kg-bw/day (NOAEL) - significant decreases in luteinizing hormone** n= 10 Dose= 0, n= 10 Dose= 0.024, n= 10 Dose= 0.24, n= 10 Dose= 240, mg/kg-bw/day	See footnotes for full summary [12]	This was a dietary study that did not report food intake or body weights; however, the reported doses in mg/kg-day are generally consistent with doses calculated using default body weight and food consumption values in female mice. There were other minor reporting deficiencies (test substance purity, animal husbandry, and number of animals per group).	Reproductive/Developmental-Ovary histopathology, serum hormones (progesterone, testosterone, estradiol, FSH, LH), and gene expression in ovarian tissue-Other (please specify below) (Endocrine)-Gene expression in pituitary tissue; Medium	11784618

* Overall Quality Determination

[1] 679889: Sprague-Dawley CD rats (70/sex/group) were exposed to 0, 500, 5000 or 10000 ppm of di-isonyl-pthalate (DINP) via dietary exposure in feed in the form of the proprietary commercial name Santicizer 900 plasticzer for 2 years. The study authors calculate the mean intake base on measured food consumption and body weight for males as 27, 271, and 553 mg/kg/day and for females as 33, 331, and 672 mg/kg/day at 500, 5000 and 10000 ppm, respectively.Animals were monitored daily for mortality and clinical signs of toxicity. Body weights and food consumption were measured weekly for the first 14 weeks, biweekly from weeks 16 through 26 and monthly though the end of the study. At month 6, 12, 18 and 24 of the study, all animals underwent ophthalmic examinations and 10 animals/sex/group had blood and urine collected to measure routine hematological parameters (erythrocytes, hemoglobin, total and differential leukocytes, platelets, hematocrit, erythrocyte morphology), blood serum chemistry (total protein, triglycerides, blood urea nitrogen, albumin, fasting glucose, globulin, glutamic pyruvic transaminase, A/G Ratio, Glutamic oxaloacetic transaminase, sodium, alkaline phosphatase, potassium, cholesterol, calcium) and urinalysis (pH, ketones, protein, bilirubin, occult blood, urobilinogen, glucose, urobilinogen, gross appearance, specific gravity). At week 54, 10 animals/sex/group were sacrificed, all surviving animals were sacrificed at 24 months. At sacrifice, gross necropsy was performed and the following organs were weighed: adrenals, brain, heart, kidneys, liver, ovaries, pituitary, biceps formis, testes with epididymides, thyroid/parathyroids) Histopathology was performed on the following tissues in the control and high-dose groups (adrenals, aorta, blood smear, bone marrow smear, brain, esophagus, eyes, head, heart, intestine, cecum, colon, duodenum, ileum, jejunum, rectum, kidneys, larynx, liver, lungs, lymph nodes, mammary gland, ovaries, pancreas, pituitary, prostate, salivary gland, seminal vesicles, skeletal muscle, skin, spinal cord, spleen, stomach, testes with epididymides, thymus, thyroid/parathyroid, tongue, trachea, urinary bladder, uterus (corpus and cervix uteri), gross lesions, tissue masses. For liver histopathology, all dose groups were examined.No differences in mortality were observed over the course of the study. Significantly decreased body weight were observed in females at 10000 ppm (7-12%). No significant differences in food consumption were observed, but there was a trend for increased food consumption in females. Observed hematological and blood serum chemistry changes included decreased hemoglobin, hematocrit and erythrocyte counts at 24 months at 10000 ppm in males and increased serum glutamic oxaloacetic transaminase, serum glutamic pyruvic transaminase and alkaline phosphatase in males at all timepoints at $\geq$500 ppm. No differences in urinalysis parameters nor ophthalmic examinations were observed. At 52 weeks, significant increases in the following organ weights were seen in males at 10000 ppm: relative heart (13%), absolute and relative kidney (19% and 25%, respectively); absolute and relative liver (30% and 34%, respectively). Relative thyroid weights were significantly increased in males at 500 ppm (26%) and 5000 ppm (26%); at 10000 ppm, weight was non-significantly increased 20% compared to control at 52 weeks. In females the following increases in organ weights were seen at 52 weeks: relative kidney weight (20%), and absolute and relative liver weight (26% and 36%, respectively) compared to control. Significant increase in absolute thyroid (106%, 102%, and 111%) and relative thyroid weights (93%, 93%, and 129%) occurred at 500, 5000, and 10000 ppm, respectively compared to control. At the end of the 2 years, significant increases in absolute and relative kidney weight (13%, 12%, respectively), liver (27% and 27%) and absolute pituitary (36%) were seen in males at 5000 ppm. In females after terminal sacrifice, significant increases in absolute kidney (12%), and relative liver (16%) were seen at 5000 ppm; and relative kidney (14%), absolute liver (14%) and relative liver (25%) at 10000 ppm, compared with control. Significant histopathological changes included increased incidence of hepatocellular carcinomas at $\geq$5000 ppm in both males (2/70, 2/69, 6/69, 4/70) and females (0/70, 0/70, 5/70, and 7/70) incidences at 0, 500, 5000, and 1000 ppm, respectively. Significant increased incidence of hepatic neoplastic nodules were seen at $\geq$500 ppm in males (2/70, 5/69, 6/69, and 5/70) and $\geq$5000 ppm in females (1/70, 1/70, 5/70, and 2/70) incidences at 0, 500, 5000 and 10000 ppm, respectively. In addition, increased incidence of testicular interstitial cell hyperplasia (in males) endometrial hyperplasia (in females), renal medullae mineral deposits (in males), parathyroid gland hyperplasia (in males) and pancreatic islet cell neoplasms (in males) were seen at 10000 ppm.A study-wide LOAEL of 500 ppm (27 mg/kg/day) was determined for endocrine and hepatic/liver effects due to increased absolute and relative thyroid weights and blood serum chemistry parameter changes. No NOAEL was determined.

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[4] 1325481: In an oncogenicity study, B6C3F1 mice (70/sex/group) were administered DINP (purity >99%) target concentrations of 0, 500, 1,500, 4,000, or 8,000 ppm, daily via the diet, for at least 104 weeks. The calculated average daily doses were 0, 90.3, 275.6, 741.8, and 1560.2 mg/kg-day for males and 0, 112.0, 335.6, 910.3, and 1887.6 mg/kg-day for females. A separate recovery group (55/sex) was administered 8,000 ppm for 78 weeks and allowed a 26-week recovery period prior to sacrifice at 104 weeks. The average daily doses for this group were 1377.4 and 1581.0 mg/kg-day for males and females, respectively. All mice were observed twice daily for mortality and moribundity. Cage-side observations were conducted daily, and detailed clinical examinations weekly. Body weights were recorded weekly for the first 17 weeks of treatment, then every 4 weeks thereafter. Food consumption was recorded weekly during the first 16 weeks, then every 4 weeks thereafter. Blood was collected for clinical chemistry and hematology during weeks 26, 52, 78, and 104. Urine was collected before each clinical sampling. Leukocyte differential and cellular morphology analysis were performed only for groups 1 (control) and 5 (8000 ppm) at weeks 26, 53, and 78 and all test groups at week 104. Myeloid/erythroid ratios

were calculated for any animals sacrificed in extremis and those sacrificed at weeks 78 and 104. Hepatocellular proliferation, biochemical analysis (protein concentration, cyanide-insensitive palmitoyl-CoA oxidation, and DNA concentration), and liver weights were assessed in mice (5/sex/group) from the control group and high dose group (8000 ppm) following 78 weeks and an additional group of mice (5/sex/group) following 104 weeks. Ten additional animals at 79 weeks were sacrificed for histomorphological evaluations. Select organs (lung, uterus, testes w/epididymis, brain w/stem, spleen, liver/gallbladder, and kidney) were weighed at 79 (10/sex) and 105/106 weeks. All animals were necropsied, and histopathological examinations were conducted on >30 tissues/organs from control and high-dose animals, as well as all animals that died throughout the study; select organs (liver, epididymides, uterus, spleen, kidney, and gross lesions) were also examined in animals from lower dose groups at the terminal sacrifice. For weeks 1-104 weeks, the survival of males at 8,000 ppm was significantly lower than controls. No significant effects on female survival were observed. Treatment-related clinical signs included those associated with poor health and/or death (hunched posture, hypoactivity, urine stains, and few feces). Increased incidences of swelling in the ventral-abdominal region occurred in males at ≥4,000 ppm and in females at 8,000 ppm and were associated with animals that had liver masses, Mean body weights of males and females in the 4,000 and 8,000 ppm groups were significantly lower than controls throughout much of the study period. In lower dose groups, mean body weights were decreased less consistently (e.g., at limited time points). Total mean body weight gains for the duration of the study (weeks 1-104) were significantly lower in males by 22% and 40% and in females by 18% and 20% in the 4000 ppm and 8000 ppm groups, respectively. There were no significant decreases in mean food consumption values in males or females in any treatment group compared to controls; conversely, total mean food consumption was significantly increased in males at weeks 78-104 in the 4000 and 8000 ppm groups.Hematological changes included significant decreases in leukocyte, lymphocyte, and/or segmented neutrophil counts compared to controls in males and females at week 78 in the 8000 ppm group and recovery group; the authors attributed this to treatment-related physiological stress; measurements were not taken in lower dose groups There were no significant changes in hematological parameters observed at week 104. There were no changes in cellular morphology or myeloid/erythroid ratios, compared with controls. Significantly increased serum total protein, albumin, and globulin were observed in males at 8000 ppm and/or recovery group at week 104. Mean serum ALT and AST were increased in males in the 8000 ppm group and recovery group across the collection time points, with a significant increase in AST in the recovery group at week 52 and the 8000 ppm and recovery groups at week 78. In female animals, changes in ALT and AST were not dose-dependent; only ALT was significantly increased in the female recovery group at week 78. Other significant changes in serum chemistry were considered incidental due to the low magnitude of change or lack of dose and/or time response. Urine chemistry results showed significantly increased mean urine volume with a corresponding decrease in mean urine osmolality. Significantly increased urine volumes, compared to controls, were observed at 1500 ppm in females (week 52), in the 8000 ppm and recovery males and females (weeks 52 and 78), in the 4000 ppm, 8000 ppm, and recovery group in males (week 104), and in the 8000 ppm group in females (week 104). Decreased urine osmolality values, compared to controls, were observed in males at ≥ 1500 ppm in the recovery group (week 78) and females in the 8000 ppm group (week 104). Decreased mean concentrations of urine sodium, potassium, chloride, and creatinine were observed in males and females. Mean creatinine clearance was generally comparable between all test groups. Urinalysis showed an increased incidence of ketones in females at 1500 and 4000 ppm (weeks 26 and 104) and at 8000 ppm (weeks 26, 53, 78, and 104); all other urinalysis findings were generally unremarkable. Liver cell proliferation evaluation in ancillary animals (5/sex/group) sacrificed during week 79 and in those sacrificed at 105 weeks did not show cell proliferation in males or females, compared with controls; DINP exposure did not result in significant changes in the mean labeling index of livers. Palmitoyl-CoA oxidase activity was significantly increased at the high dose (8000 ppm) in both sexes at 79 and at 105 weeks, compared with the controls. Analysis of liver DNA concentration showed no biologically relevant changes in males or females in the high dose group (8000 ppm) after weeks 79 or 105, compared with controls. Mean liver protein concentrations were significantly increased in both sexes at 8000 ppm at weeks 79 and 105. In the absence of body weight changes, absolute liver weight in ancillary animals was significantly increased in both sexes in the 8000 ppm group at both time points. At the interim sacrifice (n = 10/sex), male mice had significantly decreased absolute kidney weight at ≥ 1500 ppm (10%) and decreased relative (to body (16-19%) and brain wt (24-30%) kidney weights at ≥ 4,000 ppm; there were no significant kidney weight changes in females. Absolute liver weight was significantly increased in both sexes at 8000 ppm (38-39%) and relative liver weight was significantly increased in males at ≥ 4,000 ppm (37%) and in females at 8000 ppm (48%). Other significant organ weight changes included increased relative brain weight in males at ≥ 4000 ppm, decreased absolute and relative uterus weight at 500 ppm and 1500 ppm, and decreased absolute and relative (to brain wt) uterus weight at 8000 ppm. At 104 weeks, absolute and relative (to brain wt) kidney weights in males were significantly decreased at ≥ 1500 ppm (24-25%) and relative (to body wt) kidney weight was decreased only at 4000 ppm (13.4); there were no significant kidney weight changes in females. Absolute (13-33%) and relative (to body [26-60%] and brain wt [7-24%]) liver weights were significantly increased in males and statistically non-significantly increased in females at ≥ 4000 ppm. Absolute and relative (to brain wt) testis weights were significantly decreased at ≥ 4000 ppm; there were no corresponding histomorphologic effects in the testes. In addition, relative lung weight was significantly increased in males at 8000 ppm and relative brain weight was increased in males at ≥ 4000 ppm. Absolute and relative (to brain wt) kidney weights and absolute and relative (to brain wt) testis weights were still decreased and relative liver and lung weights in males were still increased following the 26-week recovery period. Mean terminal body weights at the 104-week sacrifice were significantly lower in males at ≥ 4000 (10-17%) and in females at ≥ 4000 ppm (7-8%), though not statistically significant in females.Necropsy showed lung masses in male mice, liver masses in mice of both sexes, enlarged spleen in females, and granular pitted/rough kidney is females. Microscopic evaluation showed non-treatment-related incidences of alveolar/bronchiolar neoplasms of the lung and occasional incidences of pulmonary metastasis stemming from hepatocellular carcinoma. Necropsy showed liver masses in mice at ≥ 4000 ppm that corresponded to hepatocellular neoplasms or involvement by lymphoma or histiocytic sarcoma. Histopathology findings at the 79-week sacrifice showed treatment-related histomorphologic alterations in the livers of males and females at 8000 ppm and the kidneys of females at 8000 ppm. In addition, treatment-related liver changes included increased cytoplasmic eosinophilia, diffuse hepatocellular enlargement and pigment, focal necrosis, individual cell necrosis, and hepatocellular neoplasms (adenoma and carcinoma). Incidence of hepatocellular adenomas and carcinomas (combined) in the 0, 500, 1500, 4000, and 8000 ppm groups were 1/15, 1/10, 4/10, 3/10, and 4/10, respectively in males and 0/15, 1/10, 1/10, 0/10, and 3/10, respectively in females. There was an increased incidence of chronic progressive nephropathy in all females (10/10) sacrificed at 79 weeks at 8000 ppm, compared with 4/10 in controls. Microscopic analysis of tissues at the 104-week terminal sacrifice also showed increased cytoplasmic eosinophilia, diffuse hepatocellular enlargement, and pigment in high-dose males and females; these findings were not observed in a treatment-related manner at 4000 ppm or in the high dose recovery mice. The incidence and severity of chronic progressive nephropathy was slightly increased at terminal sacrifice in females at 8000 ppm which corresponded to the pitted/rough appearance of the kidneys in high-dose females. Enlarged spleen observed in gross pathology was most often due to increased extramedullary hematopoiesis or to involvement by hemangioma/hemangiosarcoma, or hematopoietic neoplasia. All other findings were considered by the authors to be incidental and not treatment-related. The terminal sacrifice (week 104) showed increased incidences of hepatocellular neoplasms (adenomas and carcinomas) in females at 8000 ppm (3/42, 4/36, 5/37, 5/29, and 20/40 in the 0, 500, 1500, 4000, and 8000 ppm groups, respectively) and a slight increase in males at ≥ 4000 ppm (14/45, 8/41, 10/36, 16/35, and 18/32 in the 0, 500, 1500, 4000, and 8000 ppm groups, respectively). Histopathology results for all animals evaluated from unscheduled deaths and interim and terminal sacrifices showed increased incidence of hepatocellular adenomas (at 8000 ppm in females) and carcinomas (at ≥ 4000 in males and females); total combined incidence of adenomas and carcinomas was increased in males at ≥ 4000 ppm (16/70, 13/60, 18/60, 28/60 and 31/70 in the 0, 500, 1500, 4000, and 8000 ppm groups, respectively) and in females at ≥ 1500 ppm (3/70, 5/61, 10/60, 11/60, and 32/70 in the 0, 500, 1500, 4000, and 8000 ppm groups, respectively). These neoplasms in recovery animals that were treated for 78 weeks to 8000 ppm showed that effects in the liver and kidney, including liver neoplasms were partially reversible. The primary cause of both male and female deaths was hepatocellular neoplasia, which was increased in frequency in the 4,000 ppm and 8,000 ppm groups. The author reported a NOEL/NOAEL for systemic toxicity of 500 ppm, based on increased incidences of hepatocellular adenomas and carcinomas (combined) in female mice at 1500 ppm. Hepatocellular neoplasms in both sexes were apparent at ≥ 4000 ppm and gross and microscopic evidence of nonneoplastic effects were apparent in livers (males and females) and kidneys (of females) at a higher dose (8000 ppm). The test substance was positive for carcinogenicity.

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Select organs (lung, uterus, testes w/epididymis, brain w/stem, spleen, liver/gallbladder, and kidney) were weighed at 79 (10/sex) and 105/106 weeks. All animals were necropsied, and histopathological examinations were conducted on >30 tissues/organs from control and high-dose animals, as well as all animals that died throughout the study; select organs (liver, epididymides, uterus, spleen, kidney, and gross lesions) were also examined in animals from lower dose groups at the terminal sacrifice. For weeks 1-104 weeks, the survival of males at 8,000 ppm was significantly lower than controls. No significant effects on female survival were observed. Treatment-related clinical signs included those associated with poor health and/or death (hunched posture, hypoactivity, urine stains, and few feces). Increased incidences of swelling in the ventral-abdominal region occurred in males at ≥4,000 ppm and in females at 8,000 ppm and were associated with animals that had liver masses, Mean body weights of males and females in the 4,000 and 8,000 ppm groups were significantly lower than controls throughout much of the study period. In lower dose groups, mean body weights were decreased less consistently (e.g., at limited time points). Total mean body weight gains for the duration of the study (weeks 1-104) were significantly lower in males by 22% and 40% and in females by 18% and 20% in the 4000 ppm and 8000 ppm groups, respectively. There were no significant decreases in mean food consumption values in males or females in any treatment group compared to controls; conversely, total mean food consumption was significantly increased in males at weeks 78-104 in the 4000 and 8000 ppm groups.Hematological changes included significant decreases in leukocyte, lymphocyte, and/or segmented neutrophil counts compared to controls in males and females at week 78 in the 8000 ppm group and recovery group; the authors attributed this to treatment-related physiological stress; measurements were not taken in lower dose groups There were no significant changes in hematological parameters observed at week 104. There were no changes in cellular morphology or myeloid/erythroid ratios, compared with controls. Significantly increased serum total protein, albumin, and globulin were observed in males at 8000 ppm and/or recovery group at week 104. Mean serum ALT and AST were increased in males in the 8000 ppm group and recovery group across the collection time points, with a significant increase in AST in the recovery group at week 52 and the 8000 ppm and recovery groups at week 78. In female animals, changes in ALT and AST were not dose-dependent; only ALT was significantly increased in the female recovery group at week 78. Other significant changes in serum chemistry were considered incidental due to the low magnitude of change or lack of dose and/or time response. Urine chemistry results showed significantly increased mean urine volume with a corresponding decrease in mean urine osmolality. Significantly increased urine volumes, compared to controls, were observed at 1500 ppm in females (week 52), in the 8000 ppm and recovery males and females (weeks 52 and 78), in the 4000 ppm, 8000 ppm, and recovery group in males (week 104), and in the 8000 ppm group in females (week 104). Decreased urine osmolality values, compared to controls, were observed in males at ≥ 1500 ppm in the recovery group (week 78) and females in the 8000 ppm group (week 104). Decreased mean concentrations of urine sodium, potassium, chloride, and creatinine were observed in males and females. Mean creatinine clearance was generally comparable between all test groups. Urinalysis showed an increased incidence of ketones in females at 1500 and 4000 ppm (weeks 26 and 104) and at 8000 ppm (weeks 26, 53, 78, and 104); all other urinalysis findings were generally unremarkable. Liver cell proliferation evaluation in ancillary animals (5/sex/group) sacrificed during week 79 and in those sacrificed at 105 weeks did not show cell proliferation in males or females, compared with controls; DINP exposure did not result in significant changes in the mean labeling index of livers. Palmitoyl-CoA oxidase activity was significantly increased at the high dose (8000 ppm) in both sexes at 79 and at 105 weeks, compared with the controls. Analysis of liver DNA concentration showed no biologically relevant changes in males or females in the high dose group (8000 ppm) after weeks 79 or 105, compared with controls. Mean liver protein concentrations were significantly increased in both sexes at 8000 ppm at weeks 79 and 105. In the absence of body weight changes, absolute liver weight in ancillary animals was significantly increased in both sexes in the 8000 ppm group at both time points. At the interim sacrifice (n = 10/sex), male mice had significantly decreased absolute kidney weight at ≥ 1500 ppm (10%) and decreased relative (to body (16-19%) and brain wt (24-30%) kidney weights at ≥ 4,000 ppm; there were no significant kidney weight changes in females. Absolute liver weight was significantly increased in both sexes at 8000 ppm (38-39%) and relative liver weight was significantly increased in males at ≥ 4,000 ppm (37%) and in females at 8000 ppm (48%). Other significant organ weight changes included increased relative brain weight in males at ≥ 4000 ppm, decreased absolute and relative uterus weight at 500 ppm and 1500 ppm, and decreased absolute and relative (to brain wt) uterus weight at 8000 ppm. At 104 weeks, absolute and relative (to brain wt) kidney weights in males were significantly decreased at ≥ 1500 ppm (24-25%) and relative (to body wt) kidney weight was decreased only at 4000 ppm (13.4); there were no significant kidney weight changes in females. Absolute (13-33%) and relative (to body [26-60%] and brain wt [7-24%]) liver weights were significantly increased in males and statistically non-significantly increased in females at ≥ 4000 ppm. Absolute and relative (to brain wt) testis weights were significantly decreased at ≥ 4000 ppm; there were no corresponding histomorphologic effects in the testes. In addition, relative lung weight was significantly increased in males at 8000 ppm and relative brain weight was increased in males at ≥ 4000 ppm. Absolute and relative (to brain wt) kidney weights and absolute and relative (to brain wt) testis weights were still decreased and relative liver and lung weights in males were still increased following the 26-week recovery period. Mean terminal body weights at the 104-week sacrifice were significantly lower in males at ≥ 4000 (10-17%) and in females at ≥ 4000 ppm (7-8%), though not statistically significant in females.Necropsy showed lung masses in male mice, liver masses in mice of both sexes, enlarged spleen in females, and granular pitted/rough kidney is females. Microscopic evaluation showed non-treatment-related incidences of alveolar/bronchiolar neoplasms of the lung and occasional incidences of pulmonary metastasis stemming from hepatocellular carcinoma. Necropsy showed liver masses in mice at ≥ 4000 ppm that corresponded to hepatocellular neoplasms or involvement by lymphoma or histiocytic sarcoma. Histopathology findings at the 79-week sacrifice showed treatment-related histomorphologic alterations in the livers of males and females at 8000 ppm and the kidneys of females at 8000 ppm. In addition, treatment-related liver changes included increased cytoplasmic eosinophilia, diffuse hepatocellular enlargement and pigment, focal necrosis, individual cell necrosis, and hepatocellular neoplasms (adenoma and carcinoma). Incidence of hepatocellular adenomas and carcinomas (combined) in the 0, 500, 1500, 4000, and 8000 ppm groups were 1/15, 1/10, 4/10, 3/10, and 4/10, respectively in males and 0/15, 1/10, 1/10, 0/10, and 3/10, respectively in females. There was an increased incidence of chronic progressive nephropathy in all females (10/10) sacrificed at 79 weeks at 8000 ppm, compared with 4/10 in controls. Microscopic analysis of tissues at the 104-week terminal sacrifice also showed increased cytoplasmic eosinophilia, diffuse hepatocellular enlargement, and pigment in high-dose males and females; these findings were not observed in a treatment-related manner at 4000 ppm or in the high dose recovery mice. The incidence and severity of chronic progressive nephropathy was slightly increased at terminal sacrifice in females at 8000 ppm which corresponded to the pitted/rough appearance of the kidneys in high-dose females. Enlarged spleen observed in gross pathology was most often due to increased extramedullary hematopoiesis or to involvement by hemangioma/hemangiosarcoma, or hematopoietic neoplasia. All other findings were considered by the authors to be incidental and not treatment-related. The terminal sacrifice (week 104) showed increased incidences of hepatocellular neoplasms (adenomas and carcinomas) in females at 8000 ppm (3/42, 4/36, 5/37, 5/29, and 20/40 in the 0, 500, 1500, 4000, and 8000 ppm groups, respectively) and a slight increase in males at ≥ 4000 ppm (14/45, 8/41, 10/36, 16/35, and 18/32 in the 0, 500, 1500, 4000, and 8000 ppm groups, respectively). Histopathology results for all animals evaluated from unscheduled deaths and interim and terminal sacrifices showed increased incidence of hepatocellular adenomas (at 8000 ppm in females) and carcinomas (at ≥ 4000 in males and females); total combined incidence of adenomas and carcinomas was increased in males at ≥ 4000 ppm (16/70, 13/60, 18/60, 28/60 and 31/70 in the 0, 500, 1500, 4000, and 8000 ppm groups, respectively) and in females at ≥ 1500 ppm (3/70, 5/61, 10/60, 11/60, and 32/70 in the 0, 500, 1500, 4000, and 8000 ppm groups, respectively). These neoplasms in recovery animals that were treated for 78 weeks to 8000 ppm showed that effects in the liver and kidney, including liver neoplasms were partially reversible. The primary cause of both male and female deaths was hepatocellular neoplasia, which was increased in frequency in the 4,000 ppm and 8,000 ppm groups. The author reported a NOEL/NOAEL for systemic toxicity of 500 ppm, based on increased incidences of hepatocellular adenomas and carcinomas (combined) in female mice at 1500 ppm. Hepatocellular neoplasms in both sexes were apparent at ≥ 4000 ppm and gross and microscopic evidence of nonneoplastic effects were apparent in livers (males and females) and kidneys (of females) at a higher dose (8000 ppm). The test substance was positive for carcinogenicity.

[6] 1325481: In an oncogenicity study, B6C3F1 mice (70/sex/group) were administered DINP (purity >99%) target concentrations of 0, 500, 1,500, 4,000, or 8,000 ppm, daily via the diet, for at least 104 weeks. The calculated average daily doses were 0, 90.3, 275.6, 741.8, and 1560.2 mg/kg-day for males and 0, 112.0, 335.6, 910.3, and 1887.6 mg/kg-day for females. A separate recovery group (55/sex) was administered 8,000 ppm for 78 weeks

and allowed a 26-week recovery period prior to sacrifice at 104 weeks. The average daily doses for this group were 1377.4 and 1581.0 mg/kg-day for males and females, respectively. All mice were observed twice daily for mortality and moribundity. Cage-side observations were conducted daily, and detailed clinical examinations weekly. Body weights were recorded weekly for the first 17 weeks of treatment, then every 4 weeks thereafter. Food consumption was recorded weekly during the first 16 weeks, then every 4 weeks thereafter. Blood was collected for clinical chemistry and hematology during weeks 26, 52, 78, and 104. Urine was collected before each clinical sampling. Leukocyte differential and cellular morphology analysis were performed only for groups 1 (control) and 5 (8000 ppm) at weeks 26, 53, and 78 and all test groups at week 104. Myeloid/erythroid ratios were calculated for any animals sacrificed in extremis and those sacrificed at weeks 78 and 104. Hepatocellular proliferation, biochemical analysis (protein concentration, cyanide-insensitive palmitoyl-CoA oxidation, and DNA concentration), and liver weights were assessed in mice (5/sex/group) from the control group and high dose group (8000 ppm) following 78 weeks and an additional group of mice (5/sex/group) following 104 weeks. Ten additional animals at 79 weeks were sacrificed for histomorphological evaluations. Select organs (lung, uterus, testes w/epididymis, brain w/stem, spleen, liver/gallbladder, and kidney) were weighed at 79 (10/sex) and 105/106 weeks. All animals were necropsied, and histopathological examinations were conducted on >30 tissues/organs from control and high-dose animals, as well as all animals that died throughout the study; select organs (liver, epididymides, uterus, spleen, kidney, and gross lesions) were also examined in animals from lower dose groups at the terminal sacrifice. For weeks 1-104 weeks, the survival of males at 8,000 ppm was significantly lower than controls. No significant effects on female survival were observed. Treatment-related clinical signs included those associated with poor health and/or death (hunched posture, hypoactivity, urine stains, and few feces). Increased incidences of swelling in the ventral-abdominal region occurred in males at ≥4,000 ppm and in females at 8,000 ppm and were associated with animals that had liver masses, Mean body weights of males and females in the 4,000 and 8,000 ppm groups were significantly lower than controls throughout much of the study period. In lower dose groups, mean body weights were decreased less consistently (e.g., at limited time points). Total mean body weight gains for the duration of the study (weeks 1-104) were significantly lower in males by 22% and 40% and in females by 18% and 20% in the 4000 ppm and 8000 ppm groups, respectively. There were no significant decreases in mean food consumption values in males or females in any treatment group compared to controls; conversely, total mean food consumption was significantly increased in males at weeks 78-104 in the 4000 and 8000 ppm groups.Hematological changes included significant decreases in leukocyte, lymphocyte, and/or segmented neutrophil counts compared to controls in males and females at week 78 in the 8000 ppm group and recovery group; the authors attributed this to treatment-related physiological stress; measurements were not taken in lower dose groups There were no significant changes in hematological parameters observed at week 104. There were no changes in cellular morphology or myeloid/erythroid ratios, compared with controls. Significantly increased serum total protein, albumin, and globulin were observed in males at 8000 ppm and/or recovery group at week 104. Mean serum ALT and AST were increased in males in the 8000 ppm group and recovery group across the collection time points, with a significant increase in AST in the recovery group at week 52 and the 8000 ppm and recovery groups at week 78. In female animals, changes in ALT and AST were not dose-dependent; only ALT was significantly increased in the female recovery group at week 78. Other significant changes in serum chemistry were considered incidental due to the low magnitude of change or lack of dose and/or time response. Urine chemistry results showed significantly increased mean urine volume with a corresponding decrease in mean urine osmolality. Significantly increased urine volumes, compared to controls, were observed at 1500 ppm in females (week 52), in the 8000 ppm and recovery males and females (weeks 52 and 78), in the 4000 ppm, 8000 ppm, and recovery group in males (week 104), and in the 8000 ppm group in females (week 104). Decreased urine osmolality values, compared to controls, were observed in males at ≥ 1500 ppm in the recovery group (week 78) and females in the 8000 ppm group (week 104). Decreased mean concentrations of urine sodium, potassium, chloride, and creatinine were observed in males and females. Mean creatinine clearance was generally comparable between all test groups. Urinalysis showed an increased incidence of ketones in females at 1500 and 4000 ppm (weeks 26 and 104) and at 8000 ppm (weeks 26, 53, 78, and 104); all other urinalysis findings were generally unremarkable. Liver cell proliferation evaluation in ancillary animals (5/sex/group) sacrificed during week 79 and in those sacrificed at 105 weeks did not show cell proliferation in males or females, compared with controls; DINP exposure did not result in significant changes in the mean labeling index of livers. 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Absolute liver weight was significantly increased in both sexes at 8000 ppm (38-39%) and relative liver weight was significantly increased in males at ≥ 4,000 ppm (37%) and in females at 8000 ppm (48%). Other significant organ weight changes included increased relative brain weight in males at ≥ 4000 ppm, decreased absolute and relative uterus weight at 500 ppm and 1500 ppm, and decreased absolute and relative (to brain wt) uterus weight at 8000 ppm. At 104 weeks, absolute and relative (to brain wt) kidney weights in males were significantly decreased at ≥ 1500 ppm (24-25%) and relative (to body wt) kidney weight was decreased only at 4000 ppm (13.4); there were no significant kidney weight changes in females. Absolute (13-33%) and relative (to body [26-60%] and brain wt [7-24%]) liver weights were significantly increased in males and statistically non-significantly increased in females at ≥ 4000 ppm. 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Incidence of hepatocellular adenomas and carcinomas (combined) in the 0, 500, 1500, 4000, and 8000 ppm groups were 1/15, 1/10, 4/10, 3/10, and 4/10, respectively in males and 0/15, 1/10, 1/10, 0/10, and 3/10, respectively in females. There was an increased incidence of chronic progressive nephropathy in all females (10/10) sacrificed at 79 weeks at 8000 ppm, compared with 4/10 in controls. Microscopic analysis of tissues at the 104-week terminal sacrifice also showed increased cytoplasmic eosinophilia, diffuse hepatocellular enlargement, and pigment in high-dose males and females; these findings were not observed in a treatment-related manner at 4000 ppm or in the high dose recovery mice. The incidence and severity of chronic progressive nephropathy was slightly increased at terminal sacrifice in females at 8000 ppm which corresponded to the pitted/rough appearance of the kidneys in high-dose females. Enlarged spleen observed in gross pathology was most often due to increased extramedullary hematopoiesis or to involvement by hemangioma/hemangiosarcoma, or hematopoietic neoplasia. All other findings were considered by the authors to be incidental and not treatment-related. The terminal sacrifice (week 104) showed increased incidences of hepatocellular neoplasms (adenomas and carcinomas) in females at 8000 ppm (3/42, 4/36, 5/37, 5/29, and 20/40 in the 0, 500, 1500, 4000, and 8000 ppm groups, respectively) and a slight increase in males at ≥ 4000 ppm (14/45, 8/41, 10/36, 16/35, and 18/32 in the 0, 500, 1500, 4000, and 8000 ppm groups, respectively). Histopathology results for all animals evaluated from unscheduled deaths and interim and terminal sacrifices showed increased incidence of hepatocellular adenomas (at 8000 ppm in females) and carcinomas (at ≥ 4000 in males and females); total combined incidence of adenomas and carcinomas was increased in males at ≥ 4000 ppm (16/70, 13/60, 18/60, 28/60 and 31/70 in the 0, 500, 1500, 4000, and 8000 ppm groups, respectively) and in females at ≥ 1500 ppm (3/70, 5/61, 10/60, 11/60, and 32/70 in the 0, 500, 1500, 4000, and 8000 ppm groups, respectively). These neoplasms in recovery animals that were treated for 78 weeks to 8000 ppm showed that effects in the liver and kidney, including liver neoplasms were partially reversible. The primary cause of both male and female deaths was hepatocellular neoplasia, which was increased in frequency in the 4,000 ppm and 8,000 ppm groups. The author reported a NOEL/NOAEL for systemic toxicity of 500 ppm, based on increased incidences of hepatocellular adenomas and carcinomas (combined) in female mice at 1500 ppm. Hepatocellular neoplasms in both sexes were apparent at ≥ 4000 ppm and gross and microscopic evidence of nonneoplastic effects were apparent in livers (males and females) and kidneys (of females) at a higher dose (8000 ppm). The test substance was positive for carcinogenicity.

[7] 680087: In an oncogenicity study, CDF (F-344) CrlBR rats (70-85/sex/group) were administered DINP (purity >99%) target concentrations of 0, 500, 1,500, 6,000, or 12,000 ppm, daily via the diet, for at least 104 weeks. The calculated average daily doses were 0, 29.2, 88.3, 358.7, and 733.2 mg/kg-day for males and 0, 36.4, 108.6, 442.2, and 885.4 mg/kg-day for females. A separate recovery group (55/sex) was administered 12,000 ppm for 78 weeks and allowed a 26-week recovery period prior to sacrifice at 104 weeks. The average daily doses for this group were 637.3 and 773.6 mg/kg-day for males and females, respectively. A positive control group (15 male rats) for the ancillary liver proliferation tests (described further below) was administered 1,000 ppm WY 14,643, via the diet, for 13 weeks. All rats were observed twice daily for mortality and moribundity. Cage-side observations were conducted daily, and detailed clinical examinations weekly. Body weights were recorded weekly for the first 17 weeks of treatment, then weekly thereafter. Food consumption was recorded weekly during the first 16 weeks, then every 4 weeks thereafter. Blood was collected for clinical chemistry and hematology during weeks 26, 52, 78, and 104. Urine was collected before each clinical sampling. Myeloid/erythroid ratios were calculated for any animals sacrificed in extremis and those sacrificed at weeks 79 and 105/106. Liver cell proliferation, peroxisome proliferation, and liver weights were assessed in controls (negative and positive) and main group animals (5/sex/group) sacrificed at 1, 2, and 13, weeks and in negative controls and animals in the 6,000 and 12,000 ppm groups sacrificed at 79 weeks; ten additional animals at 79 weeks were sacrificed for histomorphological evaluations. Select organs (lung, uterus, testes w/epididymis, brain w/stem, spleen, liver, and kidney) were weighed at 79 (10/sex) and 104 weeks. All animals were necropsied, and histopathological examinations were conducted on >30 tissues/organs from control and high-dose animals, as well as all animals that died throughout the study; select organs (epididymides, uterus, spleen, kidney, and gross lesions were also examined in animals from lower dose groups at the terminal sacrifice. At 104 weeks, the survival of males at 12,000 ppm was significantly lower than controls. No effects on female survival were observed. Treatment-related clinical signs included increased urine stains and signs associated with death (thin appearance, hunched posture, hypoactivity, prostration, pale body appearance, rough haircoat, and few or no feces). Mean body weights of males and females in the 6,000 and 12,000 ppm groups were significantly lower than controls throughout most of the study period. Total mean body weight gains were marginally lower (10.2% in males and 14.9% in females) at the high dose. Some significant changes in food consumption were noted, but they were sporadic and showed no dose response. Additionally, food consumption was inconsistent between main high-dose and recovery females both of which were administered the same dose. The authors considered the food consumption findings to be spurious. Hematological changes included mild, but significant decreases in erythrocyte count, hemoglobin, and hematocrit at 12,000 ppm during most collection points, compared with controls; no changes were observed in the recovery group. Transient changes in these parameters were observed at 1,500 and 6,000 ppm. It was noted that these and other leukocyte changes observed fell within the reference ranges for age and sex-matched animals in the testing laboratory. There were no changes in myeloid/erythroid ratios, compared with controls. Increased serum urea nitrogen was observed in both sexes at 6,000 ppm (at 26 and/or 52 weeks only), and at 12,000 ppm primarily at 26, 52, and 78 weeks. ALT and AST were generally elevated at one or more time intervals in animals exposed to ≥ 6,000 ppm; however, there were some directional inconsistencies in females. Other clinical chemistry changes were considered to be incidental. Urinalysis showed several changes including a transient elevation in urinary protein in males at ≥ 1,500 ppm at week 26, correlating with increases in serum urea nitrogen at the same collection time. At week 104, a decrease in urine specific gravity in males at ≥6,000 ppm correlated with decreased urine osmolality. Cell proliferation in ancillary animals (5/sex/group) sacrificed during weeks 1, 2, and 13, and in those sacrificed at 104 weeks, was significantly increased only during week 1 in both sexes at 12,000 ppm. Palmitoyl-CoA oxidase activity was increased at the high dose at all time points in both sexes, and at 104 weeks in females at 6,000 ppm. In the absence of differences in terminal body weights, Liver weight changes in ancillary animals included increased absolute (weeks 2 and 13 only in males) and relative liver weights in both sexes, significant at ≥6,000 ppm. At the 79-week interim sacrifice, significant organ weight changes (n = 10/sex) included increased male and female absolute and relative kidney weights and absolute (female only) and relative liver weights at ≥6,000 ppm, increased absolute and relative spleen weights in both sexes at 12,000 ppm, and increased relative brain weight in males at 12,000 ppm; no animals in the lower dose groups were sacrificed at this time point. Terminal body weights at 72 weeks were generally lower in the exposed animals, relative to controls; the decreases were purportedly significant in males at ≥6,000 ppm, but significance was not indicated in the data tables and the changes were low in magnitude (<10%). At 104 weeks, spleen weights were elevated in females only at 6,000 ppm (absolute only) and 12,000 ppm. Absolute and relative kidney weights were increased in males at 12,000 ppm and in females at ≥6,000 ppm, and absolute and relative liver weights were increased at ≥6,000 ppm in both sexes. Absolute (female only) and relative brain weights were increased at 12,000 ppm. Relative spleen, brain, and kidney weights were still increased in females following the 26-week recovery period. Terminal body weights at the 104 week sacrifice were significantly lower in males at 12,000 ppm (22%) and in females at ≥6,000 ppm (10-12%). Necropsy showed livers that were enlarged and/or granular/pitted or rough in both sexes. Lesions in the liver were observed in high-dose males and females at the week 1 (increase in mitotic figures), week 2 (hepatocellular enlargement), and weeks 13 and 79 (cytoplasmic eosinophilia and slight to moderate hepatocellular enlargement) sacrifices. At week 79, an increased incidence of pigment in Kupffer cells/bile canaliculi was also observed in males. Kidney lesions at 79 weeks consisted of mineralization of the renal papilla (males only) and increased pigmentation of the renal tubules in 12,000 ppm group animals. Enlarged spleens were associated with incidences of mononuclear cell leukemia primarily in high-dose females. Microscopic analysis of tissues at the 104-week terminal sacrifice also showed similar alterations in the livers of high-dose rats in addition to spongiosis hepatis males at ≥6,000 ppm. Non-neoplastic kidney lesions occurred in males at ≥6,000 ppm and severity increased with dose; no kidney lesions were observed in females. All other findings were considered by the authors to be incidental or related to spontaneous disease, and not treatment-related. The primary cause of both male and female deaths was mononuclear cell leukemia, which was increased in frequency in the 6,000 ppm and 12,000 ppm groups. Incidences of hepatocellular neoplasms were significantly increased in both sexes at 12,000 ppm, compared with controls. These neoplasms were not increased in recovery animals that were treated for 78 weeks. Renal tubule cell carcinomas were noted in males at 12,000 ppm.The author reported a systemic NOEL and a NOEL for carcinogenic potential of 1,500 ppm, based on gross and microscopic liver and kidney lesions, and for increased incidences of mononuclear cell leukemia in both male and female rats at 6,000 ppm. Hepatocellular neoplasms in both sexes and renal neoplasms in males were apparent at a higher dose (12,000 ppm).

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with controls. Increased serum urea nitrogen was observed in both sexes at 6,000 ppm (at 26 and/or 52 weeks only), and at 12,000 ppm primarily at 26, 52, and 78 weeks. ALT and AST were generally elevated at one or more time intervals in animals exposed to ≥ 6,000 ppm; however, there were some directional inconsistencies in females. Other clinical chemistry changes were considered to be incidental. Urinalysis showed several changes including a transient elevation in urinary protein in males at ≥ 1,500 ppm at week 26, correlating with increases in serum urea nitrogen at the same collection time. At week 104, a decrease in urine specific gravity in males at ≥6,000 ppm correlated with decreased urine osmolality. Cell proliferation in ancillary animals (5/sex/group) sacrificed during weeks 1, 2, and 13, and in those sacrificed at 104 weeks, was significantly increased only during week 1 in both sexes at 12,000 ppm. Palmitoyl-CoA oxidase activity was increased at the high dose at all time points in both sexes, and at 104 weeks in females at 6,000 ppm. In the absence of differences in terminal body weights, Liver weight changes in ancillary animals included increased absolute (weeks 2 and 13 only in males) and relative liver weights in both sexes, significant at ≥6,000 ppm. At the 79-week interim sacrifice, significant organ weight changes (n = 10/sex) included increased male and female absolute and relative kidney weights and absolute (female only) and relative liver weights at ≥6,000 ppm, increased absolute and relative spleen weights in both sexes at 12,000 ppm, and increased relative brain weight in males at 12,000 ppm; no animals in the lower dose groups were sacrificed at this time point. Terminal body weights at 72 weeks were generally lower in the exposed animals, relative to controls; the decreases were purportedly significant in males at ≥6,000 ppm, but significance was not indicated in the data tables and the changes were low in magnitude (<10%). At 104 weeks, spleen weights were elevated in females only at 6,000 ppm (absolute only) and 12,000 ppm. Absolute and relative kidney weights were increased in males at 12,000 ppm and in females at ≥6,000 ppm, and absolute and relative liver weights were increased at ≥6,000 ppm in both sexes. Absolute (female only) and relative brain weights were increased at 12,000 ppm. Relative spleen, brain, and kidney weights were still increased in females following the 26-week recovery period. Terminal body weights at the 104 week sacrifice were significantly lower in males at 12,000 ppm (22%) and in females at ≥6,000 ppm (10-12%). Necropsy showed livers that were enlarged and/or granular/pitted or rough in both sexes. Lesions in the liver were observed in high-dose males and females at the week 1 (increase in mitotic figures), week 2 (hepatocellular enlargement), and weeks 13 and 79 (cytoplasmic eosinophilia and slight to moderate hepatocellular enlargement) sacrifices. At week 79, an increased incidence of pigment in Kupffer cells/bile canaliculi was also observed in males. Kidney lesions at 79 weeks consisted of mineralization of the renal papilla (males only) and increased pigmentation of the renal tubules in 12,000 ppm group animals. Enlarged spleens were associated with incidences of mononuclear cell leukemia primarily in high-dose females. Microscopic analysis of tissues at the 104-week terminal sacrifice also showed similar alterations in the livers of high-dose rats in addition to spongiosis hepatis males at ≥6,000 ppm. Non-neoplastic kidney lesions occurred in males at ≥6,000 ppm and severity increased with dose; no kidney lesions were observed in females. All other findings were considered by the authors to be incidental or related to spontaneous disease, and not treatment-related. The primary cause of both male and female deaths was mononuclear cell leukemia, which was increased in frequency in the 6,000 ppm and 12,000 ppm groups. Incidences of hepatocellular neoplasms were significantly increased in both sexes at 12,000 ppm, compared with controls. These neoplasms were not increased in recovery animals that were treated for 78 weeks. Renal tubule cell carcinomas were noted in males at 12,000 ppm.The author reported a systemic NOEL and a NOEL for carcinogenic potential of 1,500 ppm, based on gross and microscopic liver and kidney lesions, and for increased incidences of mononuclear cell leukemia in both male and female rats at 6,000 ppm. Hepatocellular neoplasms in both sexes and renal neoplasms in males were apparent at a higher dose (12,000 ppm).

[9] 680087: In an oncogenicity study, CDF (F-344) CrlBR rats (70-85/sex/group) were administered DINP (purity >99%) target concentrations of 0, 500, 1,500, 6,000, or 12,000 ppm, daily via the diet, for at least 104 weeks. The calculated average daily doses were 0, 29.2, 88.3, 358.7, and 733.2 mg/kg-day for males and 0, 36.4, 108.6, 442.2, and 885.4 mg/kg-day for females. A separate recovery group (55/sex) was administered 12,000 ppm for 78 weeks and allowed a 26-week recovery period prior to sacrifice at 104 weeks. The average daily doses for this group were 637.3 and 773.6 mg/kg-day for males and females, respectively. A positive control group (15 male rats) for the ancillary liver proliferation tests (described further below) was administered 1,000 ppm WY 14,643, via the diet, for 13 weeks. All rats were observed twice daily for mortality and moribundity. Cage-side observations were conducted daily, and detailed clinical examinations weekly. Body weights were recorded weekly for the first 17 weeks of treatment, then weekly thereafter. Food consumption was recorded weekly during the first 16 weeks, then every 4 weeks thereafter. Blood was collected for clinical chemistry and hematology during weeks 26, 52, 78, and 104. Urine was collected before each clinical sampling. Myeloid/erythroid ratios were calculated for any animals sacrificed in extremis and those sacrificed at weeks 79 and 105/106. Liver cell proliferation, peroxisome proliferation, and liver weights were assessed in controls (negative and positive) and main group animals (5/sex/group) sacrificed at 1, 2, and 13, weeks and in negative controls and animals in the 6,000 and 12,000 ppm groups sacrificed at 79 weeks; ten additional animals at 79 weeks were sacrificed for histomorphological evaluations. Select organs (lung, uterus, testes w/epididymis, brain w/stem, spleen, liver, and kidney) were weighed at 79 (10/sex) and 104 weeks. All animals were necropsied, and histopathological examinations were conducted on >30 tissues/organs from control and high-dose animals, as well as all animals that died throughout the study; select organs (epididymides, uterus, spleen, kidney, and gross lesions were also examined in animals from lower dose groups at the terminal sacrifice. At 104 weeks, the survival of males at 12,000 ppm was significantly lower than controls. No effects on female survival were observed. Treatment-related clinical signs included increased urine stains and signs associated with death (thin appearance, hunched posture, hypoactivity, prostration, pale body appearance, rough haircoat, and few or no feces). Mean body weights of males and females in the 6,000 and 12,000 ppm groups were significantly lower than controls throughout most of the study period. Total mean body weight gains were marginally lower (10.2% in males and 14.9% in females) at the high dose. Some significant changes in food consumption were noted, but they were sporadic and showed no dose response. Additionally, food consumption was inconsistent between main high-dose and recovery females both of which were administered the same dose. The authors considered the food consumption findings to be spurious. Hematological changes included mild, but significant decreases in erythrocyte count, hemoglobin, and hematocrit at 12,000 ppm during most collection points, compared with controls; no changes were observed in the recovery group. Transient changes in these parameters were observed at 1,500 and 6,000 ppm. It was noted that these and other leukocyte changes observed fell within the reference ranges for age and sex-matched animals in the testing laboratory. There were no changes in myeloid/erythroid ratios, compared with controls. Increased serum urea nitrogen was observed in both sexes at 6,000 ppm (at 26 and/or 52 weeks only), and at 12,000 ppm primarily at 26, 52, and 78 weeks. ALT and AST were generally elevated at one or more time intervals in animals exposed to ≥ 6,000 ppm; however, there were some directional inconsistencies in females. Other clinical chemistry changes were considered to be incidental. Urinalysis showed several changes including a transient elevation in urinary protein in males at ≥ 1,500 ppm at week 26, correlating with increases in serum urea nitrogen at the same collection time. At week 104, a decrease in urine specific gravity in males at ≥6,000 ppm correlated with decreased urine osmolality. Cell proliferation in ancillary animals (5/sex/group) sacrificed during weeks 1, 2, and 13, and in those sacrificed at 104 weeks, was significantly increased only during week 1 in both sexes at 12,000 ppm. Palmitoyl-CoA oxidase activity was increased at the high dose at all time points in both sexes, and at 104 weeks in females at 6,000 ppm. In the absence of differences in terminal body weights, Liver weight changes in ancillary animals included increased absolute (weeks 2 and 13 only in males) and relative liver weights in both sexes, significant at ≥6,000 ppm. At the 79-week interim sacrifice, significant organ weight changes (n = 10/sex) included increased male and female absolute and relative kidney weights and absolute (female only) and relative liver weights at ≥6,000 ppm, increased absolute and relative spleen weights in both sexes at 12,000 ppm, and increased relative brain weight in males at 12,000 ppm; no animals in the lower dose groups were sacrificed at this time point. Terminal body weights at 72 weeks were generally lower in the exposed animals, relative to controls; the decreases were purportedly significant in males at ≥6,000 ppm, but significance was not indicated in the data tables and the changes were low in magnitude (<10%). At 104 weeks, spleen weights were elevated in females only at 6,000 ppm (absolute only) and 12,000 ppm. Absolute and relative kidney weights were increased in males at 12,000 ppm and in females at ≥6,000 ppm, and absolute and relative liver weights were increased at ≥6,000 ppm in both sexes. Absolute (female only) and relative brain weights were increased at 12,000 ppm. Relative spleen, brain, and kidney weights were still increased in females following the 26-week recovery period. Terminal body weights at the 104 week sacrifice were significantly lower in males at 12,000 ppm (22%) and in females at ≥6,000 ppm (10-12%). Necropsy showed livers that were enlarged and/or granular/pitted or rough in both sexes. Lesions in the liver were observed in high-dose males and females at the week 1 (increase in mitotic figures), week 2 (hepatocellular enlargement), and weeks 13 and 79 (cytoplasmic eosinophilia and slight to moderate hepatocellular enlargement) sacrifices. At week 79, an increased incidence of pigment in Kupffer cells/bile canaliculi was also observed in males. Kidney lesions at 79 weeks consisted of mineralization of the renal papilla (males only) and increased pigmentation of the renal tubules in 12,000 ppm group animals. Enlarged spleens were associated with incidences of mononuclear cell leukemia primarily in high-dose females. Microscopic analysis of tissues at the 104-week terminal sacrifice also showed similar alterations in the livers of high-dose rats in addition to spongiosis hepatis males at ≥6,000 ppm. Non-neoplastic kidney lesions occurred in males at ≥6,000 ppm and severity increased with dose; no kidney lesions were observed in females. All other findings were considered by the authors to be incidental or

related to spontaneous disease, and not treatment-related. The primary cause of both male and female deaths was mononuclear cell leukemia, which was increased in frequency in the 6,000 ppm and 12,000 ppm groups. Incidences of hepatocellular neoplasms were significantly increased in both sexes at 12,000 ppm, compared with controls. These neoplasms were not increased in recovery animals that were treated for 78 weeks. Renal tubule cell carcinomas were noted in males at 12,000 ppm.The author reported a systemic NOEL and a NOEL for carcinogenic potential of 1,500 ppm, based on gross and microscopic liver and kidney lesions, and for increased incidences of mononuclear cell leukemia in both male and female rats at 6,000 ppm. Hepatocellular neoplasms in both sexes and renal neoplasms in males were apparent at a higher dose (12,000 ppm).

[10] 11784622: Six-week-old female CD-1 mice (12-14/group) were provided with a diet containing 0.15, 1.5, or 1500 ppm DEHP continuously for 11 months, or a control diet. Study authors reported target doses of 0.024, 0.240 and 240 mg DEHP/kg/day, respectively based on the assumption that a 25-gram mouse eats 5 grams of food/day. Nominal doses based on actual measured body weights and food intake were not provided. Body weights and food intake were evaluated once a week. Estrous cyclicity was monitored by examining vaginal lavage cells for 14 days after 1, 3, 5, 7, and 11 months of exposure. Urine was collected for 2 days after 6 months (n=5-8) and 11 months (n=4) of exposure to measure phthalate metabolites. After 11 months, exposed females (7-9/group) were mated with unexposed males and checked twice a day for a copulatory plug. Female weights were taken daily from the start of breeding until the presence of a copulatory plug and then a minimum of twice a week duration of the pregnancy. Mating index (# females with copulatory plugs / #females in the group), gestational index (# dams that gave birth to live pups / # of pregnant dams), pregnancy rate (# dams that were pregnant / # dams in the group), birth rate (# of dams that gave birth to live pups/number of females in group), dystocia rate (# dams with dystocia / # dames that were pregnant) and fertility index (# pregnant females / # females with a copulatory plug) were calculated. No significant difference in body weight change or food consumption was seen during the 11 months of exposure compared to controls. Body weights during breeding and gestation were not reported. Urinary levels of the phthalate metabolites MEHP, MEOHP and MEHHP were significantly increased at 6 months and further increased at 11 months in mice exposed to 1500 ppm. At months 1, 7 and 11, the time mice spent in estrus and metestrus/diestrus was not significantly different from controls. At 3 and 5 months, effects on estrous cyclicity were observed at 0.15 ppm in food, but not at the mid and high-dose groups. At 3 months, mice in the 0.15 ppm group spent significantly less time in metestrus/diestrus. At 5 months, time spent in metestrus/diestrus was significantly decreased and time spent in estrus was significantly increased in the 0.15 ppm group compared to control. Study authors conclude the effects of DEHP on estrous cycle are dependent on the age of the mice during exposure and exposure duration. No significant differences in mating index, gestational index, pregnancy rate, fertility index, birth rate or dystocia rates were seen compared to control.The study authors did not identify a NOAEL or LOAEL. A NOAEL of 1500 ppm (estimated to be 240 mg/kg/day by study authors) was determined for this review based on the lack of dose-related adverse effects.

[11] 11784622: Six-week-old female CD-1 mice (12-14/group) were provided with a diet containing 0.15, 1.5, or 1500 ppm DINP continuously for 11 months, or a control diet. Study authors reported target doses of 0.024, 0.240 and 240 mg DINP/kg/day, respectively based on the assumption that a 25-gram mouse eats 5 grams of food/day. Nominal doses based on actual measured body weights and food intake were not provided. Body weights and food intake were evaluated once a week. Estrous cyclicity was monitored by examining vaginal lavage cells for 14 days after 1, 3, 5, 7, and 11 months of exposure. Urine was collected for 2 days after 6 months (n=5-8) and 11 months (n=4) of exposure to measure phthalate metabolites. After 11 months, exposed females (7-9/group) were mated with unexposed males and checked twice a day for a copulatory plug. Female weights were taken daily from the start of breeding until the presence of a copulatory plug and then a minimum of twice a week duration of the pregnancy. Mating index (# females with copulatory plugs / #females in the group), gestational index (# dams that gave birth to live pups / # of pregnant dams), pregnancy rate (# dams that were pregnant / # dams in the group), birth rate (# of dams that gave birth to live pups/number of females in group), dystocia rate (# dams with dystocia / # dames that were pregnant) and fertility index (# pregnant females / # females with a copulatory plug) were calculated. No significant differences in body weight change or food consumption were seen during 11 months of exposure compared to controls. Body weights during breeding and gestation were not reported. At 6 months, significant increases in the levels of phthalate urinary metabolites MEOHP and MEHHP were seen in the 0.15 ppm group and MECPP at 1500 ppm compared to control. At 11 months, significant increases in MECPP and MCPP were seen in the 1500 ppm group compared to control. No significant differences in the time mice spent in estrus and metestrus/diestrus were seen compared with controls at any time point; although there was a trend for increased time in estrous and decreased time in metestrus/diestrus at 3 months (1.5 ppm) and 7 months (0.15 ppm). Reproductive indices showed dose-related decreases in the gestation index and birth rates in mated females. Compared to controls, The reduction in the gestational index (from 100% in control to approximately 20% in the exposed group) and birth rate (from approximately 60% in control to approximately 10% in the exposed group) was seen at 1500 ppm. No significant differences in the mating index, pregnancy rate, fertility index, or dystocia rate were seen, compared with controls.The study authors did not identify a NOAEL or LOAEL. This Reviewer identified a NOAEL of 1.5 ppm and a LOAEL of 1500 ppm based on statistically significant ($p < 0.05$) decreases in the gestational index and birth rate. The authors noted the decrease in the gestation index at 1.5ppm was borderline significant, but the p-value was 0.09. A test for trend was not conducted. Based on the assumption the study authors make regarding food consumption rates, these toxicity values would be equivalent to a NOAEL of approximately 0.240 and a LOAEL of 240 mg DINP/kg/day.

[12] 11784618: In a chronic dietary study, adult female CD-1 mice (number per group not specified, sample sizes suggest up to 10/group) were administered diisononylphthalate (DiNP, purity not reported) at doses of 0, 0.15, 1.5, or 1500 ppm in rodent chow ad libitum for 6 months. The doses were roughly equivalent to 0.024, 0.24, and 240 mg phthalate/kg/day. Doses were selected based on published rationale. After the treatment period, mice were euthanized during diestrus and one ovary per mouse, pituitary glands, and blood were collected. Ovaries were fixed, embedded, and stained. Slides were used to assess follicle populations by counting numbers of primordial, primary, preantral, antral, and atretic follicles and then calculating the follicle type percentage. Human counters were blinded to treatments. Blood samples were centrifuged and sera were collected for the analysis of the sex hormones progesterone, testosterone, estradiol, FSH and LH. Ovary tissues were used to analyze the expression of steroidogenic genes (Star, Hsd3b1, Hsd17b1, Cyp19a1) as well as the expression of the FSH (fshr) and LH/choriogonadotropin (Lhcgr) receptors. Pituitary tissues were analyzed for expression of genes that regulate the FSH and LH gonadotropin hormones (Nr5a1, Cga, Fshb, and Lhb).A significant increase in the number and percentage of primordial follicles was observed in mice administered 240 mg/kg-day. Percentages of preantral and antral follicles were significantly decreased at the high dose, but overall numbers did not change. The reduction in antral follicles was dose-related at was also borderline significant at 0.24 mg/kg-day. There were no changes in atretic follicles. There were no significant effects on serum progesterone, testosterone, or estradiol levels compared to controls or on ovarian expression of genes that regulate steroidogenesis (Star, Hsd3b1, Hsd17b1, and Cyp19a1). There were also no changes in ovarian Lhcgr or Fshr expression. A non-dose-related, but significant increase in serum FSH levels was observed at 0.24 mg/kg-day only. Serum LH decreased in a more dose-related manner and the reductions were significant at $\geq$ 0.24 mg/kg-day. In the pituitary, expression of Nr5a1 and Cga were significantly increased over controls, in the low-dose group only. No change in Fshb or Lhb expression was observed. The study authors concluded that long-term exposure to phthalates affects follicle growth dynamics in the ovary, differentially regulates gonadotropic secretion, and affects the expression of pituitary genes suggesting a modification at the HPG axis at multiple levels.No author-reported toxicity values were provided. Based on the available data, a NOAEL of 0.024 mg/kg-day and a LOAEL of 0.240 mg/kg-day was determined for significant decreases in luteinizing hormone levels in female mice.

Diisononyl 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 study authors cited compliance with ARRIVE guidelines for in vivo studies and that animal care was conducted in accordance with NIH. Mouse-CD-1 - [mouse]-Female	Other (specify) (Orally piped directly into the mouth)-Duration: Reproductive/Developmental-1-F0 - gestation (GD 1-7) Pregnant dams were exposed from GD 1-7	**POD: 0.02 mg/kg-bw/day (LOAEL) -Decreased gestation time, litter size, pup body weight on PND1, fetal and placental weight (GD13), and changes to placental morphology** n= 25 Dose= 0, n= 25 Dose= 0.020, mg/kg-bw/dayTotal # of generations: 1 Female Exposure: F0 - gestation, GD 1-7	See footnotes for full summary [1]	This study has mainly minor limitations, including lacking detail on confounding factors (such as other phthalates in bedding), lack of blinding and a lack of analytical verification of test substance identity and purity. The study did not use the litter as the statistical unit. Not all data were shown.	Reproductive/Developmental-Gestation length, litter size, pup weight on PND 1, and sex ratio. Maternal serum estrogen and progesterone levels, number of implantation sites, gross uterine pathology, fetal and placental weight, histopathology and immunohistochemistry (implantation chambers and placenta), measurement of total area of the placenta, junctional zone and labyrinth, ratio of labyrinth to junctional zone, and relative mRNA expression in placenta, decidua and embryo tissues for genes involved in decidualization process, angiogenic regulators, and placental cell types.; Medium	11784571

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Diisononyl 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 reference any guidance or compliance documents. Rat-Wistar - [rat]-Female	Oral-Gavage-Duration: Reproductive/Developmental-1-F0 - gestation (14/15 days)-F0- lactation (17) Dams were exposed on gestation day 7 through postnatal day 17. Offspring were not exposed. Mean gestation length was approximately 22 days; however in one subgroup, the dams were sacrificed on gestation day 21.	**POD: 300 mg/kg-bw/day (NOAEL) -Reproductive toxicity and anti-androgenic effects.** n= 16 Dose= 0, n= 16 Dose= 300, n= 16 Dose= 600, n= 16 Dose= 750, n= 16 Dose= 900, mg/kg-bw/dayTotal # of generations: 1 Female Exposure: F0 - gestation, 14/15 days, F0- lactation, 17	See footnotes for full summary [2]	The major limitation of this study was that the authors do not detail any methods to minimize outside exposure to other plasticizers. This is a limitation because the authors are investigating the effects of endocrine disrupting chemicals and exposure to other plasticizers could impact the results and confound the study.	Reproductive/Developmental-Testes histopathology, ex vivo testosterone production, serum and testes testosterone content, histopathology of reproductive organs and thyroids, gestation length, litter size, number of fetuses, number of implantations, number of live fetuses, percent post-implantation loss, litter weights, sex ratio, survival, anogenital distance, pup weights, presence/retention of nipples/areolas, age of sexual maturation, inhibin B analysis, body weights at post-natal day 90, penile malformation, testicular descent, organ weight (liver, kidney, adrenal, thyroid, testes, epididymis, seminal vesicle, ventral prostate, levator ani/bulbocavernosus muscle, bulborethral gland, ovaries, uterus), histopathology (testes, epididymides), sperm parameters, including motility, first day of estrous, motor activity and habituation capability (including Morris maze learning and memory); Medium	806135

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Diisononyl 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 reference any guidance or compliance documents. Rat-Wistar - [rat]-Female	Oral-Gavage-Duration: Reproductive/Developmental-1-F0 - gestation (14/15 days)-F0- lactation (17) Dams were exposed on gestation day 7 through postnatal day 17. Offspring were not exposed. Mean gestation length was approximately 22 days; however in one subgroup, the dams were sacrificed on gestation day 21.	**POD: 300 mg/kg-bw/day (NOAEL) -Reproductive toxicity and anti-androgenic effects.** n= 16 Dose= 0, n= 16 Dose= 300, n= 16 Dose= 600, n= 16 Dose= 750, n= 16 Dose= 900, mg/kg-bw/dayTotal # of generations: 1 Female Exposure: F0 - gestation, 14/15 days, F0- lactation, 17	See footnotes for full summary [3]	The major limitation of this study was that the authors do not detail any methods to minimize outside exposure to other plasticizers. This is a limitation because the authors are investigating the effects of endocrine disrupting chemicals and exposure to other plasticizers could impact the results and confound the study.	Reproductive/Developmental-Testes histopathology, ex vivo testosterone production, serum and testes testosterone content, histopathology of reproductive organs and thyroids, gestation length, litter size, number of fetuses, number of implantations, number of live fetuses, percent post-implantation loss, litter weights, sex ratio, survival, anogenital distance, pup weights, presence/retention of nipples/areolas, age of sexual maturation, inhibin B analysis, body weights at post-natal day 90, penile malformation, testicular descent, organ weight (liver, kidney, adrenal, thyroid, testes, epididymis, seminal vesicle, ventral prostate, levator ani/bulbocavernosus muscle, bulborethral gland, ovaries, uterus), histopathology (testes, epididymides), sperm parameters, including motility, first day of estrous, motor activity and habituation capability (including Morris maze learning and memory); Medium	806135

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Diisononyl 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 reference any guidance or compliance documents. Rat-Wistar - [rat]-Female	Oral-Gavage-Duration: Reproductive/Developmental-1-F0 - gestation (14/15 days)-F0- lactation (17) Dams were exposed on gestation day 7 through postnatal day 17. Offspring were not exposed. Mean gestation length was approximately 22 days; however in one subgroup, the dams were sacrificed on gestation day 21.	**POD: 300 mg/kg-bw/day (NOAEL) -Reproductive toxicity and anti-androgenic effects.** n= 16 Dose= 0, n= 16 Dose= 300, n= 16 Dose= 600, n= 16 Dose= 750, n= 16 Dose= 900, mg/kg-bw/dayTotal # of generations: 1 Female Exposure: F0 - gestation, 14/15 days, F0- lactation, 17	See footnotes for full summary [4]	The major limitation of this study was that the authors do not detail any methods to minimize outside exposure to other plasticizers. This is a limitation because the authors are investigating the effects of endocrine disrupting chemicals and exposure to other plasticizers could impact the results and confound the study.	Reproductive/Developmental-Testes histopathology, ex vivo testosterone production, serum and testes testosterone content, histopathology of reproductive organs and thyroids, gestation length, litter size, number of fetuses, number of implantations, number of live fetuses, percent post-implantation loss, litter weights, sex ratio, survival, anogenital distance, pup weights, presence/retention of nipples/areolas, age of sexual maturation, inhibin B analysis, body weights at post-natal day 90, penile malformation, testicular descent, organ weight (liver, kidney, adrenal, thyroid, testes, epididymis, seminal vesicle, ventral prostate, levator ani/bulbocavernosus muscle, bulborethral gland, ovaries, uterus), histopathology (testes, epididymides), sperm parameters, including motility, first day of estrous, motor activity and habituation capability (including Morris maze learning and memory); Medium	806135

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Diisononyl 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 use of study guidelines and GLP compliance are not reported. Rat-Sprague-Dawley - [rat]-Female	Oral-Diet-Duration: Reproductive/Developmental-1-F0 - gestation (GD 12-23)-F0- lactation (PND 0-14) GD 12 to PND 14	**POD: 89 mg/kg-bw/day (NOAEL) -Developmental (decreased pup body weights; induction of multinucleated germ cells in pup testes)** n= 24 Dose= 0, n= 20 Dose= 89, n= 20 Dose= 453, n= 20 Dose= 1217, mg/kg-bw/dayTotal # of generations: 1 Female Exposure: F0 - gestation, GD 12-23, F0- lactation, PND 0-14	See footnotes for full summary [5]	Palatability issues resulting in decreased food consumption were observed in the study and may be a potential confounder of the study results.	Nutritional/Metabolic; Reproductive/Developmental; Medium	1325348

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Diisononyl 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
EPA GLP 40 CRF Part 792 with deviations Rat-Sprague-Dawley - [rat]-Both	Oral-Diet-Duration: Reproductive/Developmental-2-F0- premating (10 weeks)-F0- mating-F0 - gestation (GD 0-21)-F0-lactation (PND 0-21)-F0-premating (10 weeks)-F0-mating Single Generation Exposure	**POD: 398 mg/kg-bw/day (LOAEL) -Decreased F1 body weights; and increased absolute kidney and liver weights in F0 animals.** n= 30 Dose= 0, n= 30 Dose= 398, n= 30 Dose= 790, n= 30 Dose= 1216, mg/kg-bw/dayTotal # of generations: 2 Male Exposure: F0-premating, 10 weeks, F0- mating Female Exposure: F0- premating, 10 weeks, F0- mating, F0 - gestation, GD 0-21, F0- lactation, PND 0-21	See footnotes for full summary [6]	Problems with palatability of the test substance were identified.	Nutritional/Metabolic-Body weights, body weight gain, food consumption-Reproductive/Developmental-Organ weights (left and right testis and epididymis, prostate, seminal vesicles, left and right ovaries), and gross observations. Indices for mating, fertility, fecundity, offspring survival from birth to weaning, lactation, gestation and live births, number of days of gestation, litter size, number of live and dead offspring, % of live males and females, offspring body weights,-Hepatic/Liver-Absolute and relative liver weights, gross observation-Renal/Kidney-Absolute and relative kidney weight; gross observations; Medium	1987588

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Diisononyl 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 study was performed in accordance with the following guidelines: EC Dangerous Substances Directive (67/548/EEC), Annex V, Part B, Methods for the Determination of Toxicity "Two-generation reproductive toxicity test" (adopted November, 1987); U.S. EPA, 40 CFR Part 798, TSCA "Test Guidelines for Reproductive and Fertility Effects" (1985). The study was conducted under GLP conditions. Rat-Sprague-Dawley - [rat]-Both	Oral-Diet-Duration: Reproductive/Developmental-2-F0- premating (10 weeks)-F0- mating (3 weeks)-F0 - gestation (22 days)-F0- lactation (21 days)-F1- premating (PND 21, 11 weeks before mating)-F1- mating (3 weeks)-F1 - gestation (22 days)-F1- lactation (21 days)-F0- premating (10 weeks)-F0- mating (3 weeks)-F1- premating (PND 21, 11 weeks before mating)-F1- mating (3 weeks) F0 parental animals were fed for 10 weeks prior to mating and throughout mating (~ 3 weeks) until the delivery of F1 litters (males) and through gestation and lactation (females). F1 parental animals were dosed from PND 21 for 11 weeks prior to mating, throughout mating (~ 3 weeks) until the delivery of F1 litters (males) and through gestation and lactation (females).	**POD: 114 mg/kg-bw/day (Other) -Liver (histopathological changes, increased incidence of minimal to moderate cytoplasmic eosinophilia); Developmental (decreased offspring body weight)** n= 60 Dose= 0, n= 60 Dose= 114, n= 60 Dose= 235, n= 60 Dose= 467, mg/kg-bw/dayTotal # of generations: 2 Male Exposure: F0- premating, 10 weeks, F0- mating, 3 weeks, F1- premating, PND 21, 11 weeks before mating, F1- mating, 3 weeks Female Exposure: F0- premating, 10 weeks, F0- mating, 3 weeks, F0 - gestation, 22 days, F0- lactation, 21 days, F1- premating, PND 21, 11 weeks before mating, F1- mating, 3 weeks, F1 - gestation, 22 days, F1- lactation, 21 days	See footnotes for full summary [7]	Based on the reported study results, the lowest dose tested appears to be the LOAEL (i.e., no NOAEL was identified). Some reproductive organ function measures (e.g., sperm evaluations; estrous cyclicity) and developmental measures (litter weights) were not conducted in this study.	Nutritional/Metabolic-Body weight, body weight gain, food consumption-Hepatic/Liver-Gross necropsy of liver, liver weight, histopathology of liver-Renal/Kidney-Gross necropsy of kidney and urinary bladder, kidney weight, histopathology of kidney and urinary bladder-Reproductive/Developmental-Parental reproductive endpoints: Male mating, male and female fertility, female fecundity, gestational index, and gestation length; gross necropsy and organ weights of testes, epididymides, prostate, seminal vesicles, and ovaries; histopathology of vagina, uterus (with cervix), ovaries, mammary gland (females only), coagulating gland, testes, epididymides, seminal vesicles, and prostate. Developmental endpoints: litter size, live offspring per litter, percentage of male and female offspring per litter; offspring survival, viability at weaning, body weights, body weight gain during lactation; pup clinical signs, and gross necropsy of pups at termination.; High	1987589

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Diisononyl 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 study did not report any compliance methods or if study was consistent with GLP conditions. Rat-Other (Sprague-Dawley-Harlan)-Female	Oral-Gavage-Duration: Reproductive/Developmental-1-F0 - gestation (GD 14-18) Pregnant dams were exposed from GD 14-18	**POD: 1500 mg/kg-bw/day (NOAEL) - No maternal toxicity** n= 6 Dose= 0, n= 3 Dose= 500, n= 4 Dose= 750, n= 6 Dose= 1000, n= 6 Dose= 1500, mg/kg-bw/dayTotal # of generations: 1 Female Exposure: F0 - gestation, GD 14-18	Pregnant Harlan Sprague-Dawley rats (3-6/group) were administered 0, 500, 750, 1000, or 1500 mg/kg-day of DINP (CASRN 28553-12-0) in corn oil, via gavage, on GDs 14-18. Dams were monitored for mortality, overt clinical signs, and body weight. Dams were sacrificed on GD 18 and fetal testes were collected for determination of ex vivo testicular testosterone production and changes in expression of StAR, CypllA, and Insl3 mRNA. Treatment with DINP did not cause maternal mortality, overt toxicity, reduce maternal body weight or reduce litter size (data not shown in). Ex vivo fetal testicular testosterone production was significantly reduced in a dose-dependent manner at $\geq$500 mg/kg-day (data shown for this chemical was not shown on its own; the table combined rats from this experiment with those rats treated with DINP CASRN 28553-12-0). An ED50 was calculated to be 852 mg/kg/day for reduced testicular testosterone. mRNA levels for StAR and Cyp11a were significantly reduced at $\geq$1000 mg/kg-day DIBP and the ED50 values were 901 and 1,356 mg/kg-day, respectively. A maternal NOAEL of 1500 mg/kg/day was determined based on lack of mortality, clinical signs, and body weight changes in pregnant dams. A developmental NOAEL or LOAEL for the compound of interest cannot be determined because data for two CASRN's (28553-12-0 and 68515-48-0) were combined and, therefore, the POD is based on maternal effects. The authors report there was no difference between the response of the two isomers, therefore data were combined for statistical analysis. The LOAEL for the combined data would be 500 mg/kg-day based on changes to ex-vivo fetal testicular testosterone levels.	Data for DINP (CAS RN 28553-12-0) and DINP (mixed isomers; CAS RN 68515-48-0) were reported to be similar and were therefore combined and presented together. Means +/- SE reported are of both chemicals combined.	Reproductive/Developmental-Male Reproductive - testosterone-Nutritional/Metabolic-Maternal body weight and body weight gain; Medium	788239

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Diisononyl 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 study did not report any compliance methods or if study was consistent with GLP conditions. Rat-Other (Sprague-Dawley-Harlan)-Female	Oral-Gavage-Duration: Reproductive/Developmental-1-F0 - gestation (GD 14-18) Pregnant dams were exposed from GD 14-18	**POD: 1500 mg/kg-bw/day (NOAEL) - No maternal toxicity** n= 6 Dose= 0, n= 3 Dose= 500, n= 4 Dose= 750, n= 6 Dose= 1000, n= 6 Dose= 1500, mg/kg-bw/dayTotal # of generations: 1 Female Exposure: F0 - gestation, GD 14-18	Pregnant Harlan Sprague-Dawley rats (3-6/group) were administered 0, 500, 750, 1000, or 1500 mg/kg-day of DINP (CASRN 28553-12-0) in corn oil, via gavage, on GDs 14-18. Dams were monitored for mortality, overt clinical signs, and body weight. Dams were sacrificed on GD 18 and fetal testes were collected for determination of ex vivo testicular testosterone production and changes in expression of StAR, CypllA, and Insl3 mRNA. Treatment with DINP did not cause maternal mortality, overt toxicity, reduce maternal body weight or reduce litter size (data not shown in). Ex vivo fetal testicular testosterone production was significantly reduced in a dose-dependent manner at $\geq$500 mg/kg-day (data shown for this chemical was not shown on its own; the table combined rats from this experiment with those rats treated with DINP CASRN 28553-12-0). An ED50 was calculated to be 852 mg/kg/day for reduced testicular testosterone. mRNA levels for StAR and Cyp11a were significantly reduced at $\geq$1000 mg/kg-day DIBP and the ED50 values were 901 and 1,356 mg/kg-day, respectively. A maternal NOAEL of 1500 mg/kg/day was determined based on lack of mortality, clinical signs, and body weight changes in pregnant dams. A developmental NOAEL or LOAEL for the compound of interest cannot be determined because data for two CASRN's (28553-12-0 and 68515-48-0) were combined and, therefore, the POD is based on maternal effects. The authors report there was no difference between the response of the two isomers, therefore data were combined for statistical analysis. The LOAEL for the combined data would be 500 mg/kg-day based on changes to ex-vivo fetal testicular testosterone levels.	Data for DINP (CAS RN 28553-12-0) and DINP (mixed isomers; CAS RN 68515-48-0) were reported to be similar and were therefore combined and presented together. Means +/- SE reported are of both chemicals combined.	Reproductive/Developmental-Male Reproductive - testosterone-Nutritional/Metabolic-Maternal body weight and body weight gain; Medium	788239

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Diisononyl 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 study did not report any compliance methods or if study was consistent with GLP conditions. Rat-Other (Sprague-Dawley-Harlan)-Female	Oral-Gavage-Duration: Reproductive/Developmental-1-F0 - gestation (GD 14-18) Pregnant dams were exposed from GD 14-18	**POD: 1500 mg/kg-bw/day (NOAEL) - No maternal toxicity** n= 6 Dose= 0, n= 3 Dose= 500, n= 4 Dose= 750, n= 6 Dose= 1000, n= 6 Dose= 1500, mg/kg-bw/dayTotal # of generations: 1 Female Exposure: F0 - gestation, GD 14-18	Pregnant Harlan Sprague-Dawley rats (3-6/group) were administered 0, 500, 750, 1000, or 1500 mg/kg-day of DINP (CASRN 28553-12-0) in corn oil, via gavage, on GDs 14-18. Dams were monitored for mortality, overt clinical signs, and body weight. Dams were sacrificed on GD 18 and fetal testes were collected for determination of ex vivo testicular testosterone production and changes in expression of StAR, CypllA, and Insl3 mRNA. Treatment with DINP did not cause maternal mortality, overt toxicity, reduce maternal body weight or reduce litter size (data not shown in). Ex vivo fetal testicular testosterone production was significantly reduced in a dose-dependent manner at $\geq$500 mg/kg-day (data shown for this chemical was not shown on its own; the table combined rats from this experiment with those rats treated with DINP CASRN 28553-12-0). An ED50 was calculated to be 852 mg/kg/day for reduced testicular testosterone. mRNA levels for StAR and Cyp11a were significantly reduced at $\geq$1000 mg/kg-day DIBP and the ED50 values were 901 and 1,356 mg/kg-day, respectively. A maternal NOAEL of 1500 mg/kg/day was determined based on lack of mortality, clinical signs, and body weight changes in pregnant dams. A developmental NOAEL or LOAEL for the compound of interest cannot be determined because data for two CASRN's (28553-12-0 and 68515-48-0) were combined and, therefore, the POD is based on maternal effects. The authors report there was no difference between the response of the two isomers, therefore data were combined for statistical analysis. The LOAEL for the combined data would be 500 mg/kg-day based on changes to ex-vivo fetal testicular testosterone levels.	Data for DINP (CAS RN 28553-12-0) and DINP (mixed isomers; CAS RN 68515-48-0) were reported to be similar and were therefore combined and presented together. Means +/- SE reported are of both chemicals combined.	Reproductive/Developmental-Male Reproductive - testosterone-Nutritional/Metabolic-Maternal body weight and body weight gain; Medium	788239

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Diisononyl 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 study was conducted according to OECD TG 414; EC Commission Directive 87/302/EEC of 18 November 1887; TSCA guidelines 40 CFR part 798.4900. The study was GLP compliant. Rat-Wistar - [rat]-Female	Oral-Gavage-Duration: Reproductive/Developmental-1-F0 - gestation (GD 6-15) Pregnant dams were dosed from GD6-15	**POD: 200 mg/kg-bw/day (NOAEL) - Increased incidences of fetal variations and skeletal retardations** n= 9 Dose= 0, n= 10 Dose= 40, n= 9 Dose= 200, n= 9 Dose= 1,000, mg/kg-bw/dayTotal # of generations: 1 Female Exposure: F0 - gestation, GD 6-15	See footnotes for full summary [8]	The test substance (purity) and methodological details were not included in the study. A small number of animals per group was utilized. The study did not include an appropriate window to adequately assess skeletal effects or effects on the male reproductive system.	Reproductive/Developmental-Reproductive: Uterus weight, corpora lutia/dam, implantations sites/dam, placental weight; Developmental: pre and post implantation loss, total resorptions, live fetuses, fetal weights, fetal and skeletal variations and malformations; Medium	674193
The study was conducted according to OECD TG 414; EC Commission Directive 87/302/EEC of 18 November 1887; TSCA guidelines 40 CFR part 798.4900. The study was GLP compliant. Rat-Wistar - [rat]-Female	Oral-Gavage-Duration: Reproductive/Developmental-1-F0 - gestation (GD 6-15) Pregnant dams were dosed from GD6-15	**POD: 200 mg/kg-bw/day (NOAEL) - Increased incidences of fetal variations and skeletal retardations** n= 9 Dose= 0, n= 10 Dose= 40, n= 9 Dose= 200, n= 9 Dose= 1,000, mg/kg-bw/dayTotal # of generations: 1 Female Exposure: F0 - gestation, GD 6-15	See footnotes for full summary [9]	The test substance (purity) and methodological details were not included in the study. A small number of animals per group was utilized. The study did not include an appropriate window to adequately assess skeletal effects or effects on the male reproductive system.	Reproductive/Developmental-Reproductive: Uterus weight, corpora lutia/dam, implantations sites/dam, placental weight; Developmental: pre and post implantation loss, total resorptions, live fetuses, fetal weights, fetal and skeletal variations and malformations; Medium	674193
Non-guideline study; but the analysis was performed as described by Beronius et al., 2014, and the Guide for the Care and Use of Laboratory Animals (NIH Publication No. 85-23, revised 1996). Rat-Sprague-Dawley - [rat]-Female	Oral-Gavage-Duration: Reproductive/Developmental-1-F0 - gestation (GD12-21) Exposure in utero from GD 12-21	**POD: 10 mg/kg-bw/day (LOAEL) -Leydig cell aggregation, decreased pup body weights, gene expression changes** n= 6 Dose= 0, n= 6 Dose= 10, n= 6 Dose= 100, n= 6 Dose= 500, n= 6 Dose= 1000, mg/kg-bw/dayTotal # of generations: 1 Female Exposure: F0 - gestation, GD12-21	See footnotes for full summary [10]	The dose spacing was not sufficient for the determination of a NOAEL. Data on dam body weight gains were not clearly reported. The study did not report gavage volumes or specify whether measures were taken to reduce background exposure to other plasticizers.	Reproductive/Developmental-Birth rate, % male pups, male pup body weights, length, AGD, pup testes testosterone levels, testes immunohistochemistry, histopathology, measurements of testes volume and Legdig cell number and size, gene expression analysis.; Medium	2807612

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Diisononyl 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; but the analysis was performed as described by Beronius et al., 2014, and the Guide for the Care and Use of Laboratory Animals (NIH Publication No. 85-23, revised 1996). Rat-Sprague-Dawley - [rat]-Female	Oral-Gavage-Duration: Reproductive/Developmental-1-F0 - gestation (GD12-21) Exposure in utero from GD 12-21	**POD: 10 mg/kg-bw/day (LOAEL) -Leydig cell aggregation, decreased pup body weights, gene expression changes** n= 6 Dose= 0, n= 6 Dose= 10, n= 6 Dose= 100, n= 6 Dose= 500, n= 6 Dose= 1000, mg/kg-bw/dayTotal # of generations: 1 Female Exposure: F0 - gestation, GD12-21	See footnotes for full summary [11]	The dose spacing was not sufficient for the determination of a NOAEL. Data on dam body weight gains were not clearly reported. The study did not report gavage volumes or specify whether measures were taken to reduce background exposure to other plasticizers.	Reproductive/Developmental-Birth rate, % male pups, male pup body weights, length, AGD, pup testes testosterone levels, testes immunohistochemistry, histopathology, measurements of testes volume and Legdig cell number and size, gene expression analysis.; Medium	2807612
Non-guideline study; but the analysis was performed as described by Beronius et al., 2014, and the Guide for the Care and Use of Laboratory Animals (NIH Publication No. 85-23, revised 1996). Rat-Sprague-Dawley - [rat]-Female	Oral-Gavage-Duration: Reproductive/Developmental-1-F0 - gestation (GD12-21) Exposure in utero from GD 12-21	**POD: 10 mg/kg-bw/day (LOAEL) -Leydig cell aggregation, decreased pup body weights, gene expression changes** n= 6 Dose= 0, n= 6 Dose= 10, n= 6 Dose= 100, n= 6 Dose= 500, n= 6 Dose= 1000, mg/kg-bw/dayTotal # of generations: 1 Female Exposure: F0 - gestation, GD12-21	See footnotes for full summary [12]	The dose spacing was not sufficient for the determination of a NOAEL. Data on dam body weight gains were not clearly reported. The study did not report gavage volumes or specify whether measures were taken to reduce background exposure to other plasticizers.	Reproductive/Developmental-Birth rate, % male pups, male pup body weights, length, AGD, pup testes testosterone levels, testes immunohistochemistry, histopathology, measurements of testes volume and Legdig cell number and size, gene expression analysis.; Medium	2807612

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Diisononyl 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 study was not GLP compliant. No guidelines were reported. Rat-Sprague-Dawley - [rat]-Female	Oral-Diet-Duration: Reproductive/Developmental-1-F0 - gestation (GD15-birth)-F0- lactation (birth-PND10) Dams were provided a diet containing test substance from GD15-PND10	**POD: 52 mg/kg-bw/day (NOAEL) -Developmental. Decreased body weight in male offspring sacrificed on PND27 (prepubertal)** n= 5 Dose= 0, n= 5 Dose= 52, n= 5 Dose= 517, n= 5 Dose= 2060, mg/kg-bw/dayTotal # of generations: 1 Female Exposure: F0 - gestation, GD15-birth, F0- lactation, birth-PND10	See footnotes for full summary [13]	Details on diet preparation and verification of test substance concentration in the diet was not done.	Nutritional/Metabolic-Maternal body weight gain and food consumption-Reproductive/Developmental-On PND2: the number, weights and AGD distance. On PND 27 (5/sex/group): organ weights (brain, adrenals, testes, ovaries, and uterus), brain volume measurement of SDN-POA. Remaining offspring were assessed for age and body weights at onset of puberty, estrous cyclicity (assessed via vaginal smears during PNW8-11).At post-natal week 11: organ weights (brain, adrenals, testes, ovaries, uterus, pituitary, and ventral prostate), histology (pituitary, thyroids, adrenal, mammary gland, epididymites, prostate, seminal vesicle, ovaries, uterus, and vagina), and morphometric analyses of testes (percentage of seminiferous tubules with vacuolation) and ovaries (number of secondary follicles, large atretic follicles, and corpora lutea); Medium	192872

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Diisononyl 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 study was not GLP compliant. No guidelines were reported. Rat-Sprague-Dawley - [rat]-Female	Oral-Diet-Duration: Reproductive/Developmental-1-F0 - gestation (GD15-birth)-F0- lactation (birth-PND10) Dams were provided a diet containing test substance from GD15-PND10	**POD: 52 mg/kg-bw/day (NOAEL) -Developmental. Decreased body weight in male offspring sacrificed on PND27 (prepubertal)** n= 5 Dose= 0, n= 5 Dose= 52, n= 5 Dose= 517, n= 5 Dose= 2060, mg/kg-bw/dayTotal # of generations: 1 Female Exposure: F0 - gestation, GD15-birth, F0- lactation, birth-PND10	See footnotes for full summary [14]	Details on diet preparation and verification of test substance concentration in the diet was not done.	Nutritional/Metabolic-Maternal body weight gain and food consumption-Reproductive/Developmental-On PND2: the number, weights and AGD distance. On PND 27 (5/sex/group): organ weights (brain, adrenals, testes, ovaries, and uterus), brain volume measurement of SDN-POA. Remaining offspring were assessed for age and body weights at onset of puberty, estrous cyclicity (assessed via vaginal smears during PNW8-11).At post-natal week 11: organ weights (brain, adrenals, testes, ovaries, uterus, pituitary, and ventral prostate), histology (pituitary, thyroids, adrenal, mammary gland, epididymites, prostate, seminal vesicle, ovaries, uterus, and vagina), and morphometric analyses of testes (percentage of seminiferous tubules with vacuolation) and ovaries (number of secondary follicles, large atretic follicles, and corpora lutea); Medium	192872

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Diisononyl 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 GLP compliance was stated. Study authors state that the study followed the general protocols outlined in the following references: (1) EC Official Journal of the European Communities. No. L 133. Part B. Methods for determination of toxicity, "teratogenicity." Annex V, adopted November 1987 and (2) EPA, U.S. Environmental Protection Agency, 40 CFR Part 798, Toxic Substances Control Act (TSCA), Test Guidelines for Developmental Toxicity Studies, 1985. Rat-Sprague-Dawley - [rat]-Female	Oral-Gavage-Duration: Reproductive/Developmental-1-F0 - gestation (GD 6-15)	**POD: 100 mg/kg-bw/day (NOAEL) -Repro/Dev: increased incidence of skeletal variations in fetuses** n= 24 Dose= 0, n= 25 Dose= 100, n= 24 Dose= 500, n= 23 Dose= 1000, mg/kg-bw/dayTotal # of generations: 1 Female Exposure: F0 - gestation, GD 6-15	See footnotes for full summary [15]	Ambiguity with animal allocation and possible attrition/omission of certain litters are among this study's problems. Additionally, the window of dosing did not cover the entirety of the window of sensitivity for some of the outcomes that the authors assessed.	Reproductive/Developmental-Corpora lutea/dam, implantations/dam, resorptions/dam, post-implantation loss %, viable fetuses/dam, fetal body weights, fetal sex distribution, fetuses with malformations, fetuses with variations, total affected fetuses (sum of resorptions, dead and malformed fetuses/litter), % fetuses and % litters with visceral and skeletal variations: including dilated renal pelves, skeletal variations, lumbar ribs, and cervical ribs. Uterus weights.-Nutritional/Metabolic-Maternal body weights, food consumption; High	680201

* Overall Quality Determination

[1] 11784571: In a one generation reproductive/developmental study, pregnant CD-1 mice (25/group) were exposed to 0 or 0.020 mg/kg/day of di-isononyl phthalate (DiNP) in tocopherol stripped-corn oil from gestation day (GD) 1-7 by orally pipetting the dosing solution into the mouth. At the end of the exposure period, 7 animals in each group were allowed to deliver offspring, whereas 6 animals in each group were euthanized on days on days 7, 13 or 18 to collect implantation chambers, fetus/embryo and placenta tissue. Endpoints evaluated in the group allowed to deliver naturally included: gestation length, litter size, pup weight on PND 1, and sex ratio. Endpoints evaluated on GD 7, 13, and 18 sacrificed animals included maternal serum estrogen and progesterone levels, number of implantation sites, gross uterine pathology, fetal and placental weight (GD 13 and 18), histopathology and immunohistochemistry (implantation chambers and placenta), measurement of total area of the placenta, junctional zone and labyrinth, ratio of labyrinth to junctional zone, and relative mRNA expression in placenta, decidua and embryo tissues for genes involved in decidualization process, angiogenic regulators, and placental cell types.In the group of mice that were allowed to deliver naturally, a significant decrease in gestation time was seen in exposed mice (approximately 18-24 hours earlier delivery compared with control). In addition, significant decreases in the litter size (~30% or a reduction from 16 to 11 pups per littler on average) and the pup weight on PND 1 (approximately 9%) were seen compared with control. The sex ratio in these delivered litters was not significantly different from control. On GD 7, no significant difference in serum progesterone or estrogen were seen in the dams compared with control (data in supplementary file). The number of implantation sites was not significantly different on GD 7 and histological examination did not suggest any changes in embryo attachment to the uterine wall. The study authors described many changes in mRNA expression in implantation chambers and decidua on GD 7 in animals exposed to DiNP suggesting the decidualization process and angiogenic regulators were affected by exposure. On GD 13, no significant difference in levels of serum progesterone were seen compared with control (data not shown; serum estrogen not reported). No significant difference in number of implantation sites was seen; however, significant decreases in weight of the fetuses (~47%) and placenta (~19%) were seen compared to control. Histological examination showed a significant decrease in decreased total placental area and labyrinth area, increased junctional zone area and decreased ratio of labyrinth to junctional zone area compared with control. These findings suggest placental defects that may impact nutrient transport. On GD 18, author report uteri of exposed mice had resorption sites and fewer implantation sites compared with control (data not shown). They also state the control dams had healthy fetuses, whereas mice that were exposed had “poorly perfused placentas”, dead fetuses and resorbed fetuses (data not quantified; representative photo of fetuses shown). Fetuses from the DiNP exposed mice weighed significantly less than those from the control group (~13%). Placental weight was not reported. A LOEAL of 0.020 mg/kg/day was determined for reproductive/developmental effects based on decreased gestation time, litter size, pup body weight on PND1, and changes to placental morphology. A NOAEL could not be determined.

[2] 806135: Pregnant Wistar rats (16/group) were administered DINP (purity 99%) daily at doses of 0 (corn oil vehicle control), 300, 600, 750, and 900 mg/kg in corn oil, via gavage from gestation day (GD) 7 to postnatal day (PND) 17. Animals were inspected twice daily for signs of general toxicity. Maternal body weight and maternal body weight gain between GD 7 and GD 21 were measured and recorded. On gestation day 21, a subset of animals (4 dams per group) were sacrificed with the fetuses. The testes of the fetuses were removed and sampled for histology, as well as measures of testicular testosterone production and testosterone content. Trunk blood was harvested from the fetuses for serum testosterone and luteinizing hormone (LH) measurements. Sections of unspecified reproductive organs and the thyroid were also harvested for histological analysis. In the remaining animals, gestation length was recorded. After birth, live offspring were weighted. Pups were sexed and anogenital distance, nipple retention, and age of sexual maturation were assessed. At PND 1, the interaction between mother and pups was assessed via the maternal pup retrieval test. At PND 13, pups were weighted again and examined for the presence of nipples/areolas. At PND 22, tail blood was harvested for Inhibin B analysis. At PND 90, a subset of animals (1-7 males per litter) were sacrificed for serum testosterone analysis, and animals were examined for the presence of nipples, penile malformations, and testicular descent. Testes and the epididymis were collected for histology and sperm quality and motility were assessed using a computer assisted sperm analysis program. The uteri and ovaries from female offspring were excised and weighted. The last subset of animals (1-2 males per litter and all female pups) underwent behavioral testing. These tests evaluated the motor activity levels of the animals, their ability to habituate to an unfamiliar environment, ability to learn and remember different maze environments (Morris and radial arm), and preference for sweet flavors. In fetuses sacrificed on GD21, multinucleated gonocytes were observed in all treatment groups; increased incidences multinucleated gonocytes and the total number of animals with histological changes were significantly increased at $\geq$600 mg/kg-day, compared with controls. Other significant changes included enlarged diameter of the seminiferous chords and many gonocyte with central location in the seminiferous chords in animals exposed to $\geq$750 mg/kg-day. There were no significant changes in testicular testosterone production, in plasma testosterone levels or in plasma LH levels. Animals exposed to 600 mg/kg-day had significantly lower testicular testosterone content. There was no significant difference in maternal body weight, maternal body weight gain, or any pregnancy results (gestation length, number of liters, number, of fetuses, number of implantations, number of live fetuses, percent post-implantation loss, and percent of males per litter). Exposure to 900 mg/kg-day caused a significant dose-related decrease in anogenital length in males at PND 1. This significant dose-related decreased remained when accounting for body weight. There was also a statistically significant dose-related increase in nipple retention in male pups exposed to 750 and 900 mg/kg-day at PND 13. No effects on pup birth weights were observed, but pup weights on PND13 were significantly decreased in males at 900 mg/kg-day and in females at 750 mg/kg-day. At PND 13 females at 900 mg/kg-day also had decreased body weight relative to control animals but the difference was not statistically significant. At PND 90 there was no significant difference between exposed and control groups in anogenital distance and nipple retention. At PND 90, there was a significant dose-dependent decrease in sperm motility in the 600, 750, and 900 mg/kg-day groups. Additionally, sperm count was significantly elevated at PND 90 in the 900 mg/kg-day group. Exposure to 750 mg/kg-day DINP (but not 900 mg/kg-day) caused a significant increase in saccharin intake in females, but not in males. This may have been a chance finding as the higher exposure group was not significantly impacted. Sex differences were observed in learning and memory tests. In the Morris maze test, control female time to reach the platform was nearly twice as long as the males. There were no effects of treatment on male rats; however, female animals in the exposed groups showed dose-dependent improvements in swim length and latency on the first day of memory testing, but not at other time points. These improvements reached statistical significance in the 900 mg/kg-day group, with females performing as well as control males in the Morris maze task, indicating that diisononyl phthalate has masculinization effects on female animals. There was no significant difference between exposed and control conditions in testosterone production, organ weights, or histopathology at PND 90. The authors report a NOAEL of 300 mg/kg-day based on reproductive toxicity and anti-androgenic effects. A LOAEL is not reported. A LOAEL of 600 mg/kg-day was determined for this review, based on significant decreases in sperm motility and changes in testis histopathology (significantly increased incidence of multinucleated gonocytes).

[3] 806135: Pregnant Wistar rats (16/group) were administered DINP (purity 99%) daily at doses of 0 (corn oil vehicle control), 300, 600, 750, and 900 mg/kg in corn oil, via gavage from gestation day (GD) 7 to postnatal day (PND) 17. Animals were inspected twice daily for signs of general toxicity. Maternal body weight and maternal body weight gain between GD 7 and GD 21 were measured and recorded. On gestation day 21, a subset of animals (4 dams per group) were sacrificed with the fetuses. The testes of the fetuses were removed and sampled for histology, as well as measures of testicular testosterone production and testosterone content. Trunk blood was harvested from the fetuses for serum testosterone and luteinizing hormone (LH) measurements. Sections of unspecified reproductive organs and the thyroid were also harvested for histological analysis. In the remaining animals, gestation length was recorded. After birth, live offspring were weighted. Pups were sexed and anogenital distance, nipple retention, and age of sexual maturation were assessed. At PND 1, the interaction between mother and pups was assessed via the maternal pup retrieval test. At PND 13, pups were weighted again and examined for the presence of nipples/areolas. At PND 22, tail blood was harvested for Inhibin B analysis. At PND 90, a subset of animals (1-7 males per litter) were sacrificed for serum testosterone analysis, and animals were examined for the presence of nipples, penile malformations, and testicular descent. Testes and the epididymis were collected for histology and sperm quality and motility were assessed using a computer assisted sperm analysis program. The uteri and ovaries from female offspring were excised and weighted. The last subset of animals (1-2 males per litter and all female pups) underwent behavioral testing. These tests evaluated the motor activity levels of the animals, their ability to habituate to an unfamiliar environment, ability to learn and remember different maze environments (Morris and radial arm), and preference for sweet flavors. In fetuses sacrificed on GD21, multinucleated gonocytes were observed in all treatment groups; increased incidences multinucleated gonocytes and the total number of animals with histological changes were significantly increased at $\geq$600 mg/kg-day, compared with controls. Other significant changes included enlarged diameter of the seminiferous chords and many gonocyte with central location in the seminiferous chords in animals exposed to $\geq$750 mg/kg-day. There were no significant changes in testicular testosterone production, in plasma testosterone levels or in plasma LH levels. Animals exposed to 600 mg/kg-day had significantly lower testicular testosterone content. There was no significant difference in maternal body weight, maternal body weight gain, or any pregnancy results (gestation length, number of liters, number, of fetuses, number of implantations, number of live fetuses, percent post-implantation loss, and percent of males per litter). Exposure to 900 mg/kg-day caused a significant dose-related decrease in anogenital length in males at PND 1. This significant dose-related decreased remained when accounting for body weight. There was also a statistically significant dose-related increase in nipple retention in male pups exposed to 750 and 900 mg/kg-day at PND 13. No effects on pup birth weights were observed, but pup weights on PND13 were significantly decreased in males at 900 mg/kg-day and in females at 750 mg/kg-day. At PND 13 females at 900 mg/kg-day also had decreased body weight relative to control animals but the difference was not statistically significant. At PND 90 there was no significant difference between exposed and control groups in anogenital distance and nipple retention. At PND 90, there was a significant dose-dependent decrease in sperm motility in the 600, 750, and 900 mg/kg-day groups. Additionally, sperm count was significantly elevated at PND 90 in the 900 mg/kg-day group. Exposure to 750 mg/kg-day DINP (but not 900 mg/kg-day) caused a significant increase in saccharin intake in females, but not in males. This may have been a chance finding as the higher exposure group was not significantly impacted. Sex differences were observed in learning and memory tests. In the Morris maze test, control female time to reach the platform was nearly twice as long as the males. There were no effects of treatment on male rats; however, female animals in the exposed groups showed dose-dependent improvements in swim length and latency on the first day of memory testing, but not at other time points. These improvements reached statistical significance in the 900 mg/kg-day group, with females performing as well as control males in the Morris maze task, indicating that diisononyl phthalate has masculinization effects on female animals. There was no significant difference between exposed and control conditions in testosterone production, organ weights, or histopathology at PND 90. The authors report a NOAEL of 300 mg/kg-day based on reproductive toxicity and anti-androgenic effects. A LOAEL is not reported. A LOAEL of 600 mg/kg-day was determined for this review, based on significant decreases in sperm motility and changes in testis histopathology (significantly increased incidence of multinucleated gonocytes).

[4] 806135: Pregnant Wistar rats (16/group) were administered DINP (purity 99%) daily at doses of 0 (corn oil vehicle control), 300, 600, 750, and 900 mg/kg in corn oil, via gavage from gestation day (GD) 7 to postnatal day (PND) 17. Animals were inspected twice daily for signs of general toxicity. Maternal body weight and maternal body weight gain between GD 7 and GD 21 were measured and recorded. On gestation day 21, a subset of animals (4 dams per group) were sacrificed with the fetuses. The testes of the fetuses were removed and sampled for histology, as well as measures of testicular testosterone production and testosterone content. Trunk blood was harvested from the fetuses for serum testosterone and luteinizing hormone (LH) measurements. Sections of unspecified reproductive organs and the thyroid were also harvested for histological analysis. In the

remaining animals, gestation length was recorded. After birth, live offspring were weighted. Pups were sexed and anogenital distance, nipple retention, and age of sexual maturation were assessed. At PND 1, the interaction between mother and pups was assessed via the maternal pup retrieval test. At PND 13, pups were weighted again and examined for the presence of nipples/areolas. At PND 22, tail blood was harvested for Inhibin B analysis. At PND 90, a subset of animals (1-7 males per litter) were sacrificed for serum testosterone analysis, and animals were examined for the presence of nipples, penile malformations, and testicular descent. Testes and the epididymis were collected for histology and sperm quality and motility were assessed using a computer assisted sperm analysis program. The uteri and ovaries from female offspring were excised and weighted. The last subset of animals (1-2 males per litter and all female pups) underwent behavioral testing. These tests evaluated the motor activity levels of the animals, their ability to habituate to an unfamiliar environment, ability to learn and remember different maze environments (Morris and radial arm), and preference for sweet flavors. In fetuses sacrificed on GD21, multinucleated gonocytes were observed in all treatment groups; increased incidences multinucleated gonocytes and the total number of animals with histological changes were significantly increased at ≥600 mg/kg-day, compared with controls. Other significant changes included enlarged diameter of the seminiferous chords and many gonocyte with central location in the seminiferous chords in animals exposed to ≥750 mg/kg-day. There were no significant changes in testicular testosterone production, in plasma testosterone levels or in plasma LH levels. Animals exposed to 600 mg/kg-day had significantly lower testicular testosterone content. There was no significant difference in maternal body weight, maternal body weight gain, or any pregnancy results (gestation length, number of liters, number, of fetuses, number of implantations, number of live fetuses, percent post-implantation loss, and percent of males per litter). Exposure to 900 mg/kg-day caused a significant dose-related decrease in anogenital length in males at PND 1. This significant dose-related decreased remained when accounting for body weight. There was also a statistically significant dose-related increase in nipple retention in male pups exposed to 750 and 900 mg/kg-day at PND 13. No effects on pup birth weights were observed, but pup weights on PND13 were significantly decreased in males at 900 mg/kg-day and in females at 750 mg/kg-day. At PND 13 females at 900 mg/kg-day also had decreased body weight relative to control animals but the difference was not statistically significant. At PND 90 there was no significant difference between exposed and control groups in anogenital distance and nipple retention. At PND 90, there was a significant dose-dependent decrease in sperm motility in the 600, 750, and 900 mg/kg-day groups. Additionally, sperm count was significantly elevated at PND 90 in the 900 mg/kg-day group. Exposure to 750 mg/kg-day DINP (but not 900 mg/kg-day) caused a significant increase in saccharin intake in females, but not in males. This may have been a chance finding as the higher exposure group was not significantly impacted. Sex differences were observed in learning and memory tests. In the Morris maze test, control female time to reach the platform was nearly twice as long as the males. There were no effects of treatment on male rats; however, female animals in the exposed groups showed dose-dependent improvements in swim length and latency on the first day of memory testing, but not at other time points. These improvements reached statistical significance in the 900 mg/kg-day group, with females performing as well as control males in the Morris maze task, indicating that diisononyl phthalate has masculinization effects on female animals. There was no significant difference between exposed and control conditions in testosterone production, organ weights, or histopathology at PND 90. The authors report a NOAEL of 300 mg/kg-day based on reproductive toxicity and anti-androgenic effects. A LOAEL is not reported. A LOAEL of 600 mg/kg-day was determined for this review, based on significant decreases in sperm motility and changes in testis histopathology (significantly increased incidence of multinucleated gonocytes).

[5] 1325348: In a developmental toxicity study conducted to examine the effects of DINP exposure during gestation and lactation on male rat sexual development, timed-pregnant female Sprague-Dawley (Crl:CD(SD)) rats were exposed to the test substance, DINP, in the diet at concentrations of 0, 760, 3800, and 11,400 ppm (target doses: 0, 50, 250, and 750 mg/kg/day, respectively) from gestation day (GD) 12 to postnatal day (PND) 14. Based on maternal body weights and food consumption, average maternal doses for DINP exposure groups were 56, 288, and 720 mg/kg/day for GD 13-20 and 109, 555, and 1523 mg/kg/day for PND 2-14. The time-weighted average (TWA) was calculated as follows: [(56 mg/kg/day x 8 days) + (109 mg/kg/day x 13 days)]/21 days = 89 mg/kg/day for the 760 ppm group. TWA for the 3800 ppm group was 453 mg/kg/day, and 1217 mg/kg/day for the 11400 ppm group. Maternal body weights and food consumption were recorded 4 days/week. On PND 2, the number of live pups per litter were counted and male pups were weighed. Anogenital distance (AGD) was measured. On PND 2, one male pup from each litter was randomly selected for necropsy and right testis and epididymis were collected for histopathology and testosterone measurements. Plasma samples were also collected and stored for metabolite analysis. Litters were culled to eight pups, with up to five male pups included, along with females, for a total of eight pups per litter. The left testis and epididymis were weighed. Blood samples and testes were collected for metabolite or testosterone analysis, respectively, from extra male pups. On PND 14, male pup body weight, AGD, and nipple/areolae were measured. On PND 21, maternal animals and female pups were euthanized. Male pups remained housed with littermates and were weaned. On PND 49-50, all remaining male rats were weighed and euthanized. AGE was measured and pups were examined in situ for retained nipples and the genital tract and urogenital tract were examined. The right and left gubernacular cord lengths were measured and any abnormalities such as undescended testes and epididymal agenesis, were recorded. Reproductive and non-reproductive tissues were examined in situ and weights were determined for the following: testes (right and left), epididymis (right and left), seminal vesicles (pair), glans penis, ventral prostate, levator ani plus bulbocavernosus (LABC) muscles, Cowper's glands (pair), kidney (pair), liver, and adrenal glands (pair). The right testis and epididymis were collected from one male per litter for histopathology and testosterone measurements. Animal necropsies were divided over two days due to the large number of animals. All five treatment groups were represented on each necropsy day. In maternal animals exposed to 11,400 ppm, mean body weights were significantly decreased on GD 20, PND 2, and PND 14 (8%, 12%, and 14%, respectively) and mean body weight gains were significantly decreased during GD 10-20 (30%) and PND 2-14 (35%), compared to the control group. Maternal body weight gains from PND2-14 were non-significantly decreased (35%) compared to control. Mean food consumption in maternal animals was significantly decreased at 11,400 ppm during GD 13-20 (17%) and PND 2-14 (28%), compared to the control group. There were no significant differences in the number of live pups or number of live pups per litter on PND 2. Male pup body weight was significantly decreased at 11,400 ppm on PND 2 and 14 (12% and 27%, respectively), and at 3800 ppm only on PND 14 (10%). No differences in male pup body weight were observed on PND 49-50 at study termination. At 11,400 ppm, absolute AGD and scaled AGD (AGD/BW^1/3) in male pups were significantly decreased (16% and 7%, respectively) on PND 14, but not on PND 2 or PND 49-50. No significant effects on gross findings of the reproductive organs were observed at necropsy. Sporadic incidences of flaccid epididymis and hypospadias were observed in treated and control animals and were not significantly increased in treated animals compared to controls. There were no significant differences in absolute or relative (to body weight) weights of the testes or epididymis on PND 2 or PND 49-50, testis testosterone level on PND 49-50, gubernacular cord length on PND 49-50, or the number of nipples/areolae in male pups on PND 14 or PND 49-50. The incidence of animals with multinucleated germ cells (MNGs) in the testes on PND 2 was significantly increased in the 3800 and 11,400 ppm exposure groups (incidences of 1/24, 2/20, 7/20, and 18/19 at 0, 760, 3800, and 11,400 ppm, respectively), and the incidence of animals with large Leydig cell aggregates (LCA) was significantly increased at 11,400 ppm (incidences of 4/24, 4/20, 8/20, and 19/19 at 0, 760, 3800, and 11,400 ppm, respectively), compared to the control group. For organ weight measurements on PND 49-50, only the absolute weight of LABC muscle (but not relative weight) was significantly decreased at 11,400 ppm (10%), compared to the control group. For the PND 49-50 observation, no other significant organ weight changes, or significant reproductive malformations, and/or no significant or histopathological changes in the testes were observed in test substance-exposed animals relative to controls. In pups on PND 2, serum metabolites identified in the 760, 3800, and 11,400 ppm exposure groups included monoisononyl phthalate (MiNP; concentrations of 0.02, 0.13, and 0.49 µM, respectively), monocarboxyisooctyl phthalate (MCiOP; concentrations of 1.7, 7.8, and 14.5 µM, respectively), monohydroxyisononyl phthalate (MHiNP; 0.1, 0.27, and 0.45 µM, respectively), and monooxoisononyl phthalate (MOiNP; 0, 0.07, and 0.15 µM, respectively). None of the measured metabolites were detected in plasma collected from control group animals. The study authors did not report a NOAEL or LOAEL value. The NOAEL for systemic effects in maternal animals (determined by the reviewer) is 3800 ppm (453mg/kg/day) based on decreases in body weight and body weight gain at 11,400 ppm (LOAEL; 1217 mg/kg/day). The NOAEL for developmental effects (determined by the reviewer) is 760 ppm (89mg/kg/day) based on decreases in male pup body weight on PND 14 and histopathological changes in the testes (increased incidence of MNGs) on PND 2 at 3800 ppm (LOAEL; 453 mg/kg/day).The study authors reported a NOEL in weaned animals of 11,400 ppm. The study authors note the significant changes in observed in male pups were temporary and "the call that they are adverse is questionable".

[6] 1987588: Male and female Sprague-Dawley rats (30/sex/group) were exposed to 0.5, 1.0 or 1.5% of di-isononyl phthalate (DINP) via dietary exposure in feed for 10 weeks prior to mating and throughout the mating period. Females were additionally exposed throughout gestation and lactation until weaning on postnatal day (PND) 21. The mean dose of DINP was calculated weekly by study authors based on measured food intake and body

weight of the animals. This Reviewer averaged the weekly measurements to determine mean intake. Mean intake of males over the 10 weeks was 0, 398, 790, and 1216 mg DINP/kg/day at 0, 0.5, 1.0 and 1.5%, respectively. Mean intake for females over 10 weeks of premating until PND21 was 0, 493, 970, and 1392 mg DINP/kg/day at 0, 0.5, 1.0 and 1.5%, respectively. Males were sacrificed after mating following the birth of their last litter sired and females were sacrificed after weaning (PND 21). Endpoints examined in F0 animals included: survival, clinical signs of toxicity, food consumption, body weights, indices for male and female mating, fertility, fecundity and gestation, days of gestation, and gross examination and organ weights of (liver, kidneys, left and right testis, epididymis, prostate, seminal vesicles, and left and right ovaries). Endpoints in F1 offspring included: survival, body weights (PND 0, 1, 4, 7, 14, and 21), body weight gain, litter size, number of live and dead offspring and % of live males and females. Endpoints examined in F0 animals included: survival, clinical signs of toxicity, food consumption, body weights, indices for male and female mating, fertility, fecundity and gestation, days of gestation, and gross examination and organ weights (liver, kidneys, left and right testis, epididymis, prostate, seminal vesicles, and left and right ovaries). Endpoints in F1 offspring included: survival, body weights (PND 0, 1, 4, 7, 14, and 21), body weight gain, litter size, number of live and dead offspring and % of live males and females. Deaths were considered incidental by study authors (one low dose male died on day 91, one mid dose female died during parturition). No treatment-related clinical signs of toxicity were observed in the P1 animals. Significant decreases in body weights were observed in F0 males and females in the mid- (3.4% -8.9%) and high (3.6-12%) dose groups compared to control. Significant decrease in body weights were also seen during gestation and postpartum period in the mid-dose females (5.3-15.3%) and high-dose females (10.8-23.3%) compared to control. Terminal body weights were significantly decreased in males (7% and 11%) and females (7% and 14%) in mid- and high-dose groups, respectively. Decreases in body weight gains mirrored the observed decreases in body weights in the mid-and high-dose animals. No biologically relevant changes in body weight or body weight gain were seen in the low-dose males or females. Decreased food consumption was observed in the mid-dose males and females (5.3-8.7%) and high dose males and females (5.8-10.5%) during premating compared with control. Significant decreases in food consumption were also seen during gestation and postpartum periods in the mid- (59-27.4%) and high- (11.6-42.2%) dose females compared to control. No biologically relevant changes in food consumption were seen in the low dose females during gestation and postpartum. No gross findings were observed at necropsy. Significant increase in absolute liver weight (14, 27, and 34%), relative liver weight (18, 37, and 50%), absolute kidney weight (25, 28, and 28%), and relative kidney weight (30, 39, 45%) were seen in low-, mid and high-dose F0 males, respectively. In F0 females, significant increase in absolute liver (26, 44, and 52%) and relative liver weight (12, 17, and 17%) were seen in the low-, mid and high-dose groups, and absolute kidney weight (13 and 8%) in the low- and mid-dose groups. Significant increases in absolute left testicular weight (10%), right testicular weight (9%), and right epididymis weight (7%) were seen in the high-dose males compare to control. Relative testicular and epididymal weights were significantly increased in the mid- and high-dose groups compared to control. Significant decreases in absolute right ovary weight (35%) and left ovary weight (26%), and relative right ovarian weight (25%) were seen in the high-dose group compared to control. No differences in mating or fertility indices or female gestational indices were seen compared to control. In the high-dose group, decreases in mean litter size (12.5) and mean live offspring (11.9) were seen compared to control (14.1 and 13.9, respectively). In the high-dose offspring significant decreases in live birth index (95.2%), day 4 survival index (85.6%), day 14 survival index (92.7%) and lactation index (87.2%) were seen compared to control (9.2%, 93.1%, 98.5%, and 93.9%, respectively); however, these values were within historical control range from this laboratory. No difference in sex ratios were observed. No treatment related clinical signs or observable abnormalities were seen in offspring from PND 0-21. F1 body weights were significantly decreased on PND0 in males (7, 8, and 10%) and females (8, 10, and 12%) and on PND 21 in males (10, 27, 46%) and females (8, 27, and 47%) in the low-, mid-and high-dose groups, respectively. The study authors attribute these decreases to “maternal stress and/or direct effects of DINP via exposure through lactation and not indicative of developmental abnormalities or reproductive toxicity”. A study-wide LOAEL 398 mg/kg/day was determined for reproductive/developmental, hepatic/liver and renal/kidney effects based on decreased F1 body weights and increased absolute kidney and liver weights in F1 animals. No NOAEL was determined.

[7] 1987589: In a two-generation reproductive toxicity study, virgin male and female Crl:CD BR-VAF/Plus (Sprague-Dawley) rats (30/sex/group) were exposed to 0, 0.2, 0.4 or 0.8% diisononyl phthalate (DINP) in feed for 10 weeks prior to mating and throughout mating (~ 3 weeks) until the delivery of F1 litters (males) and throughout gestation and lactation (from GD 0 to PND 21) in females. On PND 21, F1 male and female offspring (2/sex/litter) were randomly selected to be parents (P2 generation) for the F2 generation; remaining offspring were sacrificed for evaluation of terminal endpoints. P2 animals (30/sex) were administered the same test diet as received by their parents starting on PND 21, for at least 11 weeks prior to mating and throughout mating until delivery of F2 offspring (males) or throughout gestation and lactation in females as described for the P1 generation. Doses in mg/kg/day were determined based on measured body weights and food consumption. For the P1 generation, mean measured dose rates during premating for the 0.2, 0.4, and 0.8% exposure groups were 118-212 mg/kg/day (males) and 145-215 mg/kg/day (females), 236-426 mg/kg/day (males) and 278-425 mg/kg/day (females), and 477-852 mg/kg/day (males) and 562-830 mg/kg/day (females), respectively. Mean measured dose rates during gestation and lactation for P1 generation females for the 0.2, 0.4, and 0.8% exposure groups were 139-153 mg/kg/day (gestation) and 159-350 mg/kg/day (lactation), 274-301 mg/kg/day (gestation) and 347-731 mg/kg/day (lactation), and 543-571 mg/kg/day (gestation) and 673 mg/kg/day (lactation), respectively. For the P2 generation, mean measured dose rates during premating for the 0.2, 0.4, and 0.8% exposure groups were 114-264 mg/kg/day (males) and 140-254 mg/kg/day (females), 235-523 mg/kg/day (males) and 271-522 mg/kg/day (females), and 467-1090 mg/kg/day (males) and 544-1060 mg/kg/day (females), respectively. Mean measured dose rates during gestation and lactation for P2 generation females for the 0.2, 0.4, and 0.8% exposure groups were 133-153 mg/kg/day (gestation) and 174-395 mg/kg/day (lactation), 271-307 mg/kg/day (gestation) and 348-758 mg/kg/day (lactation), and 544-577 mg/kg/day (gestation) and 718-1541 mg/kg/day (lactation), respectively.Adult animals and weanlings of both generations were examined daily for mortality and clinical signs of toxicity. Detailed clinical observations of adult animals were performed at least weekly throughout the study, with additional observations conducted in females during the post-natal period (PND 0, 4, 7, 10, 14, and 21 during lactation). Parental body weight was measured weekly in males until terminal sacrifice, and weekly in females until mating and then on GD 0, 7, 14, and 21 and PND 0, 4, 7, 10, 14, and 21. Food consumption was measured concurrently with body weight in males and females throughout the study, except during mating. F1 and F2 offspring were examined daily for appearance and survival. Pups were counted, sexed, weighed, and examined externally on PND 0, 1, 4, 7, 14, and 21. Litters were culled to 4/sex on PND. Gross postmortem examinations were conducted on all animals in the study at termination. Liver, kidneys, testes, prostate, seminal vesicles, epididymides, ovaries, and brain of parental animals were weighed. Histopathology was performed on selected tissues, including the pituitary gland, testes, epididymides, seminal vesicles, vagina, uterus, ovaries, mammary gland, and gross lesions, from parental animals in the control and 0.8% groups, and the liver and kidneys of all dose groups. There were no treatment-related deaths or clinical signs in parental P1 animals. One male in the 0.4% dose group and one female in the 0.2% dose group died prior to mating and were considered incidental. Low incidences of clinical findings were observed in parental animals across all groups and were considered unrelated to treatment. No treatment-related effects on body weight, body weight gain, or food consumption were observed in males. In females of the 0.8% group, compared to controls, mean body weight was slightly, yet significantly decreased on PND 14 (-7%) and 21 (-8%), and mean body weight gain was significantly decreased during GD 0-7 (-19%) and PND 0-21 (-84%). Mean food consumption was significantly decreased in females of the 0.8% group during PND 10-14 (-14%), 14-21 (-17%), and 0-21 (-9%). No treatment-related findings were observed in males or females at gross necropsy. In males, there was a significant increase in absolute liver weight at 0.8% (16%) and in relative (to body weight) liver weight at 0.4 (8%) and 0.8% (16%), compared to the control group. There were also significant increases in absolute kidney weights in males at 0.4 (14%) and 0.8% (20%) and in relative (to body weight) kidney weight at 0.2 (9%), 0.4 (17%), and 0.8% (22%) in males. In females at 0.4 and 0.8%, there were significant increases in absolute (20 and 22%, respectively) and relative (15 and 28%, respectively) liver weights, compared to controls. There were also significant increases in absolute kidney weight in females at 0.2, 0.4, and 0.8% (8, 10, and 8%, respectively) and in relative kidney weight at 0.8% (13%). Other organ weight changes were considered incidental and unrelated to treatment. Histopathological changes observed in the livers of P1 animals included increased cytoplasmic eosinophilia at all doses in males (0/30, 28/30, 29/30, 30/30 at 0, 0.2, 0.4, and 0.8%, respectively) and females (0/30, 22/30, 26/30, and 29/30 at 0, 0.2, 0.4, and 0.8%, respectively). In the absence of correlating histopathology findings, the kidney weight changes in males and females were considered incidental and unrelated to treatment.Three, four, five, and five P1 females were not pregnant at 0, 0.2, 0.4, and 0.8%, respectively. There were no treatment-related effects on mating, fertility, fecundity, or gestational indices, gestation length, live or dead offspring, or sex ratio. In F1 offspring, there were no treatment-related effects on survival indices, clinical findings, or abnormal findings at necropsy. Mean litter size at 0.8% was slightly increased compared to controls (15.1 and 12.5, respectively). Mean litter size at 0.8% was within the historical control range; however, the value for the control group was slightly lower than the historical control range. Mean live offspring per litter was also slightly higher than controls (14.8 and 12.2, respectively), but was within the historical control range. Mean body weights

of pups were significantly decreased in males and females at 0.8% on PND 0 (5-7%), 7 (10-15%), and 14 (13-15%), and at all doses on PND 21 (10-19%), compared to controls. The study authors noted that body weights of all treated offspring at all intervals were within the range of the historical control for the laboratory.No treatment-related effects deaths or clinical signs were observed in parental animals of the second generation (P2). Mean body weights of P2 generation males were significantly decreased at 0.8% (7-13%) throughout the dosing period, compared to controls. The body weight decreases in males exceeded 10% only on Day 0, 7, and 14 and thereafter were below 10% for the remainder of the dosing period. Body weight gain was significantly decreased at 0.4 and 0.8% in P2 males only during Day 42-49 and 63-70. In P2 generation females, mean body weights were significantly decreased during premating at 0.4% on Day 0 (-6%) and on Days 0, 7, and 14 at 0.8% (-10, -8, and -6%, respectively). Mean body weight of females was significantly decreased at 0.8% on during gestation on GD 14 and during the postnatal period on PND 4, 7, 10, 14, and 21 (8-11%). The decrease in female body weight exceeded 10% only on PND 14. Mean food consumption was slightly (<8%), yet significantly decreased during the premating period at 0.8% in males (Week 1) and females (Weeks 9 and 11), compared to controls. Significant decreases in mean food consumption were also observed in females at 0.8% during gestation (13-16%) and the postnatal periods (9-12%, respectively). Treatment-related gross necropsy findings were observed in the kidneys of males and included an increased incidence of dilated renal pelves in all treatment groups, compared to controls. Changes in organ weights of the liver and kidneys and histopathological changes in the liver of P2 generation animals were similar to findings for the P1 generation. Only relative liver weight was significantly increased in males at 0.8% (15%), compared to the control group. Mean absolute kidney weight was significantly increased in males at 0.8% (14%) and relative kidney weight was significantly increased at 0.4 and 0.8% (14 and 23%, respectively). A significant increase in relative left and right epididymides weights was observed at 0.8% (14% and 16%, respectively). In females at 0.8%, there were significant increases in absolute and relative liver weight (18% and 27%, respectively) and relative kidney weight (10%), compared to controls. Due to the absence of correlating findings on histopathology or other adverse effects, the epididymides weight changes in males and the kidney weight changes in females were considered incidental and unrelated to treatment. The changes in liver weights in males and females correlated with treatment-related histopathology, including increased cytoplasmic eosinophilia, at all doses, compared to controls. Respective incidences of cytoplasmic eosinophilia in the liver at 0, 0.2, 0.4, and 0.8% were 0/30, 20/30, 29/30, and 30/30 in males and 0/30, 20/30, 26/30, and 30/30 in females. An increased incidence of renal dilatation was also observed in males at 0.4 and 0.8%, compared to controls, and was considered treatment related. Incidences for renal dilatation in males for the 0, 0.2, 0.4, and 0.8% groups were 7/30, 8/30, 12/30, and 17/30, respectively. Eight, nine, nine, and eleven P2 females were not pregnant at 0, 0.2, 0.4, and 0.8%, respectively. There were no treatment-related effects on mating, fertility, fecundity, or gestational indices, gestation length, live or dead offspring, mean litter size, mean live offspring per litter, or sex ratio. In offspring, there were no treatment-related effects on survival indices, clinical findings, or abnormal findings at necropsy. Mean body weights of male pups were significantly decreased (≤21%) in all dose groups on PND 7 and 21 and at 0.4 and 0.8% on PND 14, compared to controls. In females, mean body weights were significantly decreased (≤22%) in all dose groups on PND 0, 4, 7, 14, and 21 and at 0.4 and 0.8% on PND 1, compared to controls. The study authors noted that body weights of all treated offspring at all intervals were within the range of the historical control for the laboratory with the exception of males at 0.8% on PND 0 and 1 and females at 0.8% on PND 0. The study authors reported a LOEL for systemic effects of 0.2% based on histopathological findings in the liver (increased incidence of cytoplasmic eosinophilia), a LOEL of 0.2% for developmental effects based on decreased offspring body weights, and a NOEL for reproductive effects of 0.8% based on no adverse effects at the highest dose tested. The reviewer considers the LOAEL for systemic effects to be 0.2% (equivalent to 114 mg/kg/day, based on the lowest equivalent dose for P1 and P2 generation animals) based on the observed histopathological changes (increased incidence of cytoplasmic eosinophilia), and the LOAEL for developmental effects to be 0.2% based on decreased offspring body weight. The reviewer considers the NOAEL for reproductive effects to be 0.8% (equivalent to 467 mg/kg/day), the highest dose tested. [Note: HERO IDs 1987589 and 680202 were used for this study evaluation and extraction.]

[8] 674193: In a standard OECD TG 414 teratogenicity study, pregnant Wistar (Chbb/THOM outbred strain) rats (9-10/group/formulation) were administered two separate formulations of DINP (CASRN 28553-12-0) at 0, 40, 200, or 1,000 mg/kg-day, via gavage, from GD 6-15. In the first formulation (DINP – 2), at least 95% of the main alcohol components derived from n-butene, were alkyl-substituted octanol or heptanol. In the second formulation (DINP-3), codimerbutene was used to synthesize the main alcohol components, resulting in at least 60% alkyl-substituted hexanols. Dams were monitored for mortality and clinical signs of toxicity. Body weights were recorded on days GDs 0, 6, 10, 15, and 20, and body weight gain was determined. Food consumption was purportedly monitored, but no quantitative results were reported. The time of autopsy was not explicitly stated but is presumed to be GD20 based on another study cited for methods details (HERO 673425). Dam uterine, liver, and kidney weights were recorded. The numbers of corpora lutea and implantation sites were counted along with the numbers of live fetuses, pre and post-implantation loss, and early and late resorptions. All fetuses were weighed (sex was not recorded), and external, visceral, and skeletal examinations were conducted. The percentage of fetuses (and litters) with malformations, variations, and retardations were recorded separately. No dams administered DINP-2 or DINP-3 died. One dam treated with DINP-2 showed vaginal hemorrhage during the treatment period. No other clinical signs of toxicity were reported for either formulation. No changes to dam body weights or food consumption were reported in animals dosed with DINP-2. Mean body weights on GDs 13, 15, and 17, and body weight gains from GD 6-15 were significantly reduced in animals treated with 1,000 mg/kg-day of DINP-3. High-dose animals treated with DINP-3 also showed a significant reduction (magnitude of effect not reported) in food consumption on unspecified treatment days. No organ weight changes occurred in animals dosed with DINP-2. In those administered 1,000 mg/kg-day of DINP-3, relative liver weights were significantly increased by 11% relative to controls. Absolute liver weights were not reported. For DINP-2, the only significant developmental effect that was observed was an increase in accessory 14th ribs at 1000 mg/kg/day. The only developmental effect observed fetuses of dams treated with DINP-2 was an increase in the incidences of accessory 14th ribs in high-dose animals; statistical significance was not specified. Similarly, for DINP-3, treatment-related skeletal variations (i.e., rudimentary cervical and/or accessory 14th ribs), skeletal retardations (i.e., unossified or incompletely ossified sternebrae), and soft tissue retardations (i.e., hydroureter) were observed at 1000 mg/kg/day.The maternal NOAEL was 200 mg/kg-day for DINP-2 and DINP-3 formulations and the maternal LOAEL was 1,000 mg/kg-day for DINP-2 and DINP-3 based on vaginal hemorrhage (DINP-2), decreased body weight (DINP-3), decreased food consumption (DINP-3), and increased relative liver weight (DINP-3). The developmental NOAEL was 200 mg/kg-day for both DINP-2 and DINP-3 formulations and the developmental LOAEL was 1000 mg/kg/day based on increased incidence of skeletal variations (DINP-2 and DINP-3), and skeletal and soft tissue retardations (DINP-3 only).

[9] 674193: In a standard OECD TG 414 teratogenicity study, pregnant Wistar (Chbb/THOM outbred strain) rats (9-10/group/formulation) were administered two separate formulations of DINP (CASRN 28553-12-0) at 0, 40, 200, or 1,000 mg/kg-day, via gavage, from GD 6-15. In the first formulation (DINP – 2), at least 95% of the main alcohol components derived from n-butene, were alkyl-substituted octanol or heptanol. In the second formulation (DINP-3), codimerbutene was used to synthesize the main alcohol components, resulting in at least 60% alkyl-substituted hexanols. Dams were monitored for mortality and clinical signs of toxicity. Body weights were recorded on days GDs 0, 6, 10, 15, and 20, and body weight gain was determined. Food consumption was purportedly monitored, but no quantitative results were reported. The time of autopsy was not explicitly stated but is presumed to be GD20 based on another study cited for methods details (HERO 673425). Dam uterine, liver, and kidney weights were recorded. The numbers of corpora lutea and implantation sites were counted along with the numbers of live fetuses, pre and post-implantation loss, and early and late resorptions. All fetuses were weighed (sex was not recorded), and external, visceral, and skeletal examinations were conducted. The percentage of fetuses (and litters) with malformations, variations, and retardations were recorded separately. No dams administered DINP-2 or DINP-3 died. One dam treated with DINP-2 showed vaginal hemorrhage during the treatment period. No other clinical signs of toxicity were reported for either formulation. No changes to dam body weights or food consumption were reported in animals dosed with DINP-2. Mean body weights on GDs 13, 15, and 17, and body weight gains from GD 6-15 were significantly reduced in animals treated with 1,000 mg/kg-day of DINP-3. High-dose animals treated with DINP-3 also showed a significant reduction (magnitude of effect not reported) in food consumption on unspecified treatment days. No organ weight changes occurred in animals dosed with DINP-2. In those administered 1,000 mg/kg-day of DINP-3, relative liver weights were significantly increased by 11% relative to controls. Absolute liver weights were not reported. For DINP-2, the only significant developmental effect that was observed was an increase in accessory 14th ribs at 1000 mg/kg/day. The only developmental effect observed fetuses of dams treated with DINP-2 was an increase in the incidences of accessory 14th ribs in high-dose animals; statistical significance was not specified. Similarly, for DINP-3, treatment-related skeletal variations (i.e., rudimentary cervical and/or accessory 14th ribs), skeletal retardations (i.e., unossified or incompletely ossified sternebrae), and soft tissue retardations (i.e., hydroureter) were observed at 1000 mg/kg/day.The maternal NOAEL was 200 mg/kg-day for DINP-2 and DINP-3 formulations and the maternal LOAEL was 1,000 mg/kg-day for DINP-2 and DINP-3 based on vaginal

hemorrhage (DINP-2), decreased body weight (DINP-3), decreased food consumption (DINP-3), and increased relative liver weight (DINP-3). The developmental NOAEL was 200 mg/kg-day for both DINP-2 and DINP-3 formulations and the developmental LOAEL was 1000 mg/kg/day based on increased incidence of skeletal variations (DINP-2 and DINP-3), and skeletal and soft tissue retardations (DINP-3 only).

[10] 2807612: Pregnant Sprague Dawley rats (6/group) were administered DINP (≥99% mixture of C9 isomers with ≤ 0.15% dioctyl phthalate) at 0 (corn oil vehicle), 10, 100, 500, and 1000 mg/kg-day in corn oil, via gavage, from GD 12 to 21. After birth, pups were weighed, and body lengths and AGD were measured. Male pups were sacrificed (PND1). Testicular testosterone concentrations were measured and testes were microscopically analyzed. The normality of seminiferous tubules was assessed via immunohistochemistry, looking specifically for Desmin staining, and semi-quantitative immunohistochemical staining of Leydig cell-specific proteins 3β-hydroxysteroid dehydrogenase (3β-HSD), cholesterol side chain cleavage enzyme (CYP11A1), and insulin-like 3 (INSL3) was conducted. Enzymological staining for 3β-HSD was also performed. Fetal Leydig cell size and nuclear size were estimated using computer-assisted image analysis software. Finally, RT-PCR was performed to evaluate the expression of membrane receptor genes, cholesterol-transporting genes, and steroidogenic enzyme genes. One dam died during pregnancy, presumably just prior to birth. The pups from this dam were surgically extracted and were alive. It is unclear if these pups were included in the data analysis. Dam body weights on GD0 and GD 11, prior to the start of exposure were reported and were consistent across groups. Data for "gain weight after birth" was reported in a table, but the time frame was not specified (e.g., starting body weights till birth, GD0 till birth, or GD11 till birth). There was no indication of a statistically significant change, but the data show large differences across groups (weight gain of 2.0, 8.5, 2.2, 4.2, and 0.8 grams in the control, 10, 100, 500, and 1,000 mg/kg-day groups, respectively. Exposure to DINP had no effects on the duration of pregnancy, birth rates, number of pups born per dam, sex ratio, AGD, or AGD normalized to the cube root of pup weight. Pup body weights and cube root of body weight were significantly reduced in all treatment groups, in a non-dose-related manner compared with controls. Testicular testosterone levels decreased with dose and were significantly reduced at 1,000 mg/kg-day. The number of testes showing focal testis dysgenesis, as determined by immunological staining of desmin, and the occurrence of multi-nucleated giant cells were significantly increased at ≥ 100 mg/kg-day. There were no changes in testes volume, or fetal Leydig size, including cytoplasmic or nuclear size, that showed a relation to dose (significant changes were observed in the lowest dose groups only). However, the number of fetal Leydig cells per cluster (aggregation) was significantly increased at ≥ 10 mg/kg-day in a dose-related manner. The percentage of single-cell populations decreased at ≥100 mg/kg-day. Semi-quantitative immunohistochemical analysis showed non-dose-related reductions in 3β-HSD and INSL3 protein levels in samples from treated animals, compared with controls. The expression levels of Ins13 and 3β-HSD were also significantly reduced at ≥ 10 mg/kg-day and at ≥ 100 mg/kg-day, respectively. Other gene expression changes included reductions in luteinizing hormone receptor (Lhcgr), steroidogenic acute regulatory protein (Star), and steroidogenic enzymes Cyp11a1, Cyp17a1, and Hsd17b3. The study author reported LOAEL was 10 mg/kg-day (the lowest dose), based on fetal Leydig cell aggregation; pup body weights and protein and expression levels of Leydig cell markers were also decreased at this dose A NOAEL was not determined.

[11] 2807612: Pregnant Sprague Dawley rats (6/group) were administered DINP (≥99% mixture of C9 isomers with ≤ 0.15% dioctyl phthalate) at 0 (corn oil vehicle), 10, 100, 500, and 1000 mg/kg-day in corn oil, via gavage, from GD 12 to 21. After birth, pups were weighed, and body lengths and AGD were measured. Male pups were sacrificed (PND1). Testicular testosterone concentrations were measured and testes were microscopically analyzed. The normality of seminiferous tubules was assessed via immunohistochemistry, looking specifically for Desmin staining, and semi-quantitative immunohistochemical staining of Leydig cell-specific proteins 3β-hydroxysteroid dehydrogenase (3β-HSD), cholesterol side chain cleavage enzyme (CYP11A1), and insulin-like 3 (INSL3) was conducted. Enzymological staining for 3β-HSD was also performed. Fetal Leydig cell size and nuclear size were estimated using computer-assisted image analysis software. Finally, RT-PCR was performed to evaluate the expression of membrane receptor genes, cholesterol-transporting genes, and steroidogenic enzyme genes. One dam died during pregnancy, presumably just prior to birth. The pups from this dam were surgically extracted and were alive. It is unclear if these pups were included in the data analysis. Dam body weights on GD0 and GD 11, prior to the start of exposure were reported and were consistent across groups. Data for "gain weight after birth" was reported in a table, but the time frame was not specified (e.g., starting body weights till birth, GD0 till birth, or GD11 till birth). There was no indication of a statistically significant change, but the data show large differences across groups (weight gain of 2.0, 8.5, 2.2, 4.2, and 0.8 grams in the control, 10, 100, 500, and 1,000 mg/kg-day groups, respectively. Exposure to DINP had no effects on the duration of pregnancy, birth rates, number of pups born per dam, sex ratio, AGD, or AGD normalized to the cube root of pup weight. Pup body weights and cube root of body weight were significantly reduced in all treatment groups, in a non-dose-related manner compared with controls. Testicular testosterone levels decreased with dose and were significantly reduced at 1,000 mg/kg-day. The number of testes showing focal testis dysgenesis, as determined by immunological staining of desmin, and the occurrence of multi-nucleated giant cells were significantly increased at ≥ 100 mg/kg-day. There were no changes in testes volume, or fetal Leydig size, including cytoplasmic or nuclear size, that showed a relation to dose (significant changes were observed in the lowest dose groups only). However, the number of fetal Leydig cells per cluster (aggregation) was significantly increased at ≥ 10 mg/kg-day in a dose-related manner. The percentage of single-cell populations decreased at ≥100 mg/kg-day. Semi-quantitative immunohistochemical analysis showed non-dose-related reductions in 3β-HSD and INSL3 protein levels in samples from treated animals, compared with controls. The expression levels of Ins13 and 3β-HSD were also significantly reduced at ≥ 10 mg/kg-day and at ≥ 100 mg/kg-day, respectively. Other gene expression changes included reductions in luteinizing hormone receptor (Lhcgr), steroidogenic acute regulatory protein (Star), and steroidogenic enzymes Cyp11a1, Cyp17a1, and Hsd17b3. The study author reported LOAEL was 10 mg/kg-day (the lowest dose), based on fetal Leydig cell aggregation; pup body weights and protein and expression levels of Leydig cell markers were also decreased at this dose A NOAEL was not determined.

[12] 2807612: Pregnant Sprague Dawley rats (6/group) were administered DINP (≥99% mixture of C9 isomers with ≤ 0.15% dioctyl phthalate) at 0 (corn oil vehicle), 10, 100, 500, and 1000 mg/kg-day in corn oil, via gavage, from GD 12 to 21. After birth, pups were weighed, and body lengths and AGD were measured. Male pups were sacrificed (PND1). Testicular testosterone concentrations were measured and testes were microscopically analyzed. The normality of seminiferous tubules was assessed via immunohistochemistry, looking specifically for Desmin staining, and semi-quantitative immunohistochemical staining of Leydig cell-specific proteins 3β-hydroxysteroid dehydrogenase (3β-HSD), cholesterol side chain cleavage enzyme (CYP11A1), and insulin-like 3 (INSL3) was conducted. Enzymological staining for 3β-HSD was also performed. Fetal Leydig cell size and nuclear size were estimated using computer-assisted image analysis software. Finally, RT-PCR was performed to evaluate the expression of membrane receptor genes, cholesterol-transporting genes, and steroidogenic enzyme genes. One dam died during pregnancy, presumably just prior to birth. The pups from this dam were surgically extracted and were alive. It is unclear if these pups were included in the data analysis. Dam body weights on GD0 and GD 11, prior to the start of exposure were reported and were consistent across groups. Data for "gain weight after birth" was reported in a table, but the time frame was not specified (e.g., starting body weights till birth, GD0 till birth, or GD11 till birth). There was no indication of a statistically significant change, but the data show large differences across groups (weight gain of 2.0, 8.5, 2.2, 4.2, and 0.8 grams in the control, 10, 100, 500, and 1,000 mg/kg-day groups, respectively. Exposure to DINP had no effects on the duration of pregnancy, birth rates, number of pups born per dam, sex ratio, AGD, or AGD normalized to the cube root of pup weight. Pup body weights and cube root of body weight were significantly reduced in all treatment groups, in a non-dose-related manner compared with controls. Testicular testosterone levels decreased with dose and were significantly reduced at 1,000 mg/kg-day. The number of testes showing focal testis dysgenesis, as determined by immunological staining of desmin, and the occurrence of multi-nucleated giant cells were significantly increased at ≥ 100 mg/kg-day. There were no changes in testes volume, or fetal Leydig size, including cytoplasmic or nuclear size, that showed a relation to dose (significant changes were observed in the lowest dose groups only). However, the number of fetal Leydig cells per cluster (aggregation) was significantly increased at ≥ 10 mg/kg-day in a dose-related manner. The percentage of single-cell populations decreased at ≥100 mg/kg-day. Semi-quantitative immunohistochemical analysis showed non-dose-related reductions in 3β-HSD and INSL3 protein levels in samples from treated animals, compared with controls. The expression levels of Ins13 and 3β-HSD were also significantly reduced at ≥ 10 mg/kg-day and at ≥ 100 mg/kg-day, respectively. Other gene expression changes included reductions in luteinizing hormone receptor (Lhcgr), steroidogenic acute regulatory protein (Star), and steroidogenic enzymes Cyp11a1, Cyp17a1, and Hsd17b3. The study author reported LOAEL was 10 mg/kg-day (the lowest dose), based on fetal Leydig cell aggregation; pup body weights and protein and expression levels of Leydig cell markers were also decreased at this dose A NOAEL was not determined.

[13] 192872: In a study focused on evaluating the impact of endocrine disruption on brain and sexual differentiation, pregnant CD(SD) IGS rats (5/group) were fed a soy-free diet containing 0, 400, 4000, or 20000 ppm of DINP from GD 15 to PND 10, after which all animals were fed a soy-free diet without any test chemical. Study authors calculated the maternal DINP intake, based on food consumption on GD 15-20 as 0, 30.7, 306.7, and 1,164.5 mg/kg/day and PND 2-10 as 0, 66.2, 656.7, 2,656.7 mg/kg/day in the 0, 400, 4,000, and 20,000 ppm groups, respectively. The time-weighted average intakes calculated by this reviewer were 0, 52, 517, and 2,060 mg/kg/day at 0, 400, 4,000, and 20,000 ppm, respectively. Dams were monitored for changes in body weight and food intake. Litter size was recorded at parturition. On PND 2, pups were counted and pup body weights and AGD distance were measured. On PND 10, litters were culled randomly to maintain 5-8 pups/litter. At weaning (PND 21), offspring were placed on standard CRF-1 basal diets. On PND 27 (5 offspring/sex/group) were sacrificed to assess body weights, organ weights (brain, adrenals, testes, ovaries, and uterus), and brain volume measurements of sexually dimorphic nucleus of preoptic area (SDN-POA). The remaining offspring were monitored for age and body weights at the onset of puberty, and estrous cyclicity (assessed via vaginal smears during post-natal weeks 8-11). At post-natal week (PNW) 11, pups (5/sex/group) were sacrificed to assess body weight, organ weights (brain, adrenals, testes, ovaries, uterus, pituitary and ventral prostate), histology on pituitary, thyroids, adrenal, mammary gland, epididymis, prostate, seminal vesicle, ovaries, uterus, and vagina), and morphometric analyses of testes (percentage of seminiferous tubules with vacuolation) and ovaries (number of secondary follicles, large atretic follicles, and corpora lutea).Maternal body weight gain was significantly decreased in the high-dose group from GD 15-20 (55%) and during lactation from PND 2-10 (85%), compared with controls. Food intake was also significantly decreased in the high-dose groups from GD 15-20 (28%) and PND 2-10 (22%). There were no differences in the litter sizes, or in the numbers of live offspring, pup body weights, or AGDs on PND2 between treated animals and controls. Body weight gains in offspring were significantly decreased in the high-dose group from PND 2-10 in males (56%) and females (56%), and in males from PND 21-42 (18%). No significant differences in body weight gains were seen in males or females from PND 10-21, or in females from PND 42-77. In male offspring sacrificed at PND 27 (prepubertal), body weights were significantly decreased (18% and 43%) in the mid-and high-dose groups, respectively. Also, in the high-dose males on PND 27, significant changes in the following organ weights were seen: decreased absolute brain (30%), increased relative brain weight (54%), and decreased absolute and relative testes weights (54% and 19%, respectively), compared with controls. In the high-dose female offspring sacrificed on PND 27, significant decreases in body weight (39%), absolute brain weight (11%), absolute ovaries (30%), and absolute uterus (48%), and significant increases in relative brain weight (46%) and relative adrenals (43%) were observed. There were no significant differences in the volumes of SDN-POA in the brains of offspring at PND 27. Relative to controls, no significant differences in onset of puberty were observed in the offspring of exposed rats (age of vaginal opening or age of preputial separation). On the day of vaginal opening and preputial separation, offspring body weights were significantly decreased in the high-dose group (19% and 18%, respectively) compared to control. No changes in the estrous cyclicity of female offspring were observed. In offspring sacrificed on post-natal week 11, there were no significant differences in body weights, absolute and relative brain, pituitary, adrenal, testes, prostate, ovaries, or uterus weights, compared with controls. In high-dose male offspring, there were significant increases in the incidences of rats with slight degeneration of meiotic spermatocytes at stage XIV (4/5), minimal vacuolar degeneration of Sertoli cells (4/5), minimal scattered cell debris in ducts of epididymis (4/5), and a 5.5-fold increase in the number of seminiferous tubules that containing vacuoles; none these changes occurred in controls (0/5). No significant changes in the prostate were seen compared to control. High dose female offspring sacrificed on PNW 11 had significantly fewer numbers of corpora lutea/mm2 (27%), compared with controls.The authors concluded that treatment with DINP during the critical period for brain sexual differentiation only caused endocrine/reproductive toxicity at high doses that were also maternally toxic.A maternal NOAEL of 517 mg/kg/day (4,000 ppm) and a LOAEL of 2,060 mg/kg-day (20,000 ppm) was determined based on reduced maternal body weight gains and decreased food consumption. A developmental NOAEL of 52 mg/kg/day (400 ppm) and LOAEL of 517 mg/kg/day (4,000 ppm) was determined, based on an 18% decrease male offspring body weights on PND 27 (prepubertal). Other developmental changes (prepubertal endocrine-related organ weight changes, slight degeneration of Sertoli cells, meiotic spermatocytes, and slight decreases in the number of corpora lutea in post-puberty offspring) occurred at a dose that was also maternally toxic (2,657 mg/kg/day or 20,000 ppm).TWA doses were calculated using the following formula: (Mean intake from GD15-20 x 6 days) + (mean intake from PND2-10 X 9 days) / 15 days

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At weaning (PND 21), offspring were placed on standard CRF-1 basal diets. On PND 27 (5 offspring/sex/group) were sacrificed to assess body weights, organ weights (brain, adrenals, testes, ovaries, and uterus), and brain volume measurements of sexually dimorphic nucleus of preoptic area (SDN-POA). The remaining offspring were monitored for age and body weights at the onset of puberty, and estrous cyclicity (assessed via vaginal smears during post-natal weeks 8-11). At post-natal week (PNW) 11, pups (5/sex/group) were sacrificed to assess body weight, organ weights (brain, adrenals, testes, ovaries, uterus, pituitary and ventral prostate), histology on pituitary, thyroids, adrenal, mammary gland, epididymis, prostate, seminal vesicle, ovaries, uterus, and vagina), and morphometric analyses of testes (percentage of seminiferous tubules with vacuolation) and ovaries (number of secondary follicles, large atretic follicles, and corpora lutea).Maternal body weight gain was significantly decreased in the high-dose group from GD 15-20 (55%) and during lactation from PND 2-10 (85%), compared with controls. Food intake was also significantly decreased in the high-dose groups from GD 15-20 (28%) and PND 2-10 (22%). There were no differences in the litter sizes, or in the numbers of live offspring, pup body weights, or AGDs on PND2 between treated animals and controls. Body weight gains in offspring were significantly decreased in the high-dose group from PND 2-10 in males (56%) and females (56%), and in males from PND 21-42 (18%). No significant differences in body weight gains were seen in males or females from PND 10-21, or in females from PND 42-77. In male offspring sacrificed at PND 27 (prepubertal), body weights were significantly decreased (18% and 43%) in the mid-and high-dose groups, respectively. Also, in the high-dose males on PND 27, significant changes in the following organ weights were seen: decreased absolute brain (30%), increased relative brain weight (54%), and decreased absolute and relative testes weights (54% and 19%, respectively), compared with controls. In the high-dose female offspring sacrificed on PND 27, significant decreases in body weight (39%), absolute brain weight (11%), absolute ovaries (30%), and absolute uterus (48%), and significant increases in relative brain weight (46%) and relative adrenals (43%) were observed. There were no significant differences in the volumes of SDN-POA in the brains of offspring at PND 27. Relative to controls, no significant differences in onset of puberty were observed in the offspring of exposed rats (age of vaginal opening or age of preputial separation). On the day of vaginal opening and preputial separation, offspring body weights were significantly decreased in the high-dose group (19% and 18%, respectively) compared to control. No changes in the estrous cyclicity of female offspring were observed. In offspring sacrificed on post-natal week 11, there were no significant differences in body weights, absolute and relative brain, pituitary, adrenal, testes, prostate, ovaries, or uterus weights, compared with controls. In high-dose male offspring, there were significant increases in the incidences of rats with slight degeneration of meiotic spermatocytes at stage XIV (4/5), minimal vacuolar degeneration of Sertoli cells (4/5), minimal scattered cell debris in ducts of epididymis (4/5), and a 5.5-fold increase in the number of seminiferous tubules that containing vacuoles; none these changes occurred in controls (0/5). No significant changes in the prostate were seen compared to control. High dose female offspring sacrificed on PNW 11 had significantly fewer numbers of corpora lutea/mm2 (27%), compared with controls.The authors concluded that treatment with DINP during the critical period for brain sexual differentiation only caused endocrine/reproductive toxicity at high doses that were also maternally toxic.A maternal NOAEL of 517 mg/kg/day (4,000 ppm) and a LOAEL of 2,060 mg/kg-day (20,000 ppm) was determined based on reduced maternal body weight gains and decreased food consumption. A developmental NOAEL of 52 mg/kg/day (400 ppm) and LOAEL of 517 mg/kg/day (4,000 ppm) was determined, based on an 18% decrease male offspring body weights on PND 27 (prepubertal). Other developmental changes (prepubertal endocrine-related organ weight changes, slight degeneration of Sertoli cells, meiotic spermatocytes, and slight decreases in the number of corpora lutea in post-puberty offspring) occurred at a dose that was also maternally toxic (2,657 mg/kg/day or 20,000 ppm).TWA doses were calculated using the following formula: (Mean intake from GD15-20 x 6 days) + (mean intake from PND2-10 X 9 days) / 15 days

[15] 680201: Pregnant Sprague-Dawley rats (23-25/group) were exposed to 0, 100, 500 or 100 mg/kg/day of di-isononyl (DINP) via oral gavage in corn oil vehicle from gestational day (GD) 6 to 15. Animals were monitored for clinical signs before, during and after the exposure period. Maternal body weights and food consumption were measured on GD 0, 6, 9, 12, 15, 18 and 21. Animals were euthanized on GD 21 and the uterus was excised, weighed and examined for number of implantation sites, resorptions and number of live and dead fetuses. The ovaries were collected and the number of corpora lutea from each ovary was determined. All fetuses were weighed, sexed and examined for external, visceral and skeletal malformations and variations. Significantly reduced maternal body weights were observed from GDs 6-9 and GDs 6-15 at 1000 mg/kg/day, while food consumption was significantly reduced from GD 6-15 and 9-12 respectively at 1000 mg/kg/day. Maternal body weight gain was significantly increased from GD 15-18 at 1000 mg/kg/day, while food consumption was significantly increased from GD 18-21 at 1000 mg/kg/day. No effects were observed for numbers of corpora lutea, total implantation sites, resorptions, postimplantation loss, viable fetuses, fetal body weights and fetal sex ratios. There was no increased incidence of external, visceral nor skeletal malformations in DINP exposed fetuses. The percent of litters with visceral variations were significantly increased at 1000 mg/kg/day, while the percent of fetuses with visceral variations were significantly increased at all dose levels. Dilated renal pelves were the most common variant. The percent of litters with skeletal variations were significantly increased at 500 mg/kg/day but not at 1000 mg/kg/day, while the percent of fetuses with skeletal variations were increased at 500 and 1000 mg/kg/day. The most common skeletal variants were rudimentary lumbar ribs and supernumerary cervical ribs.In the original publication, a LOAEL of 1000 mg/kg/day and a NOAEL of 500 mg/kg/day for reproductive/developmental effects were determined based on increased incidence of visceral variations and rudimentary lumbar ribs and supernumerary cervical ribs in fetuses. A LOAEL of 1000 mg/kg/day and a NOAEL of 500 mg/kg/day for nutritional/metabolic effects were determined based on decreased body weights and food consumption during the exposure period. However, an NTP expert panel (NTP-CERHR, 2003, HERO ID: 680097) selected a developmental NOAEL of 100 mg/kg/day based on the significant incidence of skeletal variations, including rudimentary lumbar ribs at 500 and 1000 mg/kg/day and supernumerary cervical ribs at 1000 mg/kg/day. The NTP panel informed the sponsor of the Waterman et al. study that they believed that there were more recent and superior statistical approaches for analysis of the dataset and a reanalysis of the data by the study sponsor were consistent with the NTP panel's interpretation of the dataset (i.e., supported a developmental NOAEL of 100 mg/kg/day). The updated analysis is presented on pages II-15 and II-16 of NTP-CERHR (2003). The NTP expert panel concurred with the original study author's NOEL of 500 mg/kg/day for effects on maternal weight gain and food consumption.

Diisononyl Phthalate- Isomer: Di-isononyl phthalate (mixed isomers) - CASRN 68515-48-0 - Chronic (>91 days)

Guideline and Animal Species, Strain, Sex	Exposure Route and Exposure Duration	Study-wide POD and Dose/ Concentration(s)	Summary	Major Limitations	Principal Target Organs/Systems and OQD*	HERO ID
Study was conducted in accordance with the EPA Good Laboratory Practice Regulations set forth in 40 CFR Part 792. Rat-Fischer 344 - [rat]-Both	Oral-Diet-Duration: Chronic (>90 days)-7-24-2-year(s) 24 hours/day 7 days/week 18 month(s)	**POD: 300 mg/kg-bw/day (LOAEL) -Increased organ weight (liver, kidney, adrenal)** n= 10 Dose= 0, n= 10 Dose= 30, n= 10 Dose= 300, n= 10 Dose= 600, mg/kg-bw/day	See footnotes for full summary [1]	increase in food consumption during week 86 (8 days instead of 7 days) and significant decrease for 88 week (6 days instead of 7 days) due to study schedule change	Mortality; Nutritional/Metabolic; Other: (clinical observation); Hepatic/Liver; Other (Endocrine)-Organ weights (adrenals), gross necropsy (adrenals), (pituitary), pancreas, adrenals.; Cardiovascular; Immune/Hematological; Reproductive/Developmental; Neurological/Behavioral; Lung/Respiratory; Skin/Connective Tissue; Ocular/Sensory; Gastrointestinal; Musculoskeletal; Medium	1065989
Study was conducted in accordance with the EPA Good Laboratory Practice Regulations set forth in 40 CFR Part 792. Rat-Fischer 344 - [rat]-Both	Oral-Diet-Duration: Chronic (>90 days)-7-24-2-year(s) 24 hours/day 7 days/week 2 year(s)	**POD: 300 mg/kg-bw/day (LOAEL) -Increased organ weight (liver, kidney, adrenal)** n= 10 Dose= 0, n= 10 Dose= 30, n= 10 Dose= 300, n= 10 Dose= 600, mg/kg-bw/day	See footnotes for full summary [2]	increase in food consumption during week 86 (8 days instead of 7 days) and significant decrease for 88 week (6 days instead of 7 days) due to study schedule change	Nutritional/Metabolic; Renal/Kidney; Hepatic/Liver; Cancer/Carcinogenesis; Uninformative	1065989
Study was conducted in accordance with the EPA Good Laboratory Practice Regulations set forth in 40 CFR Part 792. Rat-Fischer 344 - [rat]-Both	Oral-Diet-Duration: Chronic (>90 days)-7-24-2-year(s) 24 hours/day 7 days/week 6 month(s)	**POD: 300 mg/kg-bw/day (LOAEL) -Increased organ weight (liver, kidney, adrenal)** n= 10 Dose= 0, n= 10 Dose= 30, n= 10 Dose= 300, n= 10 Dose= 600, mg/kg-bw/day	See footnotes for full summary [3]	increase in food consumption during week 86 (8 days instead of 7 days) and significant decrease for 88 week (6 days instead of 7 days) due to study schedule change	Nutritional/Metabolic; Renal/Kidney; Hepatic/Liver; Cancer/Carcinogenesis; High	1065989

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* Overall Quality Determination

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Only high doses females exhibited significant (57.14%) increase in relative spleen organ weight compared to the control. High dose males displayed statistically significant increases in heart (5.88%), brain about 10.91%, testes, about 23.84%, and thyroid relative organ weights, which can be attributed to significant decrease in terminal body weight.At study termination there were no considerable variations in the individual ALT and AST values and lead to assumption that may be related individual animal health rather than treatment. Difference in mean urea nitrogen values for males at high dose and females at mid and high dose were noted. The mean creatinine value for males at high dose were also observed as biologically different, but not statistically and reported as not treatment related. There were differences in urine protein (low and mid dose) and urine osmolality (high dose) when compared to control. Urine protein was considered not related to treatment, and more likely individual health of the animals due to individual variation values. There were no significant statistical or biological differences noted between treated female and control in mean urine chemistry. Male rat group, white bold cell count (WBCs) at mid and high dose group was high, but not statistically higher than the control values with 2 males that had extremely elevated WBCs, and the abnormal high WBCs increased with dose and were treatment related. Females at mid dose exhibited statistically significant increase in mean WBC as compared to the control; the author stated it was biologically significant and not treatment related. Males and females at mid and high dose had slightly lower red blood cell count (RBC), hemoglobin (Hgb) and hematocrit (HCT) compared to the control values and this results were both statistically (high dose male) and biologically for males and indication of anemia development which is probably related exposure and supported by increased frequency of nucleated red blood cells (NRBCs), polychromatophilic red cells and reticulocytes (Retic) incidence specially at high dose. However, these responses were biologically but not statistically significant and may not associated with treatment. Liver, kidney, pituitary, lung, and testicular, epididymites/seminal discoloration was noted frequently for both treated and controls and it appear to be a result of the aging process in rats and not treatment related. At the study termination, ovarian and uterine distention and masses were noted frequently for both treated and controls and it appear to be a result of the aging process in rats and not treatment related. The most notable necropsy observation in animals which died spontaneously or were sacrificed in moribund condition included liver, kidney, testes, lung, and pituitary discoloration as well as enlarged spleen and uterine masses which were noted in both treated and control animals. Histopathological examinations were being conducted and reported separately (see HERO ID# 1325509).No author derived toxicity values were reported. A LOAEL of 300mg/kg-BW/day was determined for this review based on statistically significant increases in absolute and relative organ weights (e.g., liver, kidney and adrenal) in both male and female rats. This determination due to the presence of supporting clinical chemistry changes.Mg/kg-BW/day= %X10,000Xfood factor (0.10 rat); 0.3%X10,000X0.10= 300mg/kg-BW/day

[5] 1065989: In this chronic toxicity study, total of 880 male and female rat Fischer-344 were divided into 4 groups of unexposed control, low, mid, and high dose groups (n=110 rats/sex), and Diisononyl Phthalate (DINP) (CASRN 68515-48-0) was orally administered in diet (0, 30, 300 and 600mg/kg-BW/day) for 24 months interim. Survival/death, in-life observation, body weight, food consumption, organ weights clinical chemistry/hematology, and gross necropsy, were quantitively assessed/measured.A total of 201/880 animals died prior to scheduled sacrifice [(20 male, 16 female control), (25 male, 24 female low dose), (30 male,31 female mid dose), and (29 male,26 female high dose). The animals survived were sacrificed as scheduled. The four groups of both sexes analyzed for estimate median and comparison between groups survivorships. Female between groups comparison indicated a negative dose response while a difference between control and mid dose and high dose was seen. For males the dose response significance difference between control and high dose. A moderate difference in females with mid-dose having the shortest survivorship and males about equal survivorship of the mid and high dose group. The author reported that the compound is associated with a moderate decrease in survivorship with strange effect between male and female.The incidences of in-life observations were relatively low throughout the 24-month test period. The most frequently noted observations were alopecia and scabs on various area of the skin, subcutaneous palpable masses, and ocular opacity, vascularization, and discharge. Similar incidence was noted in the control groups; therefore, it appeared not related to treatment toxicity. Pinworms decreased by the study termination, and few were detected in few animals with no association to other signs of disease. Pale extremities or pale-yellow extremities noted in number of animals prior to spontaneous death or sacrifice and majority of the observations were accompanied by icterus of subcutaneous tissues and presence of enlarge spleen which both are common findings in this strain of rat.Body weights by sex were statistically analyzed (mean

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[6] 1065989: In this chronic toxicity study, total of 880 male and female rat Fischer-344 were divided into 4 groups of unexposed control, low, mid, and high dose groups (n=110 rats/sex), and Diisononyl Phthalate (DINP) (CASRN 68515-48-0) was orally administered in diet (0, 30, 300 and 600mg/kg-BW/day) for 24 months interim. Survival/death, in-life observation, body weight, food consumption, organ weights clinical chemistry/hematology, and gross necropsy, were quantitively assessed/measured.A total of 201/880 animals died prior to scheduled sacrifice [(20 male, 16 female control), (25 male, 24 female low dose), (30 male,31 female mid dose), and (29 male,26 female high dose). The animals survived were sacrificed as scheduled. The four groups of both sexes analyzed for estimate median and comparison between groups survivorships. Female between groups comparison indicated a negative dose response while a difference between control and mid dose and high dose was seen. 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clinical chemistry changes.Mg/kg-BW/day= %X10,000Xfood factor (0.10 rat); 0.3%X10,000X0.10= 300mg/kg-BW/day

Diisononyl Phthalate- Isomer: Di-isononyl phthalate (mixed isomers) - CASRN 68515-48-0 - Reproductive/Developmental

Guideline and Animal Species, Strain, Sex	Exposure Route and Exposure Duration	Study-wide POD and Dose/ Concentration(s)	Summary	Major Limitations	Principal Target Organs/Systems and OQD*	HERO ID
The study did not report any compliance methods or if study was consistent with GLP conditions. Rat-Other (Sprague-Dawley-Harlan)-Female	Oral-Gavage-Duration: Reproductive/Developmental-1-F0 - gestation (GD 14-18) Pregnant dams were exposed from GD 14-18	**POD: 1500 mg/kg-bw/day (NOAEL) -No evidence of maternal toxicity** n= 3 Dose= 0, n= 3 Dose= 500, n= 3 Dose= 750, n= 3 Dose= 1000, n= 3 Dose= 1500, mg/kg-bw/dayTotal # of generations: 1 Female Exposure: F0 - gestation, GD 14-18	Pregnant Harlan Sprague-Dawley rats (3/group) were administered 0, 500, 750, 1000, or 1500 mg/kg-day of DINP (mixed isomers; CAS RN 68515-48-0) in corn oil via gavage on GDs 14-18. Dams were monitored for mortality, overt clinical signs of toxicity, and body weight. Dams were sacrificed on GD 18 and fetal testes were collected for determination of ex vivo testicular testosterone production and changes in expression of StAR, CypllA, and Insl3 mRNA. Treatment with DINP did not cause maternal mortality, overt toxicity, reduce maternal body weight, or reduce litter size (data not shown in). Ex vivo fetal testicular testosterone production was significantly reduced in a dose-dependent manner at $\geq$500 mg/kg-day (data shown for this chemical was not shown on its own; table with data combined rats from this experiment with those rats treated with DINP CAS RN 28553-12-0). An ED50 was calculated to be 852 mg/kg/day for reduced testicular testosterone. mRNA levels for StAR and Cyp11a were significantly reduced at $\geq$1000 mg/kg-day. A maternal NOAEL of 1500 mg/kg/day was determined based on lack of mortality, clinical signs, and body weight changes in pregnant dams. A developmental NOAEL or LOAEL for the compound of interest cannot be determined because data for two CASRN's were combined and, therefore, the POD is based on maternal effects. The authors report there was no difference between the response of the two isomers, therefore data were combined for statistical analysis. The LOAEL for the combined data would be 500 mg/kg-day based on changes to ex-vivo fetal testicular testosterone levels.	Data for DINP (CAS RN 28553-12-0) and DINP (mixed isomers; CAS RN 68515-48-0) were reported to be similar and were therefore combined and presented together. Means +/- SE reported are of both chemicals combined.	Reproductive/Developmental-Male Reproductive - testosterone-Nutritional/Metabolic-Maternal body weight and body weight gain; Medium	788239

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Diisononyl Phthalate- Isomer: Di-isononyl phthalate (mixed isomers) - CASRN 68515-48-0 - Reproductive/Developmental

Guideline and Animal Species, Strain, Sex	Exposure Route and Exposure Duration	Study-wide POD and Dose/ Concentration(s)	Summary	Major Limitations	Principal Target Organs/Systems and OQD*	HERO ID
The study did not report any compliance methods or if study was consistent with GLP conditions. Rat-Other (Sprague-Dawley-Harlan)-Female	Oral-Gavage-Duration: Reproductive/Developmental-1-F0 - gestation (GD 14-18) Pregnant dams were exposed from GD 14-18	**POD: 1500 mg/kg-bw/day (NOAEL) -No evidence of maternal toxicity** n= 3 Dose= 0, n= 3 Dose= 500, n= 3 Dose= 750, n= 3 Dose= 1000, n= 3 Dose= 1500, mg/kg-bw/dayTotal # of generations: 1 Female Exposure: F0 - gestation, GD 14-18	Pregnant Harlan Sprague-Dawley rats (3/group) were administered 0, 500, 750, 1000, or 1500 mg/kg-day of DINP (mixed isomers; CAS RN 68515-48-0) in corn oil via gavage on GDs 14-18. Dams were monitored for mortality, overt clinical signs of toxicity, and body weight. Dams were sacrificed on GD 18 and fetal testes were collected for determination of ex vivo testicular testosterone production and changes in expression of StAR, CypllA, and Insl3 mRNA. Treatment with DINP did not cause maternal mortality, overt toxicity, reduce maternal body weight, or reduce litter size (data not shown in). Ex vivo fetal testicular testosterone production was significantly reduced in a dose-dependent manner at $\geq$500 mg/kg-day (data shown for this chemical was not shown on its own; table with data combined rats from this experiment with those rats treated with DINP CAS RN 28553-12-0). An ED50 was calculated to be 852 mg/kg/day for reduced testicular testosterone. mRNA levels for StAR and Cyp11a were significantly reduced at $\geq$1000 mg/kg-day. A maternal NOAEL of 1500 mg/kg/day was determined based on lack of mortality, clinical signs, and body weight changes in pregnant dams. A developmental NOAEL or LOAEL for the compound of interest cannot be determined because data for two CASRN's were combined and, therefore, the POD is based on maternal effects. The authors report there was no difference between the response of the two isomers, therefore data were combined for statistical analysis. The LOAEL for the combined data would be 500 mg/kg-day based on changes to ex-vivo fetal testicular testosterone levels.	Data for DINP (CAS RN 28553-12-0) and DINP (mixed isomers; CAS RN 68515-48-0) were reported to be similar and were therefore combined and presented together. Means +/- SE reported are of both chemicals combined.	Reproductive/Developmental-Male Reproductive - testosterone-Nutritional/Metabolic-Maternal body weight and body weight gain; Medium	788239

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Diisononyl Phthalate- Isomer: Di-isononyl phthalate (mixed isomers) - CASRN 68515-48-0 - Reproductive/Developmental

Guideline and Animal Species, Strain, Sex	Exposure Route and Exposure Duration	Study-wide POD and Dose/ Concentration(s)	Summary	Major Limitations	Principal Target Organs/Systems and OQD*	HERO ID
The study did not report any compliance methods or if study was consistent with GLP conditions. Rat-Other (Sprague-Dawley-Harlan)-Female	Oral-Gavage-Duration: Reproductive/Developmental-1-F0 - gestation (GD 14-18) Pregnant dams were exposed from GD 14-18	**POD: 1500 mg/kg-bw/day (NOAEL) -No evidence of maternal toxicity** n= 3 Dose= 0, n= 3 Dose= 500, n= 3 Dose= 750, n= 3 Dose= 1000, n= 3 Dose= 1500, mg/kg-bw/dayTotal # of generations: 1 Female Exposure: F0 - gestation, GD 14-18	Pregnant Harlan Sprague-Dawley rats (3/group) were administered 0, 500, 750, 1000, or 1500 mg/kg-day of DINP (mixed isomers; CAS RN 68515-48-0) in corn oil via gavage on GDs 14-18. Dams were monitored for mortality, overt clinical signs of toxicity, and body weight. Dams were sacrificed on GD 18 and fetal testes were collected for determination of ex vivo testicular testosterone production and changes in expression of StAR, CypllA, and Insl3 mRNA. Treatment with DINP did not cause maternal mortality, overt toxicity, reduce maternal body weight, or reduce litter size (data not shown in). Ex vivo fetal testicular testosterone production was significantly reduced in a dose-dependent manner at $\geq$500 mg/kg-day (data shown for this chemical was not shown on its own; table with data combined rats from this experiment with those rats treated with DINP CAS RN 28553-12-0). An ED50 was calculated to be 852 mg/kg/day for reduced testicular testosterone. mRNA levels for StAR and Cyp11a were significantly reduced at $\geq$1000 mg/kg-day. A maternal NOAEL of 1500 mg/kg/day was determined based on lack of mortality, clinical signs, and body weight changes in pregnant dams. A developmental NOAEL or LOAEL for the compound of interest cannot be determined because data for two CASRN's were combined and, therefore, the POD is based on maternal effects. The authors report there was no difference between the response of the two isomers, therefore data were combined for statistical analysis. The LOAEL for the combined data would be 500 mg/kg-day based on changes to ex-vivo fetal testicular testosterone levels.	Data for DINP (CAS RN 28553-12-0) and DINP (mixed isomers; CAS RN 68515-48-0) were reported to be similar and were therefore combined and presented together. Means +/- SE reported are of both chemicals combined.	Reproductive/Developmental-Male Reproductive - testosterone-Nutritional/Metabolic-Maternal body weight and body weight gain; Medium	788239

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Diisononyl Phthalate- Isomer: Di-isononyl phthalate (mixed isomers) - CASRN 68515-48-0 - Reproductive/Developmental

Guideline and Animal Species, Strain, Sex	Exposure Route and Exposure Duration	Study-wide POD and Dose/ Concentration(s)	Summary	Major Limitations	Principal Target Organs/Systems and OQD*	HERO ID
The study was conducted according to OECD TG 414; EC Commission Directive 87/302/EEC of 18 November 1887; TSCA guidelines 40 CFR part 798.4900. The study was GLP compliant. Rat-Wistar - [rat]-Female	Oral-Gavage-Duration: Reproductive/Developmental-1-F0 - gestation (GD 6-15) Pregnant dams were dosed from GD6-15	**POD: 200 mg/kg-bw/day (NOAEL) - increased incidences of skeletal variations (i.e., accessory 14th rib and rudimentary cervical rib(s))** n= 9 Dose= 0, n= 9 Dose= 40, n= 8 Dose= 200, n= 10 Dose= 1,000, mg/kg-bw/dayTotal # of generations: 1 Female Exposure: F0 - gestation, GD 6-15	See footnotes for full summary [1]	The test substance (purity) and methodological details were not included in the study. A small number of animals per group was utilized. The study did not include an appropriate window to adequately assess skeletal effects or effects on the male reproductive system.	Reproductive/Developmental-Reproductive: Uterus weight, corpora lutia/dam, implantations sites/dam, placental weight; Developmental: pre and post implantation loss, total resorptions, live fetuses, fetal weights, fetal and skeletal variations and malformations; Medium	674193
The study was conducted according to OECD TG 414; EC Commission Directive 87/302/EEC of 18 November 1887; TSCA guidelines 40 CFR part 798.4900. The study was GLP compliant. Rat-Wistar - [rat]-Female	Oral-Gavage-Duration: Reproductive/Developmental-1-F0 - gestation (GD 6-15) Pregnant dams were dosed from GD6-15	**POD: 200 mg/kg-bw/day (NOAEL) - increased incidences of skeletal variations (i.e., accessory 14th rib and rudimentary cervical rib(s))** n= 9 Dose= 0, n= 9 Dose= 40, n= 8 Dose= 200, n= 10 Dose= 1,000, mg/kg-bw/dayTotal # of generations: 1 Female Exposure: F0 - gestation, GD 6-15	See footnotes for full summary [2]	The test substance (purity) and methodological details were not included in the study. A small number of animals per group was utilized. The study did not include an appropriate window to adequately assess skeletal effects or effects on the male reproductive system.	Reproductive/Developmental-Reproductive: Uterus weight, corpora lutia/dam, implantations sites/dam, placental weight; Developmental: pre and post implantation loss, total resorptions, live fetuses, fetal weights, fetal and skeletal variations and malformations; Medium	674193

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Guideline and Animal Species, Strain, Sex	Exposure Route and Exposure Duration	Study-wide POD and Dose/ Concentration(s)	Summary	Major Limitations	Principal Target Organs/Systems and OQD*	HERO ID
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The study was conducted according to OECD TG 414; EC Commission Directive 87/302/EEC of 18 November 1887; TSCA guidelines 40 CFR part 798.4900. The study was GLP compliant. Rat-Wistar - [rat]-Female	Oral-Gavage-Duration: Reproductive/Developmental-1-F0 - gestation (GD 6-15) Pregnant dams were dosed from GD6-15	**POD: 200 mg/kg-bw/day (NOAEL) - increased incidences of skeletal variations (i.e., accessory 14th rib and rudimentary cervical rib(s))** n= 9 Dose= 0, n= 9 Dose= 40, n= 8 Dose= 200, n= 10 Dose= 1,000, mg/kg-bw/dayTotal # of generations: 1 Female Exposure: F0 - gestation, GD 6-15	See footnotes for full summary [4]	The test substance (purity) and methodological details were not included in the study. A small number of animals per group was utilized. The study did not include an appropriate window to adequately assess skeletal effects or effects on the male reproductive system.	Reproductive/Developmental-Reproductive: Uterus weight, corpora lutia/dam, implantations sites/dam, placental weight; Developmental: pre and post implantation loss, total resorptions, live fetuses, fetal weights, fetal and skeletal variations and malformations; Medium	674193

* Overall Quality Determination

[1] 674193: In a standard OECD TG 414 teratogenicity study, pregnant Wistar (Chbb/THOM outbred strain) rats (8-10/group/formulation) were administered the DINP isomer (CASRN 68515-48-0, purity ≥99%) at 0, 40, 200, or 1,000 mg/kg-day, via gavage, from GD 6-15. Dams were monitored for mortality and clinical signs of toxicity. Body weights were recorded on days GDs 0, 6, 10, 15, and 20, and body weight gain was determined. Food consumption was purportedly monitored, but no quantitative results were reported. The time of autopsy was not explicitly stated but is presumed to be GD20 based on another study cited for methods details (HERO 673425). Dam uterine, liver, and kidney weights were recorded. The numbers of corpora lutea and implantation sites were counted along with the numbers of live fetuses, pre and post-implantation loss, and early and late resorptions. All fetuses were weighed (sex was not recorded), and external, visceral, and skeletal examinations were conducted. The percentage of fetuses (and litters) with malformations, variations, and retardations were recorded separately. No dams died. One dams in the 1,000 mg/kg-day group showed vaginal hemorrhage and urine-smeared fur. No significant decreases in body weight or weight gain were noted. There was a slight decrease in food consumption at the high dose during the treatment period (no further description provided). High-dose dams significantly increased relative (13%) kidney weights; absolute kidney weights were not reported. Liver and uterine weights were comparable to controls. The only significant developmental effect was an increase in the number of fetuses/litter showing variations at 1000 mg/kg/day (58.4% vs. 35.3% in controls). These included slightly higher incidences of rudimentary cervical and/or accessory 14th ribs at 1,000 mg/kg-day. No change in the percentage of litters with variations was observed. There were no increased incidences of malformations or retardations and no treatment-related effects at ≤200 mg/kg-day.The maternal NOEL was 200 mg/kg-day and LOEL was 1,000 mg/kg-day for increased relative kidney weights. A developmental NOAEL of 200 mg/kg-day and a LOAEL of 1,000 mg/kg-day was identified based on increased incidences of rudimentary cervical and/or accessory 14th ribs.

[2] 674193: In a standard OECD TG 414 teratogenicity study, pregnant Wistar (Chbb/THOM outbred strain) rats (8-10/group/formulation) were administered the DINP isomer (CASRN 68515-48-0, purity ≥99%) at 0, 40, 200, or 1,000 mg/kg-day, via gavage, from GD 6-15. Dams were monitored for mortality and clinical signs of toxicity. Body weights were recorded on days GDs 0, 6, 10, 15, and 20, and body weight gain was determined. Food consumption was purportedly monitored, but no quantitative results were reported. The time of autopsy was not explicitly stated but is presumed to be GD20 based on another study cited for methods details (HERO 673425). Dam uterine, liver, and kidney weights were recorded. The numbers of corpora lutea and implantation sites were counted along with the numbers of live fetuses, pre and post-implantation loss, and early and late resorptions. All fetuses were weighed (sex was not recorded), and external, visceral, and skeletal examinations were conducted. The percentage of fetuses (and litters) with malformations, variations, and retardations were recorded separately. No dams died. One dams in the 1,000 mg/kg-day group showed vaginal hemorrhage and urine-smeared fur. No significant decreases in body weight or weight gain were noted. There was a slight decrease in food consumption at the high dose during the treatment period (no further description provided). High-dose dams significantly increased relative (13%) kidney weights; absolute kidney weights were not reported. Liver and uterine weights were comparable to controls. The only significant developmental effect was an increase in the number of fetuses/litter showing variations at 1000 mg/kg/day (58.4% vs. 35.3% in controls). These included slightly higher incidences of rudimentary cervical and/or accessory 14th ribs at 1,000 mg/kg-day. No change in the percentage of litters with variations was observed. There were no increased incidences of malformations or retardations and no treatment-related effects at ≤200 mg/kg-day.The maternal NOEL was 200 mg/kg-day and LOEL was 1,000 mg/kg-day for increased relative kidney weights. A developmental NOAEL of 200 mg/kg-day and a LOAEL of 1,000 mg/kg-day was identified based on increased incidences of rudimentary cervical and/or accessory 14th ribs.

[3] 674193: In a standard OECD TG 414 teratogenicity study, pregnant Wistar (Chbb/THOM outbred strain) rats (8-10/group/formulation) were administered the DINP isomer (CASRN 68515-48-0, purity ≥99%) at 0, 40, 200, or 1,000 mg/kg-day, via gavage, from GD 6-15. Dams were monitored for mortality and clinical signs of toxicity. Body weights were recorded on days GDs 0, 6, 10, 15, and 20, and body weight gain was determined. Food consumption was purportedly monitored, but no quantitative results were reported. The time of autopsy was not explicitly stated but is presumed to be GD20 based on another study cited for methods details (HERO 673425). Dam uterine, liver, and kidney weights were recorded. The numbers of corpora lutea and implantation sites were counted along with the numbers of live fetuses, pre and post-implantation loss, and early and late resorptions. All fetuses were weighed (sex was not recorded), and external, visceral, and skeletal examinations were conducted. The percentage of fetuses (and litters) with malformations, variations, and retardations were recorded separately. No dams died. One dams in the 1,000 mg/kg-day group showed vaginal hemorrhage and urine-smeared fur. No significant decreases in body weight or weight gain were noted. There was a slight decrease in food consumption at the high dose during the treatment period (no further description provided). High-dose dams significantly increased relative (13%) kidney weights; absolute kidney weights were not reported. Liver and uterine weights were comparable to controls. The only significant developmental effect was an increase in the number of fetuses/litter showing variations at 1000 mg/kg/day (58.4% vs. 35.3% in controls). These included slightly higher incidences of rudimentary cervical and/or accessory 14th ribs at 1,000 mg/kg-day. No change in the percentage of litters with variations was observed. There were no increased incidences of malformations or retardations and no treatment-related effects at ≤200 mg/kg-day.The maternal NOEL was 200 mg/kg-day and LOEL was 1,000 mg/kg-day for increased relative kidney weights. A developmental NOAEL of 200 mg/kg-day and a LOAEL of 1,000 mg/kg-day was identified based on increased incidences of rudimentary cervical and/or accessory 14th ribs.

[4] 674193: In a standard OECD TG 414 teratogenicity study, pregnant Wistar (Chbb/THOM outbred strain) rats (8-10/group/formulation) were administered the DINP isomer (CASRN 68515-48-0, purity ≥99%) at 0, 40, 200, or 1,000 mg/kg-day, via gavage, from GD 6-15. Dams were monitored for mortality and clinical signs of toxicity. Body weights were recorded on days GDs 0, 6, 10, 15, and 20, and body weight gain was determined. Food consumption was purportedly monitored, but no quantitative results were reported. The time of autopsy was not explicitly stated but is presumed to be GD20 based on another study cited for methods details (HERO 673425). Dam uterine, liver, and kidney weights were recorded. The numbers of corpora lutea and implantation sites were counted along with the numbers of live fetuses, pre and post-implantation loss, and early and late resorptions. All fetuses were weighed (sex was not recorded), and external, visceral, and skeletal examinations were conducted. The percentage of fetuses (and litters) with malformations, variations, and retardations were recorded separately. No dams died. One dams in the 1,000 mg/kg-day group showed vaginal hemorrhage and urine-smeared fur. No significant decreases in body weight or weight gain were noted. There was a slight decrease in food consumption at the high dose during the treatment period (no further description provided). High-dose dams significantly increased relative (13%) kidney weights; absolute kidney weights were not reported. Liver and uterine weights were comparable to controls. The only significant developmental effect was an increase in the number of fetuses/litter showing variations at 1000 mg/kg/day (58.4% vs. 35.3% in controls). These included slightly higher incidences of rudimentary cervical and/or accessory 14th ribs at 1,000 mg/kg-day. No change in the percentage of litters with variations was observed. There were no increased incidences of malformations or retardations and no treatment-related effects at ≤200 mg/kg-day.The maternal NOEL was 200 mg/kg-day and LOEL was 1,000 mg/kg-day for increased relative kidney weights. A developmental NOAEL of 200 mg/kg-day and a LOAEL of 1,000 mg/kg-day was identified based on increased incidences of rudimentary cervical and/or accessory 14th ribs.

Epidemiology Extraction Table:

Measured Effect/ Endpoints	Study Population	Exposure	Results	Overall Quality Determination	HERO ID
Wheeze Study Design: Cross-Sectional Health Effect: Lung/Respiratory-Wheeze-Non-cancer	Children (2-18 years) Inclusion of PESS: Yes Female, Male Children (aged 7 years) from the Hokkaido Study on Environment and Children's Health cohort in Japan	DiNP (μg/g dust) median = 63.91 (25%-75%: 30.72, 152.50)	Wheeze No significant associations were found between wheeze and DiNP exposure. Comments: Table 4	Medium	4829235
Eczema Study Design: Cross-Sectional Health Effect: Skin/Connective Tissue-Eczema-Non-cancer	Children (2-18 years) Inclusion of PESS: Yes Female, Male Children (aged 7 years) from the Hokkaido cohort in Japan	DiNP (μg/g dust) median = 63.91 (25%-75%: 30.72, 152.50)	Positive dose-response relationships were found between DiNP levels and eczema (Q1 vs. Q4 p for trend=0.060) overall. Comments: Figure 1, In text results section	Medium	4829235
Sex steroid hormones (pregnenolone, progesterone, allopregnanolone, pregnanolone) Study Design: Cohort Health Effect: Reproductive/Developmental-Sex hormones (allopregnanolone, pregnanolone, progesterone, pregnenolone)-Non-cancer	Pregnant women Inclusion of PESS: Yes Female NYU CHES (2016-2018), U.S., 139 pregnant women	Early pregnancy: MCiOP, Median (ng/mL) 1.5; MiNP, Median (ng/mL) 1.0; MCNP, Median (ng/mL) 0.97; sum(DiNP) phthalate metabolites, Median (IQR) (ng/mL) 0.01 (0.00, 0.03).Midpregnancy: MCiOP, Median (ng/mL) 1.8; MiNP, Median (ng/mL) 1.0; MCNP, Median (ng/mL) 0.84; sum(DiNP) phthalate metabolites, Median (IQR) (ng/mL) 0.02 (0.00, 0.03). hormone levels in serum	Multiple informant model regression: Serum progesterone negatively associated with sum DiNP phthalates (MCiOP, MiNP); Percent change = -7.7 (CI: -13.3, -1.7). No significant associations for pregnenolone, allopregnanolone, or pregnanolone. Comments: Table 5	Medium	7978436

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Epidemiology Extraction Table:

Measured Effect/ Endpoints	Study Population	Exposure	Results	Overall Quality Determination	HERO ID
postnatal depression (postpartum depression and Edinburgh Postnatal Depression Scale (EPDS) score) Study Design: Cohort Health Effect: Neurological/Behavioral-postnatal depression, postpartum depression-Non-cancer	Pregnant women Inclusion of PESS: Yes Female NYU CHES (2016-2018), U.S., 139 pregnant women	Early pregnancy: MCiOP, Median (ng/mL) 1.5; MiNP, Median (ng/mL) 1.0; MCNP, Median (ng/mL) 0.97; sum(High Molecular Weight Phthalate metabolites (MCNP and MBzP), Median (IQR)(ng/mL) 0.14 (0.07, 0.28); sum(DiNP) phthalate metabolites, Median (IQR) (ng/mL) 0.01 (0.00, 0.03). Midpregnancy: MCiOP, Median (ng/mL) 1.8; MiNP, Median (ng/mL) 1.0; MCNP, Median (ng/mL) 0.84; sum(High Molecular Weight Phthalate metabolites (MCNP and MBzP), Median (IQR)(ng/mL) 0.14 (0.07, 0.28); sum(DiNP) phthalate metabolites, Median (IQR) (ng/mL) 0.02 (0.00, 0.03).	Multiple informant model regression: No significant associations for EPDS score or postpartum depression for sum DiNP phthalates. Comments: Table 6	Medium	7978436

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Epidemiology Extraction Table:

Measured Effect/ Endpoints	Study Population	Exposure	Results	Overall Quality Determination	HERO ID
Sick home syndrome in three domains assessed by self-report using standardized questionnaire. Prevalence was defined as >=1 symptom occurring weekly in the past 3 months and attributed to the house environment. -Mucosal symptoms = irritation of the eye, runny nose, and cough in all; dry throat in adults. -Dermal symptoms =dry/or itching hands, dry facial skin, and itchy/or flaking scalp in all -Any symptoms additionally includes general symptoms = fatigue, headache, sleeping problems in all; stomach age in children; feeling heavy-headed, nausea and lack of concentration in adults. Study Design: Cross-Sectional Health Effect: Lung/Respiratory-Sick home syndrome: self-reported weekly mucosal symptoms.-Non-cancer-Skin/Connective Tissue-Sick home syndrome: self-reported weekly dermal symptoms.-Non-cancer-Other (please specify below) (Sick home syndrome)-Sick home syndrome: self-reported weekly mucosal, dermal or general symptoms.-Non-cancer	Adults or general, Children (2-18 years) Inclusion of PESS: Yes Female, Male Cross-sectional study in Sapporo, Japan conducted in 2009-2010 including 128 households and their residents (184 boys/girls aged <=12 years, 283 male and female adolescents/adults aged >=13 years). Participants were selected from a study of 4,400 children in 2008.	DiNP was detected in 100% of living room dust samples. The median, 25th-75th percentile content of DiNP in floor duest was 139, 66- 276 μg/g, and in multi-surface dust 203, 99.7-443 μg/g.	Associations between DiNP in household dust and reported mucosal symptoms were heterogeneous. There was a significant inverse association between log-transformed DiNP in floor dust and odds of mucosal symptoms in adolescents/adults [odds ratio (95%CI) = 0.34 (0.12–0.91)]. Comments: Reverse causation and selection bias are potentially important concerns.	Low	4728476
Allergies tested using skin prick test. Study Design: Cohort (Prospective) Health Effect: Sensitization-Skin prick testing (allergy)-Non-cancer	Children (2-18 years), Infants (birth to 2 years) Inclusion of PESS: Yes Female, Male KABC (2014 - 2015), Ontario, Canada, 45 prenatally recruited children from 18 months to 3 years and 34 postnatally recruited children from 18 months to 14 years.	DiNP (ug/g) median: 561	No statistically significant results found in logistic regression model. Significance found for DINP exposure relation to allergic sensitization T2 and T3 before adjustment for confounders. Comments: Table 1 and Table S13.	Low	7613166

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Epidemiology Extraction Table:

Measured Effect/ Endpoints	Study Population	Exposure	Results	Overall Quality Determination	HERO ID
Lung function measurements (FEV1, FVC) measured via spirometry.Calculated lung function measurements (FEV1% predicted, FVC% predicted) derived by dividing measurements by predicted reference values. Study Design: Cross-Sectional Health Effect: Lung/Respiratory-Spirometry measurements (FEV1, FVC, FEV1% predicted, FVC% predicted)-Non-cancer	Adults or general Inclusion of PESS: Yes Female, Male Participants in the Dalinpu Community for Health Care cohort (2016-2018), Kaohsiung County, Taiwan, n=397 (159 men, 238 women).	DiNP: mean 18.0 ppm/cm2	In the full study population, a one-unit increase in log-transformed DiNP was associated with lower FEV1% predicted ($\beta = -2.17$; 95% CI -4.26, -0.08), FVC (-0.08; 95% CI -0.15, -0.02), and FVC% predicted ($\beta = -3.16$; 95% CI -5.21, -1.10). In analyses limited to participants age 60+ (n=54), a one-unit increase in log-transformed DiNP was associated with lower FVC% predicted ($\beta = -7.07$; 95% CI -13.33, -0.80). Comments: Results shown visually in Figures 4 and 5, listed quantitatively in the results section of the text on page 27337.	Medium	7502437

Epidemiology Extraction Table:

Measured Effect/ Endpoints	Study Population	Exposure	Results	Overall Quality Determination	HERO ID
Neurodevelopmental outcomes: cognitive development (Bayley Scales for Infant Development (Bayley-III)) at age 1 and 2 Study Design: Cohort Health Effect: Neurological/Behavioral-Cognitive development, language development, motor development-Non-cancer	Pregnant women, Infants (birth to 2 years) Inclusion of PESS: Yes Female, Male Mother and Child Cohort: (established in 2007), Łódź, Poland, 148 mother-child pairs	7-OH-MiNP, distribution not reported7-oxo-MiNP, distribution not reported	Environment-wide association study (EWAS) conducted using logistic regression: No associations noted between the relevant phthalate metabolites and cognitive development at one or two years after birth. Comments: Table 1 and Figure 4	Low	8351761
Neurodevelopmental outcomes: language development (Bayley Scales for Infant Development (Bayley-III)) at age 1 and 2 Study Design: Cohort Health Effect: Neurological/Behavioral-Cognitive development, language development, motor development-Non-cancer	Pregnant women, Infants (birth to 2 years) Inclusion of PESS: Yes Female, Male Mother and Child Cohort: (established in 2007), Łódź, Poland, 148 mother-child pairs	7-OH-MiNP, distribution not reported7-oxo-MiNP, distribution not reported	Environment-wide association study (EWAS) conducted using logistic regression: ”Language development during the second year of life is strongly associated with 20 parameters, including the child exposure levels to phthalate metabolites 7-OH-MiNP, 7-oxo-MiNP.” No quantitative results provided. Comments: Table 1, Figure 5, and text from the results section on the left side of page 11	Low	8351761
Neurodevelopmental outcomes: motor development (Bayley Scales for Infant Development (Bayley-III)) at age 1 and 2 Study Design: Cohort Health Effect: Neurological/Behavioral-Cognitive development, language development, motor development-Non-cancer	Pregnant women, Infants (birth to 2 years) Inclusion of PESS: Yes Female, Male Mother and Child Cohort: (established in 2007), Łódź, Poland, 148 mother-child pairs	7-OH-MiNP, distribution not reported7-oxo-MiNP, distribution not reported	Environment-wide association study (EWAs) conducted using logistic regression: No associations noted between the relevant phthalate metabolites and motor development at one or two years after birth. Comments: Table 1 and Figure 6	Low	8351761

Epidemiology Extraction Table:

Measured Effect/ Endpoints	Study Population	Exposure	Results	Overall Quality Determination	HERO ID
TT3 (ng/dL) measured in plasma Study Design: Cross-Sectional Health Effect: Thyroid-Thyroid function: total triiodothyronine (TT3), total thyroxine (TT4), TT3:TT4 ratio, thyroid stimulating hormone (TSH), thyroid peroxidase autoantibodies (TPOAb)-Non-cancer	Adults or general, Pregnant women Inclusion of PESS: Yes Female MoBa cohort subsample of women who gave birth in 2004-08, resided near Oslo, had available urine and blood specimens, with normal thyroid function. N = 473 in the analysis sample.	Sum of DiNP metabolites: geometric mean (GM) ± SD = 0.02 ± 1.9. Median (25-75th percentile) = 0.02 (0.01-0.03). GM ± SD for individual metabolites: OH-MiNP (μg/L) = 1.07 ± 2.1; oxo-MiNP (μg/L) = 1.24 ± 2.4; and cx-MiNP (μg/L) 3.69 ± 1.7. Total triiodothyronine (TT3)	Absolute difference in TT3 (ng/dL) per IQR increase in DiNP using GLM: -1.99 (-4.52, 0.53); using BKMR (exact method): -0.16 (-1.74, 1.41); using BKMR (approx. method): -1.36 (-3.72, 0.99). Comments: Associations significant for the TT3/TT4 ratio; less precise and non-significant associations with individual hormones.	Medium	7978495
TT3/TT4 (ng/ug) measured in plasma Study Design: Cross-Sectional Health Effect: Thyroid-Thyroid function: total triiodothyronine (TT3), total thyroxine (TT4), TT3:TT4 ratio, thyroid stimulating hormone (TSH), thyroid peroxidase autoantibodies (TPOAb)-Non-cancer	Adults or general, Pregnant women Inclusion of PESS: Yes Female MoBa cohort subsample of women who gave birth in 2004-08, resided near Oslo, had available urine and blood specimens, with normal thyroid function. N = 473 in the analysis sample.	Sum of DiNP metabolites: geometric mean (GM) ± SD = 0.02 ± 1.9. Median (25-75th percentile) = 0.02 (0.01-0.03). GM ± SD for individual metabolites: OH-MiNP (μg/L) = 1.07 ± 2.1; oxo-MiNP (μg/L) = 1.24 ± 2.4; and cx-MiNP (μg/L) 3.69 ± 1.7. Total triiodothyronine/total thyroxine ratio (TT3:TT4)	Absolute difference in TT3/TT4 (ng/ug) ratio per IQR increase in DiNP using GLM: -0.37 (-0.59, -0.15); using BKMR (exact method): -0.48 (-0.96, 0.003); using BKMR (approx. method): -0.57 (-0.90, -0.24). Comments: Associations significant for the TT3/TT4 ratio; less precise and non-significant associations with individual hormones.	Medium	7978495
TT4 (ug/dL) measured in plasma Study Design: Cross-Sectional Health Effect: Thyroid-Thyroid function: total triiodothyronine (TT3), total thyroxine (TT4), TT3:TT4 ratio, thyroid stimulating hormone (TSH), thyroid peroxidase autoantibodies (TPOAb)-Non-cancer	Adults or general, Pregnant women Inclusion of PESS: Yes Female MoBa cohort subsample of women who gave birth in 2004-08, resided near Oslo, had available urine and blood specimens, with normal thyroid function. N = 473 in the analysis sample.	Sum of DiNP metabolites: geometric mean (GM) ± SD = 0.02 ± 1.9. Median (25-75th percentile) = 0.02 (0.01-0.03). GM ± SD for individual metabolites: OH-MiNP (μg/L) = 1.07 ± 2.1; oxo-MiNP (μg/L) = 1.24 ± 2.4; and cx-MiNP (μg/L) 3.69 ± 1.7. Total thyroxine (TT4)	Absolute difference in TT4 (ng/dL) per IQR increase in DiNP using GLM: 0.13 (-0.01, 0.26); using BKMR (exact method): 0.01 (-0.08, 0.09); using BKMR (approx. method): 0.11 (-0.02, 0.23) Comments: Associations significant for the TT3/TT4 ratio; less precise and non-significant associations with individual hormones.	Medium	7978495
TSH (mU/L) measured in plasma Study Design: Cross-Sectional Health Effect: Thyroid-Thyroid function: total triiodothyronine (TT3), total thyroxine (TT4), TT3:TT4 ratio, thyroid stimulating hormone (TSH), thyroid peroxidase autoantibodies (TPOAb)-Non-cancer	Adults or general, Pregnant women Inclusion of PESS: Yes Female MoBa cohort subsample of women who gave birth in 2004-08, resided near Oslo, had available urine and blood specimens, with normal thyroid function. N = 473 in the analysis sample.	Sum of DiNP metabolites: geometric mean (GM) ± SD = 0.02 ± 1.9. Median (25-75th percentile) = 0.02 (0.01-0.03). GM ± SD for individual metabolites: OH-MiNP (μg/L) = 1.07 ± 2.1; oxo-MiNP (μg/L) = 1.24 ± 2.4; and cx-MiNP (μg/L) 3.69 ± 1.7. Thyroid stimulating hormone (TSH)	Absolute differences in TSH (mU/L) per IQR increase in DiNP using GLM: 0.03 (-0.05, 0.12); using BKMR (exact method): -0.003 (-0.06, 0.05); using BKMR (approx. method): 0.01 (-0.07, 0.10). Comments: No significant results reported for the relationship between the sum of DiNP and TSH.	Medium	7978495

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Epidemiology Extraction Table:

Measured Effect/ Endpoints	Study Population	Exposure	Results	Overall Quality Determination	HERO ID
Total testosterone, free testosterone; FSH, LH, index of aromatase activity (ratio of total testosterone to estradiol (TT/E2) Study Design: Cohort Health Effect: Reproductive/Developmental-Total testosterone (TT), free testosterone (FT), estradiol (E2), follicle stimulating hormone (FSH), and leutenizing hormone (LH)-Non-cancer	Occupational Inclusion of PESS: Yes Male Male workers (n = 97) from six French factories who use plasticizers in their industrial process.	mono-4-methyl-7-oxo-octyl phthalate (OXO-MINP) (µg/g creatinine): -Exposed first exposure [median (range)] = 3.2 (0.2-93.0)-Exposed second exposure [median (range)] = 5.2 (0.76-150)-Less exposed first exposer [median (range)] = 1.8 (0.4-7.9)-Less exposed second exposure [median (range)] = 1.9 (0.2-76)mono-4-methyl-7-hydroxy-octyl phthalate (OH-MINP) (µg/g creatinine): -Exposed first exposure [median (range)] = 8.9 (0.6-150.9)-Exposed second exposure [median (range)] = 15.1 (2.2-352.3)-Less exposed first exposer [median (range)] = 4.2 (0.9-37.9)-Less exposed second exposure [median (range)] = 7.1 (0.4-288.5)mono-4-methyl-7-carboxyheptylphthalate (CX-MINP) (µg/g creatinine):-Exposed first exposure [median (range)] = 8.2 (0.6-136.4)-Exposed second exposure [median (range)] = 14.4 (1.8-216)-Less exposed first exposer [median (range)] = 3.8 (1.1-17.3)-Less exposed second exposure [median (range)] = 6.1 (0.4-131.4)	Total Testosterone: linear mixed models with DINP metabolite modeled as less than or greater than or equal to median while adjusting for serum testosterone at T1, DEHP metabolite difference T2-T1 specific to model as indicated in table, exposed group, age, and sagittal abdominal perimeter:mono-4-methyl-7-oxo-octyl phthalate (OXO-MINP): A significant inverse association was found between the decrease in serum TT concentrations between T1 and T2 and an increase in urinary OXO-MINP [Model A, oxo-MiNP difference: (regression coefficient = -0.41 (SE: 0.18, p-value = 0.02)), Model B: (regression coefficient = -0.52 (SE: 0.18, p-value = 0.003)); Model C: (regression coefficient = -0.53 (SE: 0.17, p-value = 0.002)); Model D: (regression coefficient = -0.46 (SE: 0.17, p-value = 0.008)). No significant associations were noted for total testosterone and models for OH-MINP, or CX-MINP. Free Testosterone: linear mixed models with DINP metabolite modeled as less than or greater than or equal to median while adjusting for serum testosterone at T1, DEHP metabolite difference T2-T1 specific to model as indicated in table, exposed group, age, and sagittal abdominal perimeter: No significant associations were noted for free testosterone and oxo-MINP, OH-MINP, or CX-MINP. Sexual Health Scales: Bivariate analyses of sexual health scales (IIEF-5 and ADAM) between DINP exposed and non-exposed groups: More erectile problems (IIEF-5 score <22, ADAM score >=3) were reported using the IIEF-5 in the DINP exposed group (p=0.01). Serum reproductive hormone outcomes: Linear mixed models nested within factory: No association was observed between the level of urinary OXO-MINP concentrations ('<median OXO-MINP' group) and FSH, LH, index of aromatase activity (ratio of total testosterone to estradiol (TT/E2) (data not shown; see online supplementary file A). Comments: Tables 3, 5 and Supplementary Table A, text page 220.	Medium	7978431

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Epidemiology Extraction Table:

Measured Effect/ Endpoints	Study Population	Exposure	Results	Overall Quality Determination	HERO ID
Bone turnover markers: procollagen-type-1-N propeptide (P1NP); C terminal cross-linking telopeptide of type 1 collagen (CTX) Study Design: Cohort Health Effect: Musculoskeletal-Bone formation (serum procollagen-type-I-N propeptide (P1NP); Bone resorption (serum C terminal cross-linking telopeptide of type I collagen (CTX)-Non-cancer	Occupational Inclusion of PESS: Yes Male Male workers (n = 97) from six French factories who use plasticizers in their industrial process.	mono-4-methyl-7-oxo-octyl phthalate (OXO-MINP) (µg/g creatinine): -Exposed first exposure [median (range)] = 3.2 (0.2-93.0)-Exposed second exposure [median (range)] = 5.2 (0.76-150)-Less exposed first exposer [median (range)] = 1.8 (0.4-7.9)-Less exposed second exposure [median (range)] = 1.9 (0.2-76)mono-4-methyl-7-hydroxy-octyl phthalate (OH-MINP) (µg/g creatinine): -Exposed first exposure [median (range)] = 8.9 (0.6-150.9)-Exposed second exposure [median (range)] = 15.1 (2.2-352.3)-Less exposed first exposer [median (range)] = 4.2 (0.9-37.9)-Less exposed second exposure [median (range)] = 7.1 (0.4-288.5)mono-4-methyl-7-carboxyheptylphthalate (CX-MINP) (µg/g creatinine):-Exposed first exposure [median (range)] = 8.2 (0.6-136.4)-Exposed second exposure [median (range)] = 14.4 (1.8-216)-Less exposed first exposer [median (range)] = 3.8 (1.1-17.3)-Less exposed second exposure [median (range)] = 6.1 (0.4-131.4)	Linear mixed models nested within factory: No association was observed between the level of urinary OXO-MINP concentrations (‘<median OXO-MINP’ group) and bone turnover biomarkers (P1NP, CTX) (data not shown; see online supplementary file A). Comments: Tables 3, 5 and Supplementary Table A, text page 220.	Medium	7978431

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Epidemiology Extraction Table:

Measured Effect/ Endpoints	Study Population	Exposure	Results	Overall Quality Determination	HERO ID
Child behavioral, emotional problems were measured at 7 years and assessed by the Strengths and Difficulties Questionnaire (SDQ). Conduct problems, hyperactivity/inattention problems, emotional symptoms, peer relationship problems and prosocial behavior were measured. Child cognition, psychomotor development, measured using Polish adaptation of the Intelligence and Development Scales (IDS). Fluid intelligence, crystalized intelligence, cognition, mathematical skills, motor skills, and language skills were measured. Study Design: Cross-Sectional Health Effect: Neurological/Behavioral-Child behavioral and emotional problems at age 7 years, child cognitive and psychomotor development-Non-cancer	Children (2-18 years) Inclusion of PESS: Yes Female, Male prospective Polish Mother and Child Cohort study (REPRO_PL): 2007, Poland, (250 mother-child pairs).	sumDiNP (sum of 7-OH-mono-methyloctyl phthalate (OH-MiNP), 7-oxo-mono-methyloctyl phthalate (oxo-MiNP) and 7-carboxy-mono-methylheptyl phthalate (cx-MiNP)); central tendency not reported.	Text noted negative associations in peer relationship problems were noted for sumDiNP metabolites, and lower IDS scores were generally positively associated with higher phthalate concentrations.	Medium	5932896

Epidemiology Extraction Table:

Measured Effect/ Endpoints	Study Population	Exposure	Results	Overall Quality Determination	HERO ID
Sex hormone concentrations (luteinizing hormone, follicle stimulating hormone, testosterone, androstenedione, 17-alpha-hydroxyprogesterone, dehydroepiandrosterone sulfate) in mini-puberty from infants 3-4 months in age measured in serum Study Design: Cohort (Prospective) Health Effect: Reproductive/Developmental-hormone levels:testosterone, luteinizing hormone (LH), follicle stimulating hormone (FSH), androstenedione (adione), 17 alpha-hydroxyprogesterone (17-OHP), dehydroepiandrosterone (DHEAS), testosterone/LH ratio-Non-cancer	Pregnant women, Infants (birth to 2 years) Inclusion of PESS: Yes Female, Male 479 pregnant women participating in the Odense Child Cohort and their singleton infants	Metabolites of DiNP (MiNP, MHiNP, MOiNP, MCiOP) were measured in mother's urine at approximately 28 weeks gestation. They were summed together to give a summary DiNP metabolite measure. Central tendencies were presented not for the overall cohort but were stratified by levels of particular variables. For example, the median summary DiNP measurement for mothers <27 years of age was 7.8 ng/mL, for mothers 27-30 6.6 ng/mL, for mothers 30-34 was 7.5 ng/mL, and for mothers 34 and older was 9.4 ng/mL.Results extracted from Table 2. Sex hormone concentrations (luteinizing hormone, follicle stimulating hormone, testosterone, androstenedione, 17-alpha-hydroxyprogesterone, dehydroepiandrosterone sulfate) measured in serum	Results for male infants only: testosterone: no significant resultsluteinizing hormone: no significant resultsfollicle stimulating hormone: -Percent change (95% CI)- Q3 vs. Q1: -13.9 (-25.4-(-0.5))-Q2 vs Q1: -3.4 (-16.3-11.4), -p-trend: 0.037*androstenedione: no significant results17-OHP: no significant resultsDHEAS: no significant resultstestosterone/LH ratio: -Percent change (95% CI):-Q3 vs. Q1: –23.1 (-38.8-(-3.3))-Q2 vs. Q1: -23.0 (-38.6-(-3.4))-p-trend: 0.031*Results for female infants were presented in a supplemental table, with the text stating, "No clear association pattern was demonstrated between prenatal phthalate exposure and sex hormone concentrations in girls."Results extracted from table 3.	Medium	7978907

Epidemiology Extraction Table:

Measured Effect/ Endpoints	Study Population	Exposure	Results	Overall Quality Determination	HERO ID
Age 11 motor function in terms of total, fine and gross motor composite point scores was assessed using the short form of the Bruininks-Oseretsky Test of Motor Proficiency, 2nd edition (BOT-2). Study Design: Cohort (Prospective) Health Effect: Neurological/Behavioral-Age 11 motor skills-Non-cancer	Pregnant women, Children (2-18 years) Inclusion of PESS: Yes Female, Male Columbia Center for Children's Environmental Health (CCCEH) (recruitment 1999-2006, follow-up through age 11), United States, New York, overall n=209 mother-child pairs (116 girls, 93 boys). Sample size for the relevant metabolite (MCOP) varied based on measurement time point (n=72 prenatal MCOP, n=113 age 3 MCOP, n=199 age 5 MCOP), n=156 age 7 MCOP).	Mono-carboxy-isooctyl phthalate (MCOP, a DiNP metabolite): Prenatal Median (25th-75th percentile) = 2.3 ng/mL (1.2-4.1 ng/mL); Age 3 Median (25th-75th percentile) = 9.20 ng/mL (3.7-20.5 ng/mL); Age 5 Median (25th-75th percentile) = 11.1 ng/mL (5.85-21.20 ng/mL); Age 7 Median (25th-75th percentile) = 12.2 ng/mL (6.35-24.9 ng/mL)	MCOP measured at age 3 was significantly associated with total, fine motor, and gross motor composite scores among boys. In linear regression models, a 1 log-unit increase in age 3 MCOP was associated with lower total (beta: -3.08 [95% CI: -5.35, -0.80]), fine motor (beta: -1.64 [95% CI: -3.16, -0.12]), and gross motor (beta: -1.44 [95% CI: -2.60, -0.28]) composite scores in boys. Comparisons of the 4th versus 1st quartiles of age 3 MCOP were also associated with all three outcomes in boys (Q4 vs. Q1 total composite score beta: -7.47 [95% CI: -12.60, -2.34]; fine motor composite score beta: -4.18 [95% CI: -7.51, -0.85]; gross motor composite score beta: -3.29 [95% CI -6.06, -0.52]). No significant associations between MCOP at age 3 and outcomes in girls; p-values for sex differences at age 3 not significant. No significant associations between prenatal MCOP and outcomes in either girls or boys. Comments: Table 3, Table 4, Table S5	Medium	5039985
Age 11 motor function in terms of total, fine and gross motor composite point scores was assessed using the short form of the Bruininks-Oseretsky Test of Motor Proficiency, 2nd edition (BOT-2). Study Design: Cohort (Prospective) Health Effect: Neurological/Behavioral-Age 11 motor skills-Non-cancer	Pregnant women, Children (2-18 years) Inclusion of PESS: Yes Female, Male Columbia Center for Children's Environmental Health (CCCEH) (recruitment 1999-2006, follow-up through age 11), United States, New York, overall n=209 mother-child pairs (116 girls, 93 boys). Sample size for the relevant metabolite (MCOP) varied based on measurement time point (n=72 prenatal MCOP, n=113 age 3 MCOP, n=199 age 5 MCOP), n=156 age 7 MCOP).	Mono-carboxy-isooctyl phthalate (MCOP, a DiNP metabolite): Prenatal Median (25th-75th percentile) = 2.3 ng/mL (1.2-4.1 ng/mL); Age 3 Median (25th-75th percentile) = 9.20 ng/mL (3.7-20.5 ng/mL); Age 5 Median (25th-75th percentile) = 11.1 ng/mL (5.85-21.20 ng/mL); Age 7 Median (25th-75th percentile) = 12.2 ng/mL (6.35-24.9 ng/mL)	MCOP measured at age 3 was significantly associated with total, fine motor, and gross motor composite scores among boys. In linear regression models, a 1 log-unit increase in age 3 MCOP was associated with lower total (beta: -3.08 [95% CI: -5.35, -0.80]), fine motor (beta: -1.64 [95% CI: -3.16, -0.12]), and gross motor (beta: -1.44 [95% CI: -2.60, -0.28]) composite scores in boys. Comparisons of the 4th versus 1st quartiles of age 3 MCOP were also associated with all three outcomes in boys (Q4 vs. Q1 total composite score beta: -7.47 [95% CI: -12.60, -2.34]; fine motor composite score beta: -4.18 [95% CI: -7.51, -0.85]; gross motor composite score beta: -3.29 [95% CI -6.06, -0.52]). No significant associations between MCOP at age 3 and outcomes in girls; p-values for sex differences at age 3 not significant. No significant associations between prenatal MCOP and outcomes in either girls or boys. Comments: Table 3, Table 4, Table S5	Medium	5039985

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Epidemiology Extraction Table:

Measured Effect/ Endpoints	Study Population	Exposure	Results	Overall Quality Determination	HERO ID
Asthma measured at 7 years old via maternal report and clinical data, defined as taking asthma medication or having two or more of: respiratory symptoms, doctor diagnosis of asthma or positive bronchodilator test. FEV1 (as a measure of lung function) measured at 7 years old using spirometry. Study Design: Cohort (Prospective) Health Effect: Lung/Respiratory-Probable asthma-Non-cancer-Lung/Respiratory-Lung function (FEV1)-Non-cancer	Children (2-18 years) Inclusion of PESS: Yes Female, Male 319 mother-child pairs from the CHAMACOS study (enrollment 1999-2000), California, United States, with follow up until 7 years of age	MCOP geometric mean (ng/mL) = 3.8	BKRM analysis predicted probability (PIP) for MCOP and probable asthma is 0.47427, 0.55379 for FEV1. Changes in PIP (SDS) of probable asthma per IQR increase of MCOP is 0.08 (0.09), −0.07 (0.05) for FEV1. Comments: Table 3, Table 4	Medium	6813726
Aeroallergy measured at 7 years old via maternal report, defined as any of the following in the last year: 1) a diagnosis of hay fever/rhinitis, 2) runny or itchy eyes apart from colds, or 3) sneezing or a runny nose apart from colds. Study Design: Cohort (Prospective) Health Effect: Lung/Respiratory-Aeroallergies-Non-cancer	Children (2-18 years) Inclusion of PESS: Yes Female, Male 319 mother-child pairs from the CHAMACOS study (enrollment 1999-2000), California, United States, with follow up until 7 years of age	MCOP geometric mean (ng/mL) = 3.8	BKRM analysis predicted probability (PIP) for MCOP is 0.13803 for aeroallergy. Changes in PIP (SDS) of aeroallergies per IQR increase of MCOP is 0.04 (0.08). Comments: Table 3, Table 4	Medium	6813726
Probable asthma at age 7 Study Design: Cohort (Prospective) Health Effect: Lung/Respiratory-Probable asthma, aeroallergies-Non-cancer	Children (2-18 years) Inclusion of PESS: Yes Female, Male Center for the Health Assessment of Mothers and Children of Salinas (CHAMACOS): (1990-2000, follow-up through child age 16), United States, California, (n=329)	Monocarboxyisooctyl phthalate (MCOP): Geometric mean (25th-75th percentile): 3.8 (2.4-5.5) ng/mL	Logistic regression of log2 MCOP exposure on probable asthma: OR (95% CI)1.54 (1.12, 2.12) Comments: Results extracted represent the fully adjusted model, including maternal age, parity, household income as a proportion of poverty at baseline, child's family history of asthma, maternal education, monocarboxyisooctyl phthalate, propyl paraben, 2,4-dichlorophenol. N=329	Medium	5041286

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Epidemiology Extraction Table:

Measured Effect/ Endpoints	Study Population	Exposure	Results	Overall Quality Determination	HERO ID
Timing of pubertal milestones (thelarche) Study Design: Cohort (Prospective) Health Effect: Reproductive/Developmental-Timing of puberty (pubarche, menarche, gonadarche)-Non-cancer	Pregnant women, Children (2-18 years) Inclusion of PESS: Yes Female, Male 338 mother-child pairs from the Center for Health Assessment of Mothers and Children of Salinas (CHAMACOS) study, recruited during pregnancy from 1999-2000 with follow-up through child age 13.	MCOP, Geometric mean (25th-75th percentile) 3.8 ng/mL (2.4 - 5.6 ng/mL)	Pubarche and menarche age increased in "normal" weight girls per log2 increase in MCOP. Gonadarche and pubarche age decreased in all boys and only obese boys. All other results were not significant. Comments: Focused on extracting results from the main analysis, but results stratified by normal/overweight status are also presented with p for interaction for gonadarche reaching significance (p = 0.03).	Medium	4829221
Timing of pubertal milestones (thelarche) Study Design: Cohort (Prospective) Health Effect: Reproductive/Developmental-Timing of puberty (thelarche)-Non-cancer	Pregnant women, Children (2-18 years) Inclusion of PESS: Yes Female 338 mother-child pairs from the Center for Health Assessment of Mothers and Children of Salinas (CHAMACOS) study, recruited during pregnancy from 1999-2000 with follow-up through child age 13.	MCOP, Geometric mean (25th-75th percentile) 3.8 ng/mL (2.4 - 5.6 ng/mL)	Thelarche age increased in all girls per log2 increase in MCOP, but 95% CI included the null. Not significant when stratified by obesity status. Comments: Focused on extracting results from the main analysis, but results stratified by normal/overweight status are also presented with p for interaction for gonadarche reaching significance (p = 0.03).	Low	4829221

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Epidemiology Extraction Table:

Measured Effect/ Endpoints	Study Population	Exposure	Results	Overall Quality Determination	HERO ID
Early pregnancy outcome indicators: time from ocupation to implantation; pattern of early human chorionic gonadotropin (hCG) hormone rise; and type of corpus luteum ”rescue” (an indicator of sustained progesterone production by the ovaries, needed to maintain early pregnancy). Study Design: Cohort (Retrospective) Health Effect: Reproductive/Developmental-Early pregnancy outcome measures: time from ovulation to implantation, pattern of human chorionic gonadotropin (hCG) hormone rise (an early indicator of pregnancy), and type of ovarian corpus luteum “rescue” (timing and pattern of ovarian progesterone rise, necessary for maintaining an early pregnancy)-Non-cancer	Pregnant women Inclusion of PESS: Yes Female 137 healthy women without known fertility problems in the North Carolina Early Pregnancy Study, conducted in 1982-1986. Women were enrolled from the time they discontinued birth control and followed for up to 6 months for the occurrence of a clinical pregnancy.	Three spot urine samples collected during the conception cycle were pooled to estimate exposure. DiNP exposure was estimated using the metabolite monocarboxyoctyl phthalate (MCOP), median = 2.6 (IQR 1.8, 3.5) ng/mg creatinine. Urinary measures of major metabolites of estrogen (estrone 3-glucuronide (E1G)) and progesterone (pregnanediol 3-glucuronide (PdG), along with human chorionic gonadotropin (hCG) hormone.	-Time from ovulation to implantation: There was no significant association between MCOP and time to implantation. -hCG rise: There was no significant association between MCOP and hCG rise. -Type of corpus luteum ”rescue”: There was no significant association between MCOP and type of corpus luteum rescue. Comments: Table 2 (time to implantation), results text (hCG rise), type of corpus luteum rescue (table 3).	Medium	5043528
BMI and BMI z-score, characterized as weight/height^2 (kg/m^2) Study Design: Cohort (Prospective) Health Effect: Reproductive/Developmental-Body mass index (BMI)-Non-cancer-Nutritional/Metabolic-Body mass index (BMI)-Non-cancer	Pregnant women, Children (2-18 years) Inclusion of PESS: Yes Female, Male CHAMACOS: 1999-2000 (up to 14 years of follow-up), United States/California, 162 male and 173 female children	MCOP median (Q1-Q3): 3.1 ng/mL (1.8-5.1 ng/mL)	No significant results reported - however, functional principal components analysis found that MCOP was an explanatory variable in variation of BMI trajectories among girls. Comments: Fig. 5; Table 6	Medium	5514974

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Epidemiology Extraction Table:

Measured Effect/ Endpoints	Study Population	Exposure	Results	Overall Quality Determination	HERO ID
[1] Executive Function – 3 assessments. (i) Behavior Rating Inventory of Executive Function (BRIEF) - Behavioral Regulation, Metacognition, Global Executive indices; parent (7, 9, 12 y), teacher (7 y). (ii) NEPSY tower task - planning, monitoring, self-regulation, problem solving (9 y). (iii) Wisconsin Card Sort Task (WCST) - strategic planning, ability to shift strategies, impulse control (9, 12 y). [2] Cognition – 4 IQ subscales. Weschler Intelligence Scale for Children (WISC-IV) – Full score, Verbal Comprehension, Perceptual Reasoning, Working Memory, Processing Speed scales (7, 10.5 y). [3] Social Cognition – 3 assessments. (i) Evaluación neuropsicológica del niño (ENI) - identify mental state in photos (9 y). (ii) NEPSY-II Affect Recognition (12 y). (iii) Social Responsiveness Scale (SRS-2) – autism traits; parent (14 y). [4] Attention Behavior - 4 assessments. (i) Attention Behavior Assessment System for Children (BASC- 2) - hyperactivity, attention, depression, anxiety, internalizing problems, externalizing problems; parent (7, 10.5, 14, 16 y), teacher (7 y). (ii) Self-Report of Personality (SRP) - internalizing problems, hyperactivity, attention, depression, anxiety (14, 16 y). (iii) Conners' Attention Deficit Hyperactivity Disorder (ADHD)/ DSM-IV Scales (CADS) - ADHD index, DSM-IV inattentive, hyperactive/impulse, total ADHD; parent (7, 9, 12 y), teacher (7 y) (iv) Conners' Continuous Performance Test, v5 (CPT II) - hit rate, accuracy, impulse control analyzed as errors of commission, omission, and ADHD confidence index (9, 12 y). Study Design: Cohort (Prospective)	Pregnant women, Children (2-18 years) Inclusion of PESS: Yes Female, Male 334 children from the CHAMACOS (Center for the Health Assessment of Mothers and Children of Salinas) birth cohort followed through age 16 years	Diisononylphthalate (DiNP) metabolite MCOP [mono(carboxyoctyl)phthalate]: median ng/mL 3.8, IQR 2.4-5.6, max 93.2)	Adjusted beta (95% CI). Effects per unit log2 specific gravity adjusted exposure (ng/mL) except when use of tertiles is indicated. [1] Cognition. Overall associations null for MCOP, MCNP and HMW phthalates. Negative associations in boys for HMW phthalates (no sex-stratified analyses for MCOP, MCNP). Example: WISC-IV Full scale IQ at 7 and 10.5y. Results for all children: MCOP = 0.1 (-1.0, 1.3); MCNP = 0.6 (-0.7, 2.0); sum-HMW = 0.0 (−1.4, 1.4). Sex stratified results for sum-HMW: boys = −1.9 (-4.1, 0.3) and girls = 1.8 (0.1, 3.3). [2] Behavior. Results suggest associations with increased problems for teacher-reported outcomes, particularly for MCNP; potential sex differences suggested for selected HMW phthalate results. Null associations based on parent and self-report outcomes. Example: Teacher based on BASC-2. All children, internalizing problems - anxiety scale MCOP = -1.4 (-2.6, -0.2), MCNP = -1.7 (-3.1, -0.3); depression scale MCOP = -0.1 (-1.2, 0.9), MCNP = -1.8 (-3.1, -0.4). All children, externalizing problems - hyperactivity scale MCOP = -0.6 (-1.8, 0.7), MCNP = -1.3 (-2.4, -0.3); attention problems scale MCOP = -0.4 (-1.2, 0.4), MCNP = -0.8 (-1.7, 0.0). Example: Teacher based on CADS DSM-IV total scale. MCOP = -0.4 (-1.5, 0.8); MCNP = -1.2 (-2.5, 0.0). DSM-IV total scale analyzed using tertiles of sum-HMW: all children T2 =-1.1 (-4.1, 1.9), T3 =-0.4 (-3.5, 2.7) boys T2 = -1.2 (-5.3, 2.9), T3 = 2.5 (-2.0, 7.0); girls T2 = -1.1 (-5.7, 3.5), T3 =-3.3 (-7.9, 1.3). [3] Executive function associations largely null. Example: BRIEF parent report at 7, 9 and 12y global executive composite: MCOP = 0.4 (-0.6, 1.4); MCNP = -0.4 (-1.2, 0.5). [4] Social cognition largely null except NEPSY-II affect recognition (age 12 y). NEPSY-II MCOP = -0.5 (-0.9, -0.2); MCNP = -0.2 (-0.5, 0.2). Comments: Utility for specifically evaluating effects of DiNP and DiDP is limited by the fact that sex differences and potential non-linear associations were not examined for individual metabolites, given that findings for the sum of 4 high molecular weight (HMW) phthalates, which included MCOP and MCNP, suggest that prenatal HMW phthalates were associated with lower IQ scores in boys and higher scores in girls.	Medium	6815846

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Epidemiology Extraction Table:

Measured Effect/ Endpoints	Study Population	Exposure	Results	Overall Quality Determination	HERO ID
blood glucose levels (results from non-fasting gestational diabetes mellitus screening conducted at 24-28 weeks gestation) Study Design: Cohort (Prospective) Health Effect: Nutritional/Metabolic-pregnancy glucose levels-Non-cancer	Pregnant women Inclusion of PESS: Yes Female Sub-analysis of the EARTH study: 2005-2015, USA, Massachusetts, 245 pregnant women aged 18-46 years	MCOP (ng/mL) trimester 1 geometric mean (SD): 28.2 (2.9), trimester 1 50th percentile: 28.28trimester 2 geometric mean (SD): 21.9 (2.3), trimester 2 50th percentile: 20.38 blood glucose	When assessing associations between quartiles of MCOP exposure in the 1st and 2nd trimesters and blood glucose levels measured at 24-28 weeks gestation, there were no statistically significant results reported. Comments: Results from modeling analysis found in Table 3	High	4728454
Full scale IQ was measured by trained examiners at age 5 years (Wechsler Preschool and Primary Scale of Intelligence-III [WPPSI-III] and at age 8 years (Wechsler Intelligence Scale for Children-IV [WISC-IV]). Study Design: Cohort Health Effect: Neurological/Behavioral-Full-scale IQ at age 5 years (Wechsler Preschool and Primary Scale of Intelligence-III [WPPSI-III]) and full scale IQ at age 8 years (Wechsler Intelligence Scale for Children-IV [WISC-IV]))-Non-cancer	Children (2-18 years) Inclusion of PESS: Yes Female, Male 253 mother-child pairs from the HOME study, pregnant women aged $\geq$18 years recruited ~16 weeks' gestation in 2003 to 2006, residing in housing built prior to 1978. This study included children with cognitive testing at aged 5 and/or 8 years.	DiNP metabolite monocarboxyoctyl phthalate (MCOP) in annual spot urines from ages 1 to 5 years, and at age 8 years. Median (25th-75th percentile) at age 3 = 13.5 (7.2-25.0) ng/mL. MCOP increased over time (medians at ages 1 and 8 years 10.1 and 27.5 ng/mL, respectively).	Associations between child IQ scores and urinary MCOP measured at different ages were not statistically significant and were heterogeneous (positive and negative). For exposure at age 3 years, when associations with several other phthalate metabolites were significantly inverse, adjusted beta (95% confidence interval) for MCOP = -1.2 (-3.2, 0.9) Comments: Statistical power may have been limited, particularly to detect any effect modification.	Medium	5053633

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Epidemiology Extraction Table:

Measured Effect/ Endpoints	Study Population	Exposure	Results	Overall Quality Determination	HERO ID
Child behavior (at 2, 3, 4, 5 and 8 years) was evaluated by parent or caregivers using the Behavioral Assessment System for Children-2 (BASC-2) T-scores. Primary outcomes: internalizing problems, externalizing problems, and the Behavioral Symptoms Index [BSI]. Additional outcomes: anxiety, depression, somatization, aggression, conduct problems, hyperactivity, attention problems, atypicality, and withdrawal. Study Design: Cohort (Prospective) Health Effect: Neurological/Behavioral-Child behavior, as reported by parents or caregivers using the Behavioral Assessment System for Children-2 (BASC-2) (internalizing problems, externalizing problems, Behavioral Symptoms Index [BSI]) and nine clinical subscales.-Non-cancer	Children (2-18 years) Inclusion of PESS: Yes Female, Male This study included 314 (171 girls, 143 boys) children in the longitudinal Cincinnati HOME cohort with repeated measures of phthalates exposure and behavioral outcomes assessed from ages 1 to 8 years.	Child log-10 creatinine-adjusted monocarboxyoctyl phthalate (MCOP) at age 1 year: median (p25-p75) 1.70 (1.49-1.96) ng/mL without measurement error correction. Values declined slightly with increasing age (median at age 8y 1.52 ng/mL). Corresponding measurement error-corrected values were 1.67 (1.62-1.72) at at 1 year, median 1.57 at age 8 years.	Associations are beta coefficients (95%) per IQR increase in log-10 transformed creatinine adjusted and error corrected exposure variables and T scores (mean 50 SD 10) in BASC-2 behavioral outcomes. MCOP was associated with significantly increased behavioral problem composite scores. Associations were somewhat higher in boys (differences NS). -Behavioral Symptoms Index (BSI): MCOP overall = 0.9 (0.0, 1.7), boys = 1.5 (0.3, 2.7), girls = 0.4 (−0.8, 1.5) (sex interaction p=0.83).A negative association between externalizing problems in girls was reported and significant, but this was not observed for boys.-Externalizing problems: MCOP overall =−0.2 (−1.2, 0.7), boys = 0.9 (−0.4, 2.2), girls = −1.5 (−2.7, −0.2) (sex interaction p=0.64)MCOP was associated with significantly higher internalizing problem scores in boys but not in girls. -Internalizing problems: MCOP overall = 0.2 (−0.7, 1.0), boys = 1.3 (0.3, 2.4), girls = −0.9 (−2.2, 0.5) (sex interaction p=0.08). Comments: Gestational measures of MCNP and MCOP were not available because methods to assay these metabolites were not available when maternal samples were analyzed.	Medium	9419532
Placental weight (g), birth weight to placental weight ratio (BW:PW) measured by obstetrical nurses Study Design: Cohort (Prospective) Health Effect: Reproductive/Developmental-Placental weight, birth weight to placental weight ratio-Non-cancer	Adults or general, Pregnant women Inclusion of PESS: Yes Female, Male Environment and Reproductive Health (EARTH) Study, a prospective preconception cohort of couples recruited from a fertility center in Massachusetts, 132 mothers and 68 fathers	Exposure was the mean of multiple spot urine samples. Specific gravity-adjusted geometric mean (GSD) for MCOP: maternal preconception samples =24.3 (2.84) ng/mL; maternal prenatal samples =25.8 (2.57) ng/mL; paternal preconception samples =29.4 (4.37) ng/mL.	Associations were negative and non-significant. Beta (95% confidence interval for MCOP exposure and placental weight (g): paternal preconception = 8 (−13, 29); maternal preconception = 11 (−5, 27); maternal prenatal = −6 (−24, 12). Comments: Some statistically significant associations were found for MEP and DEHP.	Medium	5742214

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Epidemiology Extraction Table:

Measured Effect/ Endpoints	Study Population	Exposure	Results	Overall Quality Determination	HERO ID
IQ (full-scale, performance, verbal) assessed through French version of Wechsler Preschool and Primary Scale of Intelligence Third Edition (WPPSI-III) Study Design: Cohort (Prospective) Health Effect: Neurological/Behavioral-, Full-Scale iQ, Verbal IQ, Performance IQ-Non-cancer	Pregnant women, Children (2-18 years) Inclusion of PESS: Yes Male February 2003 through January 2006, France, 452 mother/son (5 years of age)	Median (5th, 95th percentiles) concentrations for MCOP were 1.3 ug/L (0.4, 9.7 ug/L)	No statistically significant findings of the association between performance and verbal IQs and DINP metabolite concentrations (Table 3, 4, S4) Comments: No significant findings were reported. Across different modeling approaches MCNP reported mostly non-significant positive associations.	Medium	4728401
Breast cancer mortality measured using ICD-9/10 codes 174.9 and C-50.9 Study Design: Cohort (Prospective) Health Effect: Reproductive/Developmental-Breast cancer mortality-Cancer-Mortality-Breast cancer mortality-Cancer-Cancer/Carcinogenesis-Breast cancer mortality-Cancer	Adults or general Inclusion of PESS: Yes Female Long Island Breast Cancer Study Project (LIBCSP): (1996-1997), United States, New York, 320 women	MCOP (ug/L), median = 4.50 ug/L	No significant results Comments: Table 4	Medium	4728408
Breast cancer confirmed by physician and medical record review Study Design: Case-Control Health Effect: Cancer/Carcinogenesis-Breast cancer-Cancer-Reproductive/Developmental-Breast cancer-Cancer	Adults or general Inclusion of PESS: Yes Female Long Island Breast Cancer Study Project (LIBCSP): (1996-1997), United States, New York, 525 women	MCOP (ug/L), median = 4.50 ug/L	Adjusted odds ratios for breast cancer:Quintile 2 (3.45-4.98 ug/L) vs. Quintile 1 (0.850-3.40 ug/L) = 0.69 (95% CI: 0.39, 1.24)Quintile 3 (5.08-7.42 ug/L) vs. Quintile 1 (0.850-3.40 ug/L) = 0.65 (95% CI: 0.36, 1.37)Quintile 4 (7.66-13.44 ug/L) vs. Quintile 1 (0.850-3.40 ug/L) = 0.54 (95% CI: 0.30, 0.97)Quintile 3 (13.69-474 ug/L) vs. Quintile 1 (0.850-3.40 ug/L) = 0.73 (95% CI: 0.71, 1.30)per increase in ln(MCOP) = 0.90 (95% CI: 0.75, 1.08) Comments: Table 2	Medium	4728408
All-cause mortality Study Design: Cohort (Prospective) Health Effect: Mortality-All-cause mortality-Non-cancer	Adults or general Inclusion of PESS: Yes Female Long Island Breast Cancer Study Project (LIBCSP): (1996-1997), United States, New York, 320 women	MCOP (ug/L), median = 4.50 ug/L	No significant results Comments: Table 4	Medium	4728408

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Epidemiology Extraction Table:

Measured Effect/ Endpoints	Study Population	Exposure	Results	Overall Quality Determination	HERO ID
Placental weight and birth weight obtained from medical records; placental-to-birth weight ratio calculated as [placental weight/birth weight] × 100. Study Design: Cohort Health Effect: Reproductive/Developmental-Placental weight-Non-cancer-Reproductive/Developmental-Birth weight-Non-cancer-Reproductive/Developmental-Placental-to-birth weight ratio (PFR)-Non-cancer	Pregnant women, Infants (birth to 2 years) Inclusion of PESS: Yes Male Pregnant women (mean age=29.6 years), infant boys (at birth).	MCOP (ug/L), median=3.86 ug/L, 5th percentile=1.17 ug/L, 95th percentile=17.4 ug/L.	MCOP was associated with lower PFR in multipollutant elastic net penalized regression models. The effect estimate from a multiple linear regression model (unpenalized effect estimate) was beta=-0.23, 95% CI=(-0.58, 0.11), p=0.18. MCOP was not associated with birth weight or placental weight based on elastic net regression models. Comments: Table 3	Medium	5041225
Breast cancer via self-report and physician confirmation via medical records Study Design: Case-Control (Nested) Health Effect: Cancer/Carcinogenesis-Breast cancer-Cancer-Reproductive/Developmental-Breast cancer-Cancer	Adults or general, Older Adults (65 years or older) Inclusion of PESS: Yes Female Women's Health Initiative: (October 1, 1993-2013), United States, 1,257 women (419 cases, 838 controls)	MCOP (ug/g creatinine), geometric mean (SD) cases = 6.15 (1.94), controls = 6.34 (1.96).	No significant results in MCOP analysis using either ln-transformed or quartile exposure variables. Adjusted OR (95% CI) in models using ln-MCOP = 1.02 (0.90 to 1.16). Findings were similar in models stratified by estrogen/progesterone receptor status and BMI. Comments: Associations somewhat stronger but NS among cases diagnosed closer to sample collection time. See Table S3. Repeated measures of phthalate metabolites were used to estimate exposure, but low intraclass correlations suggested that additional measures would have been optimal.	Medium	5043615
Overweight and obese measured at clinic visits during baseline and year 3 and 6 clinic visits. Phthalate metabolites measured in urine. Study Design: Case-Control, Cross-Sectional Health Effect: Nutritional/Metabolic-Overweight and obesity-Non-cancer	Adults or general, Older Adults (65 years or older) Inclusion of PESS: Yes Female Women's Health Initiative: October 1, 1993-December 21, 1998 (with follow-up through 2013), United States (Alabama, Pennsylvania, Arizona), 337 female cases and 660 female controls	Mono-carboxyoctyl phthalate, mean ng/mg creatinine (95% CI)Underweight/normal: 5.55 (5.15-5.98)Overweight: 6.71 (6.21-7.24)Obese: 6.77 (6.29-7.28)	OverweightPhthalate concentration (ng/mL): OR (95% CI)0.14-2.10: Reference2.20-3.60: 2.00 (1.30, 3.08)3.70-6.50: 2.06 (1.27, 3.34)6.60-239.0: 2.93 (1.74, 4.92)p-trend < 0.001Obese0.14-2.10: Reference2.20-3.60: 1.50 (0.91, 2.49)3.70-6.50: 2.38 (1.40, 4.05)6.60-239.0: 2.55 (1.42, 4.58)p-trend = 0.001 Comments: Table 3, PDF page 7. Results from model 2, most adjusted.	Medium	5613207

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Epidemiology Extraction Table:

Measured Effect/ Endpoints	Study Population	Exposure	Results	Overall Quality Determination	HERO ID
Weight change measured at clinic visits during baseline and year 3 and 6 clinic visits. Study Design: Case-Control, Cross-Sectional Health Effect: Nutritional/Metabolic-Weight change-Non-cancer	Adults or general, Older Adults (65 years or older) Inclusion of PESS: Yes Female Women's Health Initiative: October 1, 1993-December 21, 1998 (with follow-up through 2013), United States (Alabama, Pennsylvania, Arizona), 660 female controls	Mono-carboxyoctyl phthalate, mean ng/mg creatinine (95% CI)Underweight/normal: 5.55 (5.15-5.98)Overweight: 6.71 (6.21-7.24)Obese: 6.77 (6.29-7.28)	There were no significant trend tests for weight change at year 3 or year 6 Comments: Table 4, PDF page 9	Medium	5613207
Autism Spectrum Disorder (ASD) and Non-Typical Development (Non-TD) assessed by licensed clinical psychologists using the Autism Diagnostic Observation Schedules (ADOS) and by administration of the Mullen Scales of Early Learning (MSEL). Study Design: Cohort Health Effect: Neurological/Behavioral-Autism spectrum disorder (ASD), non-typical development (Non-TD)-Non-cancer	Pregnant women, Children (2-18 years) Inclusion of PESS: Yes Female, Male MARBLES (Markers of Autism Risk in Babies – Learning Early Signs) (2007-2014), California, United States, n = 201 (boys = 122, girls = 79)	MCOP (ug/L), median = 12.6 μg/L	Significant associations: Multinomial logistic regression of MCOP during mid to late pregnancy and ASD (vs. TD) among mothers who took prenatal vitamins: RRR = 0.49 (95% CI: 0.27, 0.88). Multinomial logistic regression of MCOP during mid to late pregnancy and Non-TD (vs. TD) among mothers who did not take prenatal vitamins: RRR = 1.86 (95% CI: 1.01, 3.39). Multinominal logistic of MCOP during 2nd trimester and ASD (vs. TD) among mothers who took prenatal vitamins: RRR = 0.41 (95% CI: 0.21, 0.79). Non-significant associations: MCOP in mid to late pregnancy and both ASD and Non-TD, unstratified analysis. MCOP in the 2nd trimester and both ASD and Non-TD, unstratified analysis. MCOP in the 3rd trimester and both ASD and Non-TD, unstratified analysis. MCOP in mid to late pregnancy and ASD among mothers who did not take prenatal vitamins. MCOP in mid to late pregnancy and Non-TD among mothers who took prenatal vitamins. MCOP in mid to late pregnancy and both ASD and Non-TD, stratified by sex. MCOP in the 2nd trimester and ASD among mothers who did not take prenatal vitamins. MCOP in the 2nd trimester and Non-TD, stratified by prenatal vitamin use. MCOP in the 3rd trimester and both ASD and Non-TD, stratified by prenatal vitamin use. MCOP in the 2nd trimester and both ASD and Non-TD, stratified by sex. MCOP in the 3rd trimester and both ASD and Non-TD, stratified by sex. Comments: Tables 3, 4, 5, S9, S10, S11, S12	High	5043457

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Epidemiology Extraction Table:

Measured Effect/ Endpoints	Study Population	Exposure	Results	Overall Quality Determination	HERO ID
Elevated total serum IgE (CAP assay) Study Design: Cohort (Prospective) Health Effect: Immune/Hematological-Eczema-Non-cancer	Children (2-18 years) Inclusion of PESS: Yes Male EDEN cohort: (2003-2006), France (Nancy and Poitiers), 604 male children	Monocarboxy-isooctyl phthalate (MCOP) median (25th-75th percentile) = 3.9 (2.4-6.5) ug/L IgE	No significant associations with elevated serum IgE (>=60 IU/mL). Comments: PDF page 5	Medium	4728712
Eczema measured via validated questionnaire and physician diagnosis. Study Design: Cohort (Prospective) Health Effect: Immune/Hematological-Eczema-Non-cancer	Children (2-18 years) Inclusion of PESS: Yes Male EDEN cohort: (2003-2006), France (Nancy and Poitiers), 604 male children	Monocarboxy-isooctyl phthalate (MCOP) median (25th-75th percentile) = 3.9 (2.4-6.5) ug/L	Multivariate logistic regression of MCOP and odds (95% CI) of eczema diagnosed at select ages [OR (95% CI)]: age 1 = 1.25 (0.70, 2.20) ns, age 3 = 1.28 (0.79, 2.09) ns, age 4 = 1.37 (95% CI: 0.99, 1.98) p<0.10. age 5 = 1.60 (95% CI: 1.16, 2.23) p<0.05. Multivariate logistic regression of MCOP on early onset eczema (first 2 years of life) = 1.29 (95% CI: 1.04, 1.60), p<0.05, late-onset (age 3-5 years) eczema: OR = 1.63 (95% CI: 1.20, 2.21), p<0.05. Cox proportional hazard model of MCOP and ever diagnosed with eczema: HR = 1.09 (95% CI: 0.95, 1.25), p=0.05. Comments: Table 3	Medium	4728712
IQ measured using the Wechsler Intelligence Scale for Children, 4th edition (WISC-IV) Study Design: Cohort Health Effect: Neurological/Behavioral-full scale IQ-Non-cancer	Pregnant women, Children (2-18 years) Inclusion of PESS: Yes Female, Male Swedish Environmental Longitudinal Mother and Child, Asthma and Allergy (SELMA) study: 718 mother-child pairs from Varmland county, Sweden, 2007-2010, recruited during first trimester; follow-up at child age 7.	MCiOP exposure distribution not directly provided. MCiOP concentrations were used to calculate DiNP (molar sum of MHiNP, MOiNP, and MCiOP). DiNP (ng/mL), geometric mean = 26.7 ng/mL, geometric standard deviation = 3.0 ng/mL.	MCiOP not directly analyzed. MCiOP concentrations were used to calculate DiNP (molar sum of MHiNP, MOiNP, and MCiOP). DiNP weights were not above the threshold of concern in the main weighted quantile sum analyses. In sensitivity analyses using a positive constraint, the weight for DiNP was 16% in the full sample approach among all children, 9% in the validation approach among all children, 25% in the full sample approach above girls, and 13% in the validation approach among girls. Comments: This is a mixtures analysis and phthalates of interest were only above the threshold of concern in sensitivity analyses using positive weights.	Medium	5933606

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Epidemiology Extraction Table:

Measured Effect/ Endpoints	Study Population	Exposure	Results	Overall Quality Determination	HERO ID
All-cause and CVD mortality, measured through the NHANES Public-Use Linked Mortality File and ICD-10 codes. Study Design: Cohort Health Effect: Mortality-All-cause mortality, CVD mortality-Non-cancer-Cardiovascular-CVD mortality-Non-cancer	Adults or general Inclusion of PESS: No Female, Male NHANES: (2005-2006; 2007-2008; 2009-2010), United States, 3,310 adult participants aged 40+ years. Mortality follow-up through 2015.	Specific concentrations not reported in text but likely available via NHANES data.	All-cause mortality Hazard Ratio (95%CI)Continuous: 1.03 (0.91-1.17)Tertile 2 vs. Tertile 1: 1.11 (0.83-1.47)Tertile 3 vs. Tertile 1: 1.14 (0.78-1.66)CVD mortality Hazard Ratio (95%CI)Continuous: 0.97 (0.71-1.33)Tertile 2 vs. Tertile 1: 0.63 (0.28-1.44)Tertile 3 vs. Tertile 1: 1.05 (0.46-2.40)(Table 3) Comments: No significant associations for mortality and DiNP. Non-significant positive associations were consistently reported for all-cause mortality.	Medium	9495379
Cancer mortality measured through the NHANES Public-Use Linked Mortality File and ICD-10 codes. Study Design: Cohort Health Effect: Mortality-Cancer mortality-Cancer-Cancer/Carcinogenesis-Cancer mortality-Cancer	Adults or general Inclusion of PESS: No Female, Male NHANES: (2005-2006; 2007-2008; 2009-2010), United States, 3,310 adult participants aged 40+ years. Mortality follow-up through 2015.	Specific concentrations not reported in text but likely available via NHANES data.	Cancer mortality Hazard Ratio (95%CI)Continuous: 1.01 (0.85-1.20)Tertile 2 vs. Tertile 1: 1.02 (0.64-1.64)Tertile 3 vs. Tertile 1: 1.14 (0.64-2.03)(Table 3) Comments: No significant associations for cancer mortality and DiNP. Non-significant positive associations were consistently reported.	Medium	9495379

Epidemiology Extraction Table:

Measured Effect/ Endpoints	Study Population	Exposure	Results	Overall Quality Determination	HERO ID
Uterine volume >= median Study Design: Cross-Sectional Health Effect: Reproductive/Developmental-uterine volume-Non-cancer	Adults or general Inclusion of PESS: No Female Women within the Fibroids Observational Research on Genes and the Environment (FORGE) study presenting to the George Washington University (GWU) gynecology clinic for evaluation for symptomatic fibroid tumors and surgical management were recruited 2014-2017. Eligible women were non-pregnant, premenopausal, English speaking, 18 years old or older, and intending to have their surgery at the GWU hospital. Ninety percent (n=61) of the n=68 women initially approached consented to participate. Final analysis was limited to the women (n=57) with urinary phthalate metabolite data.	MHiBP, Geometric Mean (GSD) (ng/mL) 2.06 (2.96)	Results from multivariate logistic regression analysis of urinary phthalate exposure on odds of uterine volume increase reported that each log-unit increase in MHiBP was significantly ($p<0.05$) associated with 2.6 (95% confidence interval (CI): 1.0-6.4) times increased odds of greater uterine volume, Results from additional multivariate linear regression analyses of urinary phthalate exposure on percent increase in uterine volume were positive but non-significant.	Medium	5043589

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Epidemiology Extraction Table:

Measured Effect/ Endpoints	Study Population	Exposure	Results	Overall Quality Determination	HERO ID
Uterine volume >= median Study Design: Cross-Sectional Health Effect: Reproductive/Developmental-uterine volume-Non-cancer	Adults or general Inclusion of PESS: No Female Women within the Fibroids Observational Research on Genes and the Environment (FORGE) study presenting to the George Washington University (GWU) gynecology clinic for evaluation for symptomatic fibroid tumors and surgical management were recruited 2014-2017. Eligible women were non-pregnant, premenopausal, English speaking, 18 years old or older, and intending to have their surgery at the GWU hospital. Ninety percent (n=61) of the n=68 women initially approached consented to participate. Final analysis was limited to the women (n=57) with urinary phthalate metabolite data.	MCOP, Geometric Mean (GSD) (ng/mL) 14.95 (4.66)	Results from multivariate logistic regression analysis of urinary phthalate exposure on odds of uterine volume increase reported that each log-unit increase in MCOP was significantly ($p<0.05$) associated with 2.1 (95% confidence interval (CI): 1.2-3.5) times increased odds of greater uterine volume, Results from additional multivariate linear regression analyses of urinary phthalate exposure on percent increase in uterine volume were positive but non-significant.	Medium	5043589

Epidemiology Extraction Table:

Measured Effect/ Endpoints	Study Population	Exposure	Results	Overall Quality Determination	HERO ID
Sex steroid hormones (pregnenolone, progesterone, allopregnanolone, pregnanolone) Study Design: Cohort Health Effect: Reproductive/Developmental-Sex hormones (allopregnanolone, pregnanolone, progesterone, pregnenolone)-Non-cancer	Pregnant women Inclusion of PESS: Yes Female NYU CHES (2016-2018), U.S., 139 pregnant women	Early pregnancy: MCiOP, Median (ng/mL) 1.5; MiNP, Median (ng/mL) 1.0; MCNP, Median (ng/mL) 0.97; sum(DiNP) phthalate metabolites, Median (IQR) (ng/mL) 0.01 (0.00, 0.03).Midpregnancy: MCiOP, Median (ng/mL) 1.8; MiNP, Median (ng/mL) 1.0; MCNP, Median (ng/mL) 0.84; sum(DiNP) phthalate metabolites, Median (IQR) (ng/mL) 0.02 (0.00, 0.03). hormone levels in serum	Multiple informant model regression: Serum progesterone negatively associated with sum DiNP phthalates (MCiOP, MiNP); Percent change = -7.7 (CI: -13.3, -1.7). No significant associations for pregnenolone, allopregnanolone, or pregnanolone. Comments: Table 5	Medium	7978436
postnatal depression (postpartum depression and Edinburgh Postnatal Depression Scale (EPDS) score) Study Design: Cohort Health Effect: Neurological/Behavioral-postnatal depression, postpartum depression-Non-cancer	Pregnant women Inclusion of PESS: Yes Female NYU CHES (2016-2018), U.S., 139 pregnant women	Early pregnancy: MCiOP, Median (ng/mL) 1.5; MiNP, Median (ng/mL) 1.0; MCNP, Median (ng/mL) 0.97; sum(High Molecular Weight Phthalate metabolites (MCNP and MBzP), Median (IQR)(ng/mL) 0.14 (0.07, 0.28); sum(DiNP) phthalate metabolites, Median (IQR) (ng/mL) 0.01 (0.00, 0.03). Midpregnancy: MCiOP, Median (ng/mL) 1.8; MiNP, Median (ng/mL) 1.0; MCNP, Median (ng/mL) 0.84; sum(High Molecular Weight Phthalate metabolites (MCNP and MBzP), Median (IQR)(ng/mL) 0.14 (0.07, 0.28); sum(DiNP) phthalate metabolites, Median (IQR) (ng/mL) 0.02 (0.00, 0.03).	Multiple informant model regression: No significant associations for EPDS score or postpartum depression for sum DiNP phthalates. Comments: Table 6	Medium	7978436
cognition - physical reasoning task (difference in total looking time between videos of impossible and possible events (looking time at impossible minus possible in seconds)) Study Design: Cohort (Prospective) Health Effect: Neurological/Behavioral-cognition (physical reasoning–looking time difference (seconds))-Non-cancer	Infants (birth to 2 years) Inclusion of PESS: Yes Female, Male Illinois Kids Development Study (IKIDS) pregnant women (n=159) age 18-40 years and recruited at their first prenatal visit, enrolled in the current study 2014-2018.	sumDINP, median 0.02 micromol/L (IQR=0.04 micromol/L)	An IQR increase in ΣDINP in pooled urine samples across pregnancy was associated with a negative looking time difference in males ($\beta = -1.0$; 95% CI: -1.8, -0.1; p-value = 0.03) Comments: Table 3b	Medium	7978433

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Epidemiology Extraction Table:

Measured Effect/ Endpoints	Study Population	Exposure	Results	Overall Quality Determination	HERO ID
Respiratory symptoms (asthma, hay fever, rhinitis, and wheeze) in the past 12 months Study Design: Cross-Sectional Health Effect: Lung/Respiratory-Asthma, wheeze, hay fever, rhinitis (symptoms in the past 12 months)-Non-cancer	Adults or general Inclusion of PESS: No Female, Male NHANES (2005-2006), United States, n = 1,091 adults aged >= 18 years (men = 547, women = 544)	Mono(carboxyoctyl) phthalate (MCOP), geometric mean = 5.03 ng/mL, SE = 0.19 ng/mL. Associations with mono-isononyl phthalate (MINP) were not analyzed as only 13.3% of participants (n=145, GM = 1.06, SE= 0.02) had detectable levels.	- For current asthma, there was a significant positive association between MCOP and odds of current asthma, which increased significantly among those with higher dust endotoxin exposure. Odds ratio (95% CI) per unit increase in log10 MCOP = 1.64 (1.05, 2.54) overall, low endotoxin = 0.96 (0.51, 1.79); medium endotoxin: 2.27 (1.34, 3.86); high endotoxin: 1.96 (1.16, 3.32). MCOP x endotoxin interaction p=0.01 for asthma. Current asthma definition: self-reported symptoms in the past 12 months among doctor-diagnosed participants. - For current wheeze, there was a non-significant increase between MCOP and odds of current wheeze overall. Associations were significantly stronger with higher endotoxin exposure but did not reach statistical significancce. OR (95% CI) per unit increase in log10 MCOP = 1.18 (0.82, 1.71) overall, low endotoxin = 0.82 (0.50, 1.33); medium endotoxin = 1.35 (0.85, 2.14); high endotoxin = 1.52 (0.98, 2.36). MCOP x endotoxin interaction p=0.03 for wheeze. Current wheeze definition: self-reported symptoms in the past 12 months. - For both hay fever and rhinitis symptoms, no significant main effects or endotoxin interactions were found for MCNP (results in a supplement not available at the time of extraction). Comments: Tabled 2, 3, and 4. For asthma, this study found significant main effects that were not observed in their previous study on phthalates and respiratory symptoms of NHANES 2005-06. The focus of this study was effect modification of phthalates by endotoxin (n=1,091); the previous study analyzed a larger sample as it did not exclude participants missing endotoxin data (n=1,546). The magnitude of difference in associations is unknown. Despite these differences in significance, there was no direct evidence of bias.	Medium	4728797

Epidemiology Extraction Table:

Measured Effect/ Endpoints	Study Population	Exposure	Results	Overall Quality Determination	HERO ID
Total oocytes, mature oocytes, fertilized oocytes, top quality embryos, live birth Study Design: Cohort Health Effect: Reproductive/Developmental-Total Oocytes, mature oocytes, fertilized oocytes, top quality embryos, live births, implantation-Non-cancer	Pregnant women Inclusion of PESS: Yes Female Women undergoing in vitro fertilization (IVF) (n = 136) from January 2014 through August 2016 in Israel	Mono carboxyisooctyl phthalate (MCOP): specific gravity adjusted median (IQR) = 8.2 (5.3, 17.1)T1 = (1.68–6.15)T2 = (6.16–11.14)T3 = (11.15–1344)	Mono carboxyisooctyl phthalate (MCOP): -Association (adjusted means) between urinary MCOP concentration and intermediate outcomes of assisted reproduction (Total oocytes and mature oocytes) [Total oocytes T2 = 10.2 (95% CI: 9.3, 11.2), T2 vs. T1 $<$ 0.05; mature oocytes T2 = 8.4 (95% CI: 7.6, 9.3) T2 vs. T1 $<$ 0.05]. Not significant: -Association (adjusted means) between urinary MCOP concentration and intermediate outcomes of assisted reproduction (fertilized oocytes, top quality embryos)-Association (adjusted means) between tertiles of specific gravity adjusted MCOP and live birth, implantations following assisted reproduction. Comments: Table 3, Table 5, Supplemental Table 3	Medium	5743382
Total oocytes, mature oocytes, fertilized oocytes, top quality embryos, live birth Study Design: Cohort Health Effect: Reproductive/Developmental-Total Oocytes, mature oocytes, fertilized oocytes, top quality embryos, live births, implantation-Non-cancer	Pregnant women Inclusion of PESS: Yes Female Women undergoing in vitro fertilization (IVF) (n = 136) from January 2014 through August 2016 in Israel	Mono-iso-nonyl phthalate (MiNP): specific gravity adjusted median (IQR) = 1.0 (<LOD, 1.6)T1 = (<LOD)T2 = (0.50–1.40)T3 = (1.41–263)	Mono-iso-nonyl phthalate (MiNP): -Association (adjusted means) between urinary MiNP concentration and intermediate outcomes of assisted reproduction (Total oocytes) [Total oocytes T2 = 9.2 (95% CI: 8.2, 10.2), T2 vs. T1 $<$ 0.05]. Not significant: -Association (adjusted means) between urinary MiNP concentration and intermediate outcomes of assisted reproduction (mature oocytes, fertilized oocytes, top quality embryos)-Association (adjusted means) between tertiles of specific gravity adjusted MiNP and live birth or implantation following assisted reproduction. Comments: Table 3, Table 5, Supplemental Table 3	Medium	5743382
Total oocytes, mature oocytes, fertilized oocytes, top quality embryos, live birth Study Design: Cohort Health Effect: Reproductive/Developmental-Total Oocytes, mature oocytes, fertilized oocytes, top quality embryos, live births, implantation-Non-cancer	Pregnant women Inclusion of PESS: Yes Female Women undergoing in vitro fertilization (IVF) (n = 136) from January 2014 through August 2016 in Israel	Mono(oxo-iso-nonyl) phthalate (MOiNP or MONP): specific gravity adjusted median (IQR) = 3.5 ug/L (2.4, 6.0 ug/L)T1 = (0.56-2.79)T2 = (2.80-4.83)T3 = (4.84-902)	Mono(oxo-nonyl) phthalate (MONP): Association between urinary MONP and intermediate outcomes of assisted reproduction (total oocytes, mature oocytes, fertilized oocytes, top quality embryos) and live birth following assisted reproduction: all non-significant for T2, T3 versus T1 intermediate outcomes and for p-trend of live birth, implantations. Comments: Table 3, Table 5, Supplemental Table 3	Medium	5743382

Epidemiology Extraction Table:

Measured Effect/ Endpoints	Study Population	Exposure	Results	Overall Quality Determination	HERO ID
-Child behavior (conduct problems, emotional symptoms, hyperactivity-inattention problems, peer relationship problems, total difficulties, prosocial behavior) measured at age 7 using maternal report on the Strengths and Difficulties Questionnaire. -Child cognition and psychomotor development (fluid intelligence, crystallized intelligence, cognition, mathematical skills, psychomotor skills, language skills) measured at age 7 using psychologist assessment on the Intelligence and Development Scales. Study Design: Cohort (Prospective) Health Effect: Neurological/Behavioral-Child behavior (domains: conduct problems, emotional symptoms, hyperactivity-inattention problems, peer relationship problems, total difficulties, prosocial behavior)-Non-cancer-Neurological/Behavioral-Child cognition and psychomotor development (domains: fluid intelligence, crystallized intelligence, cognition, mathematical skills, psychomotor skills, language skills)-Non-cancer	Pregnant women, Children (2-18 years), Infants (birth to 2 years) Inclusion of PESS: Yes Female, Male A subset of mother-child pairs from the Polish Mother and Child Cohort (recruitment beginning 2007), Poland, Lodz district, n=134 mother child pairs	OH-MiNP (ug/g creatinine maternal samples, ug/L child samples): median (IQR) in maternal 3rd trimester samples 0.76 (0.5 - 2.3 ug/g creatinine), median (IQR) in child age 2 samples 3.07 (0.99 - 9.55 ug/L).	No statistically significant associations between OH-MiNP and any of the outcomes. There was no clear pattern of associations with behavioral outcomes; associations with cognitie and psychomotor scores were generally weakly negative. -For example, the odds ratio (95% CI) for having a borderline or clinical total difficulties behavioral score (18.2%) per unit increase in log10 OH-MiNP were 0.65 (0.29: 1.44) for prenatal and 1.54 (0.69: 3.42) for postnatal (age 2 years) levels. -For crystallized intelligence, beta coefficients (95% CI) per unit increase in log10 OH-MiNP were -1.79 (-5.59: 2.01) for prenatal and -0.41 (-4.28: 3.46) for postnatal measures. Psychomotor score associations were -1.04 (-2.35: 0.27) and -1.23 (-2.57: 0.11) for pre- and postnatal measures, respectively. Comments: Table 4 (Strengths and Difficulties Questionnaire), Table 5 (Intelligence and Developmental Scales)	Medium	5933662

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Epidemiology Extraction Table:

Measured Effect/ Endpoints	Study Population	Exposure	Results	Overall Quality Determination	HERO ID
IQ measured using the Wechsler Intelligence Scale for Children, 4th edition (WISC-IV) Study Design: Cohort Health Effect: Neurological/Behavioral-full scale IQ-Non-cancer	Pregnant women, Children (2-18 years) Inclusion of PESS: Yes Female, Male Swedish Environmental Longitudinal Mother and Child, Asthma and Allergy (SELMA) study: 718 mother-child pairs from Varmland county, Sweden, 2007-2010, recruited during first trimester; follow-up at child age 7.	MHiNP exposure distribution not directly provided. MHiNP concentrations were used to calculate DiNP (molar sum of MHiNP, MOiNP, and MCiOP). DiNP (ng/mL), geometric mean = 26.7 ng/mL, geometric standard deviation = 3.0 ng/mL.	MHiNP not directly analyzed. MHiNP concentrations were used to calculate DiNP (molar sum of MHiNP, MOiNP, and MCiOP). DiNP weights were not above the threshold of concern in the main weighted quantile sum analyses. In sensitivity analyses using a positive constraint, the weight for DiNP was 16% in the full sample approach among all children, 9% in the validation approach among all children, 25% in the full sample approach above girls, and 13% in the validation approach among girls. Comments: This is a mixtures analysis and phthalates of interest were only above the threshold of concern in sensitivity analyses using positive weights.	Medium	5933606

Epidemiology Extraction Table:

Measured Effect/ Endpoints	Study Population	Exposure	Results	Overall Quality Determination	HERO ID
Severe uterine fibroids measured through diagnosis Study Design: Case-Control Health Effect: Reproductive/Developmental-Uterine fibroids-Non-cancer	Adults or general Inclusion of PESS: No Female 2015-2016, Seoul, Ansan, Incheon, and Jeju South Korea, 111 women (20-49 years of age) (32 uterine fibroid cases and 79 controls)	Median (25th, 75th percentiles) concentrations for case OH_MINP were 2.05 ng/mL (1.12, 3.80 ng/mL) and controls were 1.37 ng/mL (0.83-2.39 ng/mL), while those for cxMINP cases were 2.34 ng/mL (1.51, 4.65 ng/mL) and controls were 2.57 ng/mL (1.52, 3.50 ng/mL).	No statistically significant findings of the association between uterine fibroids and DINP metabolite concentrations. Significance found between cases and controls for OH-MINP concentrations (p-value: 0.042) as mono(4-methyl-7-hydroxyoctyl) phthalate (OH-MINP) concentrations were significantly higher in the cases than controls. Comments: Tables 2 and 3	Medium	7274600

Epidemiology Extraction Table:

Measured Effect/ Endpoints	Study Population	Exposure	Results	Overall Quality Determination	HERO ID
Attention-deficit hyperactivity disorder (ADHD) Study Design: Case-Control (Nested) Health Effect: Neurological/Behavioral-Attention-deficit hyperactivity disorder (ADHD)-Non-cancer	Children (2-18 years) Inclusion of PESS: Yes Female, Male Norwegian Mother and Child Cohort (MoBa) (2003-2008), ADHD cases (n=297 with n=213 boys, n=82 girls), controls (n=533 with n=273 boys, n=278 girls),	Concentrations [median (25th-75th percentile)] ug/L of the three measured metabolites of DiNP in cases vs controls were: mono-4-methyl-7-hydroxyoctylphthalate (OH-MiNP) = 0.86 (0.59-1.22 ug/L) vs. 0.95 (0.69-1.42); mono-4-methyl-7-oxooctylphthalate (oxo-MiNP) = 0.95 ug/L (0.62-1.58 ug/L) vs. 1.04 (0.70-1.76); and mono-4-methyl-7-carboxyheptylphthalate (cx-MiNP) = 2.96 ug/L (2.27-4.45) vs. 3.49 (2.50-4.73). The percentage of samples above LOQ for these metabolites were 100%, 98.5% and 100%, respectively. The distribution of the sum of DiNP metabolites was 0.02 (0.01-0.02) umol/L in cases vs. 0.02 (0.01-0.03) in controls. Geometric means for the sum of DiNP metabolites in cases vs. controls were 1.75 vs. 1.95 umol/L.	The authors reported no association of ADHD with phthalate metabolites relevant for this review (sum of di-iso-nonyl phthalate (DiNP) metabolites). In Bayesian logistic regression models, the association (OR, 95% credible interval) with log sum of DiNP was 0.85 (0.61,1.15); there were no sex differences. Associations with individual DiNP metabolites (not shown) were also null.	Medium	4728558

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Epidemiology Extraction Table:

Measured Effect/ Endpoints	Study Population	Exposure	Results	Overall Quality Determination	HERO ID
ADHD/subthreshold ADHD at age 3-4 years. Cases screened in the parent cohort (Child Behavior Checklist, DSM-IV items) were identified in a clinical exam by trained and supervised graduate psychology students using the Preschool Age Psychiatric Assessment (PAPA). Study Design: Cohort (Prospective), Case-Control (Nested) Health Effect: Neurological/Behavioral-Attention Deficit Hyperactivity Disorder (ADHD)-Non-cancer	Children (2-18 years) Inclusion of PESS: Yes Female, Male Case-cohort study of ADHD (260 cases, 115 girls; 549 non-cases, 274 girls) nested in the MoBa cohort. Participants were born in 2004-2008 and followed through age 3.8 years.	Sum of 3 DiNP metabolites, cases: geometric mean ± SD (min, 25th, 50th, 75th, max) = 0.02 ± 2.04 umol/L (0.01, 0.01, 0.02, 0.03, and 0.96) Sum of 3 DiNP metabolites, non-cases: geometric mean ± SD (min, 25th, 50th, 75th, max) = 0.02 ± 1.86 umol/L (0.01, 0.01, 0.02, 0.03, and 1.07) oh-MiNP, cases: geometric mean ± SD (min, 25th, 50th, 75th, max) = 1.12 ± 2.23 ug/L (0.31, 0.72, 0.97, 1.36, and 138)oh-MiNP, non-cases: geometric mean ± SD (min, 25th, 50th, 75th, max) = 1.07 ± 2.01 ug/L (0.20, 0.69, 0.96, 1.43, and 60.7)oxo-MiNP, cases: geometric mean± SD (min, 25th, 50th, 75th, max) = 1.30 ± 2.58 ug/L (0.27, 0.72, 1.04, 1.76, and 122) oxo-MiNP, non-cases: geometric mean± SD (min, 25th, 50th, 75th, max) = 1.22 ± 2.34 ug/L (0.18, 0.70, 1.04, 1.76, and 201) cx-MiNP, cases: geometric mean± SD (min, 25th, 50th, 75th, max) = 3.80 ±1 .83 ug/L (1.27, 2.51, 3.37, 5.15, and 49.7)cx-MiNP, non-cases: geometric mean± SD (min, 25th, 50th, 75th, max) = 3.65 ±1 .71 ug/L (1.14, 2.50, 3.49, 4.74, and 141)	The association between DiNP and odds of ADHD was significantly non-linear; associations were significant in the 2nd and 5th quintiles. Results of multivariate logistic regression ORs (95% CI) for the association between increasing DiNP quintiles vs. Q1 (<0.12 umol/L) and odds of ADHD were: Q2 (0.012 - 0.016 umol/L) = 2.07 (1.27 to 3.37) Q3 (0.016 - 0.020 umol/L) = 0.89 (0.52 to 1.55) Q4 (0.020 - 0.027 umol/L) = 1.13 (0.67 to 1.92) Q5 (>0.027 umol/L) = 1.70 (1.03 to 2.82) -From the model using ln-transformed DiNP, the odds ratio (95% CI) per 1 ln increase = 1.18 (0.94 to 1.49).In model 2, which includes additional adjustment for DEHP): Q2 (0.012 - 0.016 umol/L) = 2.04 (1.2 to 3.33) Q3 (0.016 - 0.020 umol/L) = 0.86 (0.50 to 1.50) Q4 (0.020 - 0.027 umol/L) = 1.07 (0.62 to 1.82) Q5 (>0.027 umol/L) = 1.54 (0.91 to 2.61) -From the model using ln-transformed DiNP, the odds ratio (95% CI) per 1 ln increase = 1.10 (0.85 to 1.42). Comments: Table 3. See Table 4 for sex stratified results, which used only ln-transformed exposure (i.e., did not take non-linearity into account). Individual DiNP metabolites were not analyzed.	Medium	9559555

Epidemiology Extraction Table:

Measured Effect/ Endpoints	Study Population	Exposure	Results	Overall Quality Determination	HERO ID
age at pubertal onset (testicular volume >3 mL, genitalia >= stage 2, pubarche >= Stage 2) Study Design: Cohort (Prospective) Health Effect: Reproductive/Developmental-age at pubertal onset (as measured by testicular volume, genitalia Tanner stage, and pubarche Tanner stage_-Non-cancer	Children (2-18 years) Inclusion of PESS: Yes Male 304 boys recruited at ages 8-9 for the Russia Children's Study, (recruited 2003-2005; follow-up to 18-19 years)	MOiNP, Median (ng/mL) 2.9	Testicular volume > 3mL positively associated with all quartiles vs. 1 of MOiNP;For Q2, mean shift (months)= 5.1 (95% CI, 0.2, 9.9); For Q3, mean shift (months)= 7.0 (95% CI, 1.9, 12.1); For Q4, mean shift (months)= 6.5 (95% CI, 1.2, 11.7); p-trend = 0.02Genitalia stage >= stage 2 positively associated with all quartiles vs. 1 of MOiNP;For Q2, mean shift (months)= 6.3 (95% CI, 0.2, 12.4); For Q3, mean shift (months)= 8.8 (95% CI, 2.4, 15.2); For Q4, mean shift (months)= 8.0 (95% CI, 1.4, 14.5); p-trend = 0.02 Comments: Table 4, S3	Medium	10294569
age at pubertal onset (testicular volume >3 mL, genitalia >= stage 2, pubarche >= Stage 2) Study Design: Cohort (Prospective) Health Effect: Reproductive/Developmental-age at pubertal onset (as measured by testicular volume, genitalia Tanner stage, and pubarche Tanner stage_-Non-cancer	Children (2-18 years) Inclusion of PESS: Yes Male 304 boys recruited at ages 8-9 for the Russia Children's Study, (recruited 2003-2005; follow-up to 18-19 years)	MCOP, Median (ng/mL) 6.4	Testicular volume > 3mL positively associated with all quartiles vs. 1 of MCOP;For Q2, mean shift (months)= 7.3 (95% CI, 2.5, 12.1); For Q3, mean shift (months)= 6.2 (95% CI, 1.1, 11.3); For Q4, mean shift (months)= 8.7 (95% CI, 3.7, 13.7); p-trend = 0.02Genitalia stage >= stage 2 positively associated with all quartiles vs. Q1 of MCOP;For Q2, mean shift (months)= 7.7 (95% CI, 1.6, 13.7); For Q3, mean shift (months)= 8.0 (95% CI, 1.5, 14.4); For Q4, mean shift (months)= 9.9 (95% CI, 3.5, 16.2); p-trend= 0.005Pubarche stage >= Stage 2 positively associated with Q3 and Q4 vs. Q1of MCOP;For Q3, mean shift (months)= 10.7 (95% CI, 3.6, 17.8); For Q4, mean shift (months)= 11,1 (95% CI, 4.2, 18.1); p-trend= 0.001 Comments: Table 4, S3	Medium	10294569
age at pubertal onset (testicular volume >3 mL, genitalia >= stage 2, pubarche >= Stage 2) Study Design: Cohort (Prospective) Health Effect: Reproductive/Developmental-age at pubertal onset (as measured by testicular volume, genitalia Tanner stage, and pubarche Tanner stage_-Non-cancer	Children (2-18 years) Inclusion of PESS: Yes Male 304 boys recruited at ages 8-9 for the Russia Children's Study, (recruited 2003-2005; follow-up to 18-19 years)	Summed DiNP, Median (umol/L) 0.06	Testicular volume > 3mL positively associated with Q4 vs. Q1 of urinary summed DiNP levels; For Q4, mean shift (months)= 5.4 (95% CI, 0.01, 10.7); Genitalia stage >= stage 2 positively associated with Q3 vs. Q1 of urinary summed DiNP levels; For Q3, mean shift = 6.5 (95% CI, 0.03, 13.0); Pubarche stage >= Stage 2 positively associated with Q3 and Q4 vs. Q1of urinary summed DiNP levels; For Q3, mean shift = 8.9 (95% CI, 1.8, 15.9); For Q4, mean shift = 8.4 (95% CI, 1.1, 15.7); Comments: Table 4	Medium	10294569

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Epidemiology Extraction Table:

Measured Effect/ Endpoints	Study Population	Exposure	Results	Overall Quality Determination	HERO ID
age at pubertal onset (testicular volume >3 mL, genitalia >= stage 2, pubarche >= Stage 2) Study Design: Cohort (Prospective) Health Effect: Reproductive/Developmental-age at pubertal onset (as measured by testicular volume, genitalia Tanner stage, and pubarche Tanner stage_-Non-cancer	Children (2-18 years) Inclusion of PESS: Yes Male 304 boys recruited at ages 8-9 for the Russia Children's Study, (recruited 2003-2005; follow-up to 18-19 years)	MHiNP, Median (ng/mL) 8.2	Pubarche stage >= Stage 2 positively associated with Q3 vs. Q1 of MHiNP;For Q3, mean shift (months)= 8.4 (95% CI, 1.4, 15.3); p-trend= 0.001 Comments: Table 4, S3	Medium	10294569
Any episodes of wheeze during infant's first year of life assessed by maternal report using the ISAAQ questionnaire Study Design: Cohort (Prospective) Health Effect: Lung/Respiratory-Wheeze-Non-cancer	Infants (birth to 2 years) Inclusion of PESS: Yes Female, Male SELMA cohort participants: pregnant women recruited during their first visit to a public antenatal care center in Sweden and their infants (n = 1,062 mother-infant pairs)	Geometric means (95% CI) for DiNP metabolites were MHiNP = 6.2 (5.8–6.7) ng/mL; MCiOP = 2.9 (2.7–3.1) ng/mL; and MOiNP 9.9 (9.3–11.0) ng/mL.	Several DiNP metabolites were associated with wheeze, although there was no clear pattern of dose-response, with some sex differences. [1] MHiNP. All quartiles of MHiNP were associated with wheeze [adjusted OR (95% CI) vs Q1 were Q2 = 1.55 (1.04, 2.29), Q3 = 1.49 (1.00, 2.21) Q4 = 1.83 (1.24, 2.71)]. Log10 transformed MHiNP was also associated with increased odds of wheeze (visual results only). Sex-stratified associations were significant for the 4th quartile in girls [OR = 2.24 (1.01–4.95)] but not in boys [OR = 0.86 (0.30–2.47)]. [2] MOiNP. In quartile-based analysis, MOiNP was associated with wheeze (adjusted OR (95% CI) were Q2 = 1.70 (1.14, 2.52), Q3 = 1.75 (1.18, 2.60), Q4 =1.69 (1.13, 2.51)). No association between MOiNP as a continuous variable and wheeze. Sex-stratified associations were significant in boys for Q3. The magnitude of associations was stronger in girls, and signifiant for Q3 and Q4. [3] MCiOP. In quartile-based analysis, MCiOP was associated with wheeze in the 2nd and 4th quartiles (OR for Q2 = 1.49 (1.00, 2.20), Q4 = 1.72 (1.17, 2.54). No association between MCiOP as a continuous variable and wheeze. In boys, the association was U-shaped (stronger associations that reached significance in Q2 [1.75 (1.06–2.88)] and Q3 [1.67 (1.00–2.78)] while in girls the associations were null for Q2 and Q3 [0.98 (0.52–1.86)], with a strong and statistically significant association in Q4 [1.87 (1.03–3.40)]. Comments: Figure 1, Figure 2, Table 3, Table 4	Medium	4728698

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Epidemiology Extraction Table:

Measured Effect/ Endpoints	Study Population	Exposure	Results	Overall Quality Determination	HERO ID
Any episodes of croup or otitis media during infant's first year of life assessed by maternal report Study Design: Cohort (Prospective) Health Effect: Lung/Respiratory-Croup-Non-cancer	Infants (birth to 2 years) Inclusion of PESS: Yes Female, Male SELMA cohort participants: pregnant women recruited during their first visit to a public antenatal care center in Sweden and their infants (n = 1,062 mother-infant pairs)	Geometric means (95% CI) for DiNP metabolites were MHiNP = 6.2 (5.8–6.7) ng/mL; MCiOP = 2.9 (2.7–3.1) ng/mL; and MOiNP 9.9 (9.3–11.0) ng/mL.	DiNP metabolites were not associated with croup overall or in girls. In boys, Q4 vs Q1 of DiNP was associated with a significant increase in odds of croup: OR (95% CI) 2.24 (1.01–4.95); associations with other quartiles did not reach significance. Comments: Figure 1, Figure 2, Table 3, Table 4	Medium	4728698
Any episodes of croup or otitis media during infant's first year of life assessed by maternal report Study Design: Cohort (Prospective) Health Effect: Immune/Hematological-Otitis media-Non-cancer	Infants (birth to 2 years) Inclusion of PESS: Yes Female, Male SELMA cohort participants: pregnant women recruited during their first visit to a public antenatal care center in Sweden and their infants (n = 1,062 mother-infant pairs)	Geometric means (95% CI) for DiNP metabolites were MHiNP = 6.2 (5.8–6.7) ng/mL; MCiOP = 2.9 (2.7–3.1) ng/mL; and MOiNP 9.9 (9.3–11.0) ng/mL.	There were no significant associations between any phthalates and maternal reported odds of otitis media in the first year of life. Comments: Figure 1, Figure 2, Table 3, Table 4	Medium	4728698

Epidemiology Extraction Table:

Measured Effect/ Endpoints	Study Population	Exposure	Results	Overall Quality Determination	HERO ID
A total of 10 executive function symptom outcomes were analyzed. Habitual executive function was evaluated by parent and teacher-rated reports using the Behavior Rating Inventory of Executive Function-Preschool [BRIEF-P]. Emotional control, inhibition, and working memory scores were analyzed. Three performance-based assessments administered by psychologists in the study clinic were also analyzed: Stanford Binet IV short version [SB5] to measure assess non-verbal and verbal working memory; a developmental Neuro PSYchological Assessment [NEPSY] test subtask to assess inhibition; and cookie delay task [CDT] to assess self-control. Study Design: Cohort (Prospective) Health Effect: Neurological/Behavioral-Executive function symptoms-Non-cancer	Pregnant women, Children (2-18 years) Inclusion of PESS: Yes Female, Male The study included 340 children: 146 and 116 boys and girls respectively with high ADHD symptoms, and 42 and 36 boys and girls respectively clinically confirmed as neurotypical following the clinical on-site assessment.	Diisononyl phthalate (DiNP) geometric mean [GM] ± SD 0.02 ± 1.60 umol/L; IQR increase = 0.01 umol/L. DiNP exposure was estimated using the molar sum of mono-4-methyl-7-hydroxyoctyl phthalate (OH-MiNP, GM ± SD 0.92 ± 1.79 ng/mL) , mono-4-methyl-7oxooctyl phthalate (oxo-MiNP, GM ± SD 1.01 ± 1.93 ng/mL) and mono-4-methyl-7-carboxyheptyl phthalate (cx-MiNP, GM ± SD 3.14 ± 1.55 ng/mL).	Associations between DiNP and all outcomes were null. For example, multivariate linear regression beta coefficient (95% CI) per 1 IQR DiNP increase for inhibition outcome measures were: teacher report = -0.004 (-0.40, 0.39), parent report = 0.35 (-0.02, 0.72), and NEPSY clinic assessment -0.02 (-0.06, 0.01). For working memory, results were: teacher report = -0.11 (-0.49, 0.26), parent report = 0.02 (-0.38, 0.41), Standford-Binet non-verbal working memory = -0.02 (-0.06, 0.02) and verbal working memory -0.01 (-0.05, 0.03). Comments: Supplementary analyses shown only for MBzP found considerably stronger associations for 8 of the 10 outcomes in the neurotypical subgroup. However, incorporating sample weight adjustments to account for oversampling of ADHD children (77% of the sample) yielded results similar to those in the neurotypical group.	Medium	8010273

Epidemiology Extraction Table:

Measured Effect/ Endpoints	Study Population	Exposure	Results	Overall Quality Determination	HERO ID
IQ measured using the Wechsler Intelligence Scale for Children, 4th edition (WISC-IV) Study Design: Cohort Health Effect: Neurological/Behavioral-full scale IQ-Non-cancer	Pregnant women, Children (2-18 years) Inclusion of PESS: Yes Female, Male Swedish Environmental Longitudinal Mother and Child, Asthma and Allergy (SELMA) study: 718 mother-child pairs from Varmland county, Sweden, 2007-2010, recruited during first trimester; follow-up at child age 7.	MOiNP exposure distribution not directly provided. MOiNP concentrations were used to calculate DiNP (molar sum of MHiNP, MOiNP, and MCiOP). DiNP (ng/mL), geometric mean = 26.7 ng/mL, geometric standard deviation = 3.0 ng/mL.	MOiNP not directly analyzed. MOiNP concentrations were used to calculate DiNP (molar sum of MHiNP, MOiNP, and MCiOP). DiNP weights were not above the threshold of concern in the main weighted quantile sum analyses. In sensitivity analyses using a positive constraint, the weight for DiNP was 16% in the full sample approach among all children, 9% in the validation approach among all children, 25% in the full sample approach above girls, and 13% in the validation approach among girls. Comments: This is a mixtures analysis and phthalates of interest were only above the threshold of concern in sensitivity analyses using positive weights.	Medium	5933606

Epidemiology Extraction Table:

Measured Effect/ Endpoints	Study Population	Exposure	Results	Overall Quality Determination	HERO ID
Overweight at ages 4, 8, 16 and 24 years. BMI, waist circumference, body fat percentage, trunk fat percentage at age 24 years. Study Design: Cohort (Prospective) Health Effect: Nutritional/Metabolic-Obesity: overweight/obesity, body mass index (BMI), waist circumference (WC), body fat %, and trunk fat %.-Non-cancer	Adults or general, Children (2-18 years) Inclusion of PESS: Yes Female, Male A subsample of children from the Swedish BAMSE birth cohort (enrolled 1994-1996) who were followed through age 24 years (n = 100).	Specific-gravity adjusted ng/mL: mono(hydroxy-isononyl) phthalate (MHiNP) = mean ± sd = 13.9 ± 21, median (range) = 8.4 (1.1-166); mono(oxo-isononyl) phthalate (MOiNP) mean ± sd = 5.9 ± 9.1, median (range) = 3.3 (0.2-74.3); mono(carboxy-isooctyl) phthalate (MCiOP) mean ± sd = 14.9 ± 18.7, median (range) = 9.0 (2.2-121); DiNP mean ± sd = 34.5 ± 47.4, median (range) = 21.6 (4.1-318).	Urinary age 4 MHiNP, MOiNP, MCiOP and ΣDiNP measures were significantly associated with an increased odds of overweight at ages 8, 16, and 24 years, and with higher BMI , waist circumference, body fat %, and trunk fat % at 24 years. For overweight/obesity up to 24 years, MOiNP: (OR: 1.18, 95% CI: 1.05, 1.33), MCiOP: (OR: 1.06, 95% CI: 1.01, 1.11) and ΣDiNP: (OR: 1.02, 95% CI: 1.003, 1.04). Additionally, the DiNP metabolite MHiNP was borderline significantly associated (p = 0.053) with overweight/obesity = (OR: 1.04, 95% CI: 1.00, 1.08). For outcomes of BMI, waist circumference, body fat % and trunk fat % at 24 years, ΣDiNP, beta coefficients (95% CI) at age 24 y were: BMI = 1.60 (0.37-2.84), waist circumference = 4.42 (1.35-7.49), body fat % = 2.65 (0.52-4.77), and trunk fat % 2.70 (0.33-5.07). For MCiOP, beta coefficients (95% CI) at age 24 y were: BM1 = 1.60 (0.30-2.89), waist circumference = 4.34 (1.12-7.57), body fat % = 2.65 (0.41-4.89), and trunk fat % 2.68 (0.18-5.18). For MOiNP beta coefficients (95% CI) at age 24 y were: BM1 = 1.35 (0.26-2.44), waist circumference = 3.57 (0.85-6.30), body fat % = 2.32 (0.46-4.18), and trunk fat % 2.43 (0.36-4.51). For MHiNP beta coefficients (95% CI) at age 24 y were: BM1 = 1.55 (0.39-2.70), waist circumference = 4.27 (1.40-7.14), body fat % = 2.42 (0.44-4.39), and trunk fat % 2.44 (0.23-4.65). Comments: Figure 1, Table 4	Medium	7978414

Epidemiology Extraction Table:

Measured Effect/ Endpoints	Study Population	Exposure	Results	Overall Quality Determination	HERO ID
Forced Expiratory Volume in 1 second as % predicted (FEV1%) Study Design: Cohort (Prospective) Health Effect: Lung/Respiratory-Forced Expiratory Volume in 1s as % predicted value (FEV1%)-Non-cancer	Children (2-18 years) Inclusion of PESS: Yes Female, Male HELIX comprises 1,301 mother-child pairs drawn from 6 prospective, general population birth cohorts in Europe (France, Greece, Lithuania, Norway, Spain, and the UK). Eligible participants (age 6-11, sufficient stored blood and urine samples from pregnancy, complete address history, no serious health problems) were randomly selected from each sub-cohort and invited to participate.	Median (25-75th percentiles (n=914 prenatal, n=1,301 childhood)(1) Mono-4-methyl-7-oxooctyl phthalate (oxo-MiNP) prenatal = 1.03 (0.62-1.75) μg/g creatinine, childhood = 2.83 (1.86-4.87) μg/g creatinine.(2) Mono-4-methyl-7-hydroxyoctyl phthalate (oh-MiNP) prenatal = 0.91 (0.61-1.47) μg/g creatinine, childhood = 5.36 (3.38-9.26) μg/g creatinine.	This exposome study examined 85 prenatal and 125 concurrent postnatal measures. (1) In the exposome-wide association (ExWAS) one-by-one exposure analysis: coefficient (95% CI) for association between FEV1% and childhood oxo-MiNP = –0·9 (–1·7 to 0·0), p=0.04 per log2 IQR increase (IQR=1.34). Associations were not significant accounting for multiple comparisons and were attenuated after adjusting for co-exposures. Associations with oh-MiNP did not reach significance. (2) No exposures were significant using the deletion-substitution-addition (DSA) algorithm. Comments: The childhood DiNP-lung function association is cross-sectional. Childhood DiNP concentrations were higher than prenatal concentrations, reflecting the increase in DiNP use in Europe.	High	5043613

Epidemiology Extraction Table:

Measured Effect/ Endpoints	Study Population	Exposure	Results	Overall Quality Determination	HERO ID
Infant cognition at 7-8 months was measured using a visual recognition memory test with automated measures of duration or proportion of time spent looking at image sets. Outcomes included: information processing speed (run duration during familiarization trial), visual attention (time to familiarization), and visual recognition memory (novelty preference in test trial). Study Design: Cohort Health Effect: Neurological/Behavioral-Cognition at 7-8 months as assessed by information processing speed (average run duration during familiarization trial), visual attention (time to reach familiarization criterion during familiarization trial), and visual recognition memory (novelty preference in test trial) using eye tracking within a paired comparison visual recognition memory (VRM) test.-Non-cancer	Infants (birth to 2 years) Inclusion of PESS: Yes Female, Male The study included a subset of infants (123 male, 121 female)) from the IKIDS cohort (Champaign-Urbana, IL area) aged 7-8 months. Participants were recruited between December 2013-August 2018. Prenatal exposure to phthalates was measured in using pooled aliquots from multiple maternal urine samples during pregnancy.	ΣDINP2 (μmol/L) = the molar sum of mono-isononyl phthalate (MINP), mono-carboxyisooctyl phthalate (MCOP) in n=244 infants. Median (minimum, maximum) = 0.03884 (0.00504, 1.18001). IQR = 0.07677	Urinary ΣDiNP2 metabolites (MINP and MCOP) was associated with significant increases in average information processing speed (run duration) among infants administered set 2 images. An IQR increase in maternal urine levels of ΣDiNP2 was associated ($p<0.01$) with 0.58 (95 % CI: 0.26, 0.89) seconds longer run duration for infants who saw set 2 stimuli as familiar, but not those who saw set 1 stimuli as the familiar -0.11, 95 % CI: -0.33, 0.10), with p -interaction noted as < 0.05. ΣDINP2 was also associated with a non-significant decrease in visual recognition memory (novelty preference), suggesting poorer recognition memory. In contrast to novelty preference and run duration, prenatal exposure targeted phthalates was not associated with time to familiarization (Figs. 3C and 4 C). Comments: Results were reported within text and Figures 3 and 4 and Supplemental Table 1. Sensitivity and specificity of outcome measures uncertain.	Medium	7978460
Significant ADHD-related Behavior Problems based on parent, teacher and self-assessment by adolescents using the Behavior Assessment System for Children (BASC-2) and Conners Attention Deficit Scale (CADS) checklists. Study Design: Cross-Sectional Health Effect: Neurological/Behavioral-Attention Deficit-Hyperactivity Disorder (ADHD) related behaviors-Non-cancer	Children (2-18 years) Inclusion of PESS: Yes Female, Male 205 children in the age 15-year follow-up of the New Bedford Cohort, a study of children born near a Superfund site. The analysis included children with available urine samples for phthalates metabolites measurement.	DiNP metabolites monocarboxyoctyl phthalate (MCOP) and mono-isononyl phthalate (MNP) were assessed in one or two (70%) urine samples collected in each participant. Median (IQR) concentrations were 49.4 (26.0, 103.0) ug/L for MCOP and 1.60 (0.70, 4.30) ug/L for MNP. Specific gravity was included in models to account for urine dilution.	MNP and MCOP were not significantly associated with risk of elevated ADHD-related behaviors. Comments: See eTable 3	Medium	9419487

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Epidemiology Extraction Table:

Measured Effect/ Endpoints	Study Population	Exposure	Results	Overall Quality Determination	HERO ID
CPT-3 Block Change score Study Design: Cohort, Cross-Sectional Health Effect: Neurological/Behavioral-Conners' Continuous Performance Test, Second Edition (CPT-II) at age 6-11 years and an updated version of the Conners' CPT (CPT-3) at age 9-18 years-Non-cancer-Reproductive/Developmental-Conners' Continuous Performance Test, Second Edition (CPT-II) at age 6-11 years and an updated version of the Conners' CPT (CPT-3) at age 9-18 years-Non-cancer	Pregnant women, Children (2-18 years) Inclusion of PESS: Yes Female, Male ELEMENT (Recruitment: 1997-2004; Follow-up: 6-11 child years, 9-18 child years), Mexico, 221 mother-child pairs (longitudinal analyses); 491 mother-child pairs (cross-sectional analyses)	MCOP during adolescence, Geometric mean (GSD) 4.89 (2.81) ug/L	Significant decreases in CPT-3 Block Change scores (although lower bound of 95% CI is at null). Percent change per IQR increase (95% CI) = -1.9 (-3.9, 0). No other significant MCOP results for other ADHD measures. Comments: Figure 4, Table S6	Medium	8348423

Epidemiology Extraction Table:

Measured Effect/ Endpoints	Study Population	Exposure	Results	Overall Quality Determination	HERO ID
Overweight, obese measured at clinic visits during baseline and year 3 and 6 clinic visits. Study Design: Case-Control, Cross-Sectional Health Effect: Nutritional/Metabolic-Overweight and obesity-Non-cancer	Adults or general, Older Adults (65 years or older) Inclusion of PESS: Yes Female Women's Health Initiative: October 1, 1993-December 21, 1998 (with follow-up through 2013), United States (Alabama, Pennsylvania, Arizona), 337 female cases and 660 female controls	Mono-hydroxyisobutyl phthalate (MHiBP), mean ng/mg creatinine (95% CI)Underweight/normal: 1.44 (1.35-1.53)Overweight: 1.49 (1.38-1.61)Obese: 1.23 (1.14-1.32)	No significant results in cross-sectional analyses by quartile of exposure. Comments: Table 3, PDF page 6	Medium	5613207
Weight change measured at clinic visits during baseline and year 3 and 6 clinic visits. Phthalate metabolites measured in urine. Study Design: Case-Control, Cross-Sectional Health Effect: Nutritional/Metabolic-Weight change-Non-cancer	Adults or general, Older Adults (65 years or older) Inclusion of PESS: Yes Female Women's Health Initiative: October 1, 1993-December 21, 1998 (with follow-up through 2013), United States (Alabama, Pennsylvania, Arizona), 660 female controls	Mono-hydroxyisobutyl phthalate (MHiBP), mean ng/mg creatinine (95% CI)Underweight/normal: 1.44 (1.35-1.53)Overweight: 1.49 (1.38-1.61)Obese: 1.23 (1.14-1.32)	Weight change examined via longitudinal analysis at year 3MHiBP concentration range (ng/mL): Adjusted beta-coefficients (95% CI)0.28-0.40: Reference0.50-0.80: 0.28 (-1.06, 1.62)0.90-1.60: -0.34 (-1.71, 1.04)1.70-91.70: 1.98 (0.62, 3.33)p-trend: 0.02Non-statistically significant results at year 6. Comments: Table 4, PDF page 8	Medium	5613207

Epidemiology Extraction Table:

Measured Effect/ Endpoints	Study Population	Exposure	Results	Overall Quality Determination	HERO ID
Sex hormone levels measured in serum Oxidative stress/Inflammation measured in serumBenign prostatic hyperplasia measured using urologist diagnosis, I-PSS, urinary creatinine, uroflowmetry, DRE, and prostate biopsy Study Design: Cross-Sectional Health Effect: Reproductive/Developmental-Sex hormone levels (luteinizing hormone, follicle-stimulating hormone, sex hormone binding globulin, inhibinB, dehydroepiandrosterone, dehydroepiandrosterone sulfate, androstenedione, estrone, estradiol, total testosterone, free testosterone, dihydrotestosterone, dihydrotestosterone/total testosterone ratio, estradiol/total testosterone ratio, estradiol/estrone ratio)-Non-cancer-Other (please specify below) (Oxidative stress/Inflammation)-Oxidative stress/Inflammation (malondialdehyde, inducible nitric oxide synthetase, 8-hydroxy-2'-deoxyguanosine)-Non-cancer-Reproductive/Developmental-benign prostatic hyperplasia (prostate specific antigen, prostate volume)-Non-cancer	Adults or general, Older Adults (65 years or older) Inclusion of PESS: Yes Male elderly males from National Cheng Kung University Hospital: Taiwan, 207 elderly meals with diagnosed BPH, 2015-2017	MINP (ng/mL), geometric mean = 0.18 ng/mL	There were significant positive associations between the outcomes FSH, InhibinB, DHEA, iNOS and MINP with regression coefficients of 0.91 (CI, 0.85, 0.98), 0.90 (CI, 0.83, 0.97), 1.58 (CI, 1.40, 1.79) and 1.61 (CI, 1.29, 2.03) respectively with $P < 0.05$. Multivariate regression coefficients showed significant resuls for FHS, InhibinB, iNOS and DHEA, but showed nonsignificant results for LH, SHBG, DHEA-s, AD, E1, E2, TT, FT, DHT, MDA, 8-OHdG, PSA, and prostate volume. Comments: Table 3	Medium	5499417
Endometriosis assessed by videolaparoscopy surgery with visual inspection of the pelvis and biopsy of suspected lesions, except for 3 cases which were assessed by MRI. Controls were screened laparoscopically to rule out endometriosis. Study Design: Case-Control Health Effect: Reproductive/Developmental-Endometriosis-Non-cancer	Adults or general Inclusion of PESS: Yes Female Women aged 18-45 with and without endometriosis, study years not provided, Brazil, n=52 (30 cases, 22 controls)	MiNP (ug/g), cases, mean = 73.2 ug/g, median = 21.8 ug/g. MiNP (ug/g), controls, mean = 18.9 ug/g, median = 14.7 ug/g. Note measures of central tendency appear to be computed only among samples with values above the LOD.	Odds ratio (95% CI) for the association between MiNP and endometriosis (MiNP above versus below the median): 2.500 (0.457, 13.778). Comments: Table 3The authors did not discuss whether controls were patients with other gynecologic or reproductive disorders who were being screened to rule out a diagnosis of endometriosis. No adjustment for confounding.	Low	5432788

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Epidemiology Extraction Table:

Measured Effect/ Endpoints	Study Population	Exposure	Results	Overall Quality Determination	HERO ID
Recurrent pregnancy loss diagnosed by a physician Study Design: Case-Control Health Effect: Reproductive/Developmental-Recurrent pregnancy loss-Non-cancer	Adults or general Inclusion of PESS: Yes Female 2013-2017 Taiwanese women recruited at a hospital obstetrics and gynecology department (103 cases, 74 controls)	Median MiNP sample was below limit of detection; highest sample was 70.4 ng/mL in controls (detection rate 2.6%) and 1.43 ng/mL in cases (detection rate 2.9%).	Mann-Whitney test p-value for the difference in MiNP for cases vs. controls was not statistically significant (0.927). No multivariate analyses conducted for this metabolite.	Low	4728516
Autism Spectrum Disorder (ASD) and Non-Typical Development (Non-TD) assessed by licensed clinical psychologists using the Autism Diagnostic Observation Schedules (ADOS) and by administration of the Mullen Scales of Early Learning (MSEL). Study Design: Cohort Health Effect: Neurological/Behavioral-Autism spectrum disorder (ASD), non-typical development (Non-TD)-Non-cancer	Pregnant women, Children (2-18 years) Inclusion of PESS: Yes Female, Male MARBLES (Markers of Autism Risk in Babies – Learning Early Signs) (2007-2014), California, United States, n = 201 (boys = 122, girls = 79)	MiNP (ug/L), median = 1.1 ug/L	MiNP was not evaluated in regression models due to only 50% of samples being above the limit of detection. Comments: Tables 3, 4, 5, S9, S10, S11, S12	Uninformative	5043457

Epidemiology Extraction Table:

Measured Effect/ Endpoints	Study Population	Exposure	Results	Overall Quality Determination	HERO ID
Infant cognition at 7-8 months was measured using a visual recognition memory test with automated measures of duration or proportion of time spent looking at image sets. Outcomes included: information processing speed (run duration during familiarization trial), visual attention (time to familiarization), and visual recognition memory (novelty preference in test trial). Study Design: Cohort Health Effect: Neurological/Behavioral-Cognition at 7-8 months as assessed by information processing speed (average run duration during familiarization trial), visual attention (time to reach familiarization criterion during familiarization trial), and visual recognition memory (novelty preference in test trial) using eye tracking within a paired comparison visual recognition memory (VRM) test.-Non-cancer	Infants (birth to 2 years) Inclusion of PESS: Yes Female, Male The study included a subset of infants (123 male, 121 female)) from the IKIDS cohort (Champaign-Urbana, IL area) aged 7-8 months. Participants were recruited between December 2013-August 2018. Prenatal exposure to phthalates was measured in using pooled aliquots from multiple maternal urine samples during pregnancy. The DINP metabolite mono-oxononyl phthalate (MONP) became available after methodological improvements and was measured for 142 infants.	ΣDINP3 (μmol/L) = the molar sum of mono-isononyl phthalate (MINP), mono-carboxyisooctyl phthalate (MCOP), and mono-oxononyl phthalate (MONP) n n=142 infants. Median (minimum, maximum) = 0.02361 (0.00505, 1.18098). IQR = 0.02714MONP (ug/L). Median (minimum, maximum) = 0.00003 (0.00001, 0.00107). IQR = 0.00003	Urinary ΣDiNP3 metabolites (MINP, MCOP, and MONP) and MONP were associated with significant increases in average information processing speed (run duration) among male infants administered set 2 images. Specifically, an IQR increase in ΣDiNP3 levels was associated with 0.33 (95 % CI: 0.07, 0.74) seconds longer run duration for males in set 2, but not other strata (p-interaction <0.05). Findings suggested potential faster (better) information processing speed (run duration) in association with ΣDINP3 exposure among males in set 1, although confidence limits included the null (ß=-0.50, 95 % CI: -1.01, 0.02 seconds shorter run duration for each IQR increase in ΣDINP3). ΣDINP3 was also associated with a non-significant decrease in visual recognition memory (novelty preference) overall suggesting poorer recognition memory, while MONP was associated with a non-significant increase in novelty preference among infants administered set 2 image. Specifically, each IQR increase in urine MONP concentration was associated with a 0.003 increase in the proportion of novelty preference in infants who saw set 2 as the familiar stimuli, but confidence limits for this association were wide and included the null ((95% Confidence Interval: -0.001, 0.007).In contrast to novelty preference and run duration, prenatal exposure to relevant targeted phthalates was not significantly associated with time to familiarization (Figs. 3C and 4 C). Comments: In results text and Figures 3 and 4 and Supplemental Table 1. Sensitivity and specificity of outcome measures uncertain.	Medium	7978460

Epidemiology Extraction Table:

Measured Effect/ Endpoints	Study Population	Exposure	Results	Overall Quality Determination	HERO ID
Outcomes analyzed among cases. Sex hormones: FSH, LSH, estradiol. Study Design: Case-Control Health Effect: Reproductive/Developmental- Sex hormones: serum luteinizing hormone (LH), plasma follicle stimulating hormone (FSH), serum estradiol.-Non-cancer	Children (2-18 years) Inclusion of PESS: Yes Female cases - Turkey, Antalya City, 29 girls (4-8 years old) with premature thelarche. controls - Turkey, Antalya City, 25 healthy girls (4-8 years old).	Mean± SEM concentrations were significantly lower in controls vs cases for MOiNP and MCiOP, a marginally non-significant difference for sumDiNP, and a large but non-significant difference in MHiNP. MiNP levels were similarly low in both groups. However, the concentrations reported for individual metabolites was not consistent with the similar levels reported for the sum of DiNP/ The sum of individual metabolite means = 144.18 in controls vs. 15.66 in cases, while the sumDINP was 221.21 vs 220.81. No explanation was provided, and it is unclear whether there was a conversion or reporting error. MCiOP controls = 86.77 ug/g ± 65.48 vs. cases = 8.00 ug/g ± 1.39 (p=0.014); MHiNP controls =40.02 ug/g ± 20.20 vs. cases 4.97 ug/g ± 0.88 (p=0.021); MiNP controls = 1.94 ug/g ± SEM 1.02 vs cases = 0.51 ug/g ± 0.20 (p=0.278); MOiNP 15.45 ug/g ± 9.80 vs cases 2.18 ug/g ± 0.47. Sum DiNP controls 287.39 ug/g ± 47.19 vs. cases 284.60 ± 41.35 ug/g (p=0.051). Follicle stimulating hormone, leutenizing hormone, estradiol.	Spearman correlations with sex hormone levels were positive and significant for MCiOP, but otherwise generally weak and non-significant. MCiOP. -FSH levels: significant positive correlation (rho = 0.334, p = 0.048). -LH levels weak correlation (rho = 0.013, p = 0.899). –Estradiol levels weak correlation (rho = 0.185, p = 0.157).MiNP. FSH levels weak correlation (rho = -0.167, p = 0.114) -LH levels weak correlation (rho = -0.068, p = 0.921). -Estradiol levels weak correlation (rho = -0.009, p = 0.994).MHiNP. FSH levels weak correlation HiNP (rho = 0.228, p = 0.161) -LH levels weak correlation (rho = 0.106, p = 0.085).-Estradiol levels weak correlation (rho = 0.025, p = 0.889).MOiNP. FSH levels weak correlation (rho = 0.113, p = 0.089) -LH levels weak correlation (rho = 0.097, p = 0.091).-Estradiol levels weak correlation (rho = 0.148, p = 0.101).sum DiNP. FSH levels weak correlation (rho = 0.114, p = 0.964) -LH levels weak correlation (rho = 0.102, p = 0.951).-Estradiol levels weak correlation (rho = -0.093, p = 0.077).	Low	5512126

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Epidemiology Extraction Table:

Measured Effect/ Endpoints	Study Population	Exposure	Results	Overall Quality Determination	HERO ID
Physical markers of reproductive development: uterine volume, ovarian volumes, public hair growth. Study Design: Case-Control Health Effect: Reproductive/Developmental-Ovary and uterus volumes; pubic hair growth-Non-cancer	Children (2-18 years) Inclusion of PESS: Yes Female cases - Turkey, Antalya City, 29 girls (4-8 years old) with premature thelarche. controls - Turkey, Antalya City, 25 healthy girls (4-8 years old).	Mean± SEM concentrations were significantly lower in controls vs cases for MOiNP and MCiOP, a marginally non-significant difference for sumDiNP, and a large but non-significant difference in MHiNP. MiNP levels were similarly low in both groups. However, the concentrations reported for individual metabolites was not consistent with the similar levels reported for the sum of DiNP/ The sum of individual metabolite means = 144.18 in controls vs. 15.66 in cases, while the sumDINP was 221.21 vs 220.81. No explanation was provided, and it is unclear whether there was a conversion or reporting error. MCiOP controls = 86.77 ug/g ± 65.48 vs. cases = 8.00 ug/g ± 1.39 (p=0.014); MHiNP controls =40.02 ug/g ± 20.20 vs. cases 4.97 ug/g ± 0.88 (p=0.021); MiNP controls = 1.94 ug/g ± SEM 1.02 vs cases = 0.51 ug/g ± 0.20 (p=0.278); MOiNP 15.45 ug/g ± 9.80 vs cases 2.18 ug/g ± 0.47. Sum DiNP controls 287.39 ug/g ± 47.19 vs. cases 284.60 ± 41.35 ug/g (p=0.051).	Spearman correlations with uterine volumes, ovarian volume and pubic hair growth varied but were largely negative, with some significant values. MCiOP. Uterus volume levels had a weak negative correlation (rho = -0.219, p = 0.064), right ovary volume levels negative weak correlation (rho = -0.128, p = 0.091), left ovary volume levels negative weak correlation (rho = -0.154, p = 0.101), pubic hair growth had a significant positive correlation (rho = 0.440, p = 0.002)MiNP. uterus volume levels weak correlation (rho = -0.168, p = 0.084), right ovary volume levels weak correlation (rho = 0.038, p = 0.897). left ovary volume levels weak correlation (rho = 0.074, p = 0.896). pubic hair growth had a significant positive correlation (rho = 0.480, p = 0.000). MHiNP. uterus volume levels weak correlation (rho = 0.091, p = 0.070), right ovary volume levels weak correlation (rho = -0.203, p = 0.142), left ovary volume levels weak correlation (rho = -0.242, p = 0.067). pubic hair growth had a positive non-significant correlation (rho = 0.126, p = 0.084). MOiNP. uterus volume levels weak correlation (rho = -0.112, p = 0.075), right ovary volume levels weak correlation (rho = -0.118, p = 0.089), left ovary volume levels weak correlation (rho = -0.149, p = 0.086). pubic hair growth had a positive non-significant correlation (rho = 0.184, p = 0.101). sumDINP. uterus volume levels weak correlation (rho = -0.132, p = 0.099), right ovary volume levels weak correlation (rho = -0.156, p = 0.079), left ovary volume levels weak correlation (rho = -0.149, p = 0.086). pubic hair growth had a negative non-significant correlation (rho = -0.351, p = 0.052).	Low	5512126

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Epidemiology Extraction Table:

Measured Effect/ Endpoints	Study Population	Exposure	Results	Overall Quality Determination	HERO ID
Thyroid hormones: TSH and free T4 Study Design: Case-Control Health Effect: Thyroid-Serum thyroid stimulating hormone (TSH) and serum free T4 (fT4)-Non-cancer	Children (2-18 years) Inclusion of PESS: Yes Female cases - Turkey, Antalya City, 29 girls (4-8 years old) with premature thelarche. controls - Turkey, Antalya City, 25 healthy girls (4-8 years old).	Mean± SEM concentrations were significantly lower in controls vs cases for MOiNP and MCiOP, a marginally non-significant difference for sumDiNP, and a large but non-significant difference in MHiNP. MiNP levels were similarly low in both groups. However, the concentrations reported for individual metabolites was not consistent with the similar levels reported for the sum of DiNP/ The sum of individual metabolite means = 144.18 in controls vs. 15.66 in cases, while the sumDINP was 221.21 vs 220.81. No explanation was provided, and it is unclear whether there was a conversion or reporting error. MCiOP controls = 86.77 ug/g ± 65.48 vs. cases = 8.00 ug/g ± 1.39 (p=0.014); MHiNP controls =40.02 ug/g ± 20.20 vs. cases 4.97 ug/g ± 0.88 (p=0.021); MiNP controls = 1.94 ug/g ± SEM 1.02 vs cases = 0.51 ug/g ± 0.20 (p=0.278); MOiNP 15.45 ug/g ± 9.80 vs cases 2.18 ug/g ± 0.47. Sum DiNP controls 287.39 ug/g ± 47.19 vs. cases 284.60 ± 41.35 ug/g (p=0.051). Thyroid stimulating outcome, free T4	Thyroid hormone levels had largely negative Spearman correlations with DiNP metabolites; a few reached significance. MCiOP. TSH levels had a non-significant negative correlation (rho = -0.322, p = 0.055), fT4 levels had a significant negative correlation with MCiOP (rho = -0.335, p = 0.041). MiNP. TSH levels had a non-significant negative correlation (rho = -0.222, p = 0.911), fT4 levels had a non-significant positive correlation (rho = 0.119, p = 0.084)MHiNP. TSH levels had a non-significant positive correlation (rho = -0.028, p = 0.902), fT4 levels had a non-significant negative correlation (rho = -0.282, p = 0.065)MOiNP. TSH levels had a non-significant negative correlation (rho = -0.218, p = 0.067), fT4 levels had a non-significant negative correlation (rho = -0.028, p = 0.917)sumDiNP. TSH levels had a significant negative correlation (rho = -0.327, p = 0.048), fT4 levels had a non-significant negative correlation (rho = -0.021, p = 0.931)	Medium	5512126

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Epidemiology Extraction Table:

Measured Effect/ Endpoints	Study Population	Exposure	Results	Overall Quality Determination	HERO ID
BMI and weight Study Design: Case-Control Health Effect: Nutritional/Metabolic-Body weight, BMI-Non-cancer	Children (2-18 years) Inclusion of PESS: Yes Female cases - Turkey, Antalya City, 29 girls (4-8 years old) with premature thelarche. controls - Turkey, Antalya City, 25 healthy girls (4-8 years old).	Mean± SEM concentrations were significantly lower in controls vs cases for MOiNP and MCiOP, a marginally non-significant difference for sumDiNP, and a large but non-significant difference in MHiNP. MiNP levels were similarly low in both groups. However, the concentrations reported for individual metabolites was not consistent with the similar levels reported for the sum of DiNP/ The sum of individual metabolite means = 144.18 in controls vs. 15.66 in cases, while the sumDINP was 221.21 vs 220.81. No explanation was provided, and it is unclear whether there was a conversion or reporting error. MCiOP controls = 86.77 ug/g ± 65.48 vs. cases = 8.00 ug/g ± 1.39 (p=0.014); MHiNP controls =40.02 ug/g ± 20.20 vs. cases 4.97 ug/g ± 0.88 (p=0.021); MiNP controls = 1.94 ug/g ± SEM 1.02 vs cases = 0.51 ug/g ± 0.20 (p=0.278); MOiNP 15.45 ug/g ± 9.80 vs cases 2.18 ug/g ± 0.47. Sum DiNP controls 287.39 ug/g ± 47.19 vs. cases 284.60 ± 41.35 ug/g (p=0.051).	Spearman correlations between DiNP phthalate metabolites and BMi and weight were generally positive and significant. MCiOP. weight levels had a significant positive correlation with MCiOP (rho = 0.754, p = 0.000) BMI levels had a significant positive correlation with MCiOP (rho = 0.606, p = 0.000)MiNP weight levels had a significant positive correlation (rho = 0.426, p = 0.025) BMI levels had a significant positive correlation (rho = 0.416, p = 0.022)MHiNP. weight levels had a significant positive correlation (rho = 0.671, p = 0.000) BMI levels had a significant positive correlation (rho = 0.565, p = 0.000)MOiNP. weight levels had a significant positive correlation (rho = 0.709, p = 0.000) BMI levels had a significant positive correlation (rho = 0.703, p = 0.000)sumDiNP. weight levels had a significant positive correlation (rho = 0.426, p = 0.328); looks like a typo in table this p-value has an asteriskBMI levels had a significant positive correlation (rho = 0.551, p = 0.003)	Low	5512126

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Epidemiology Extraction Table:

Measured Effect/ Endpoints	Study Population	Exposure	Results	Overall Quality Determination	HERO ID
BMI and weight Study Design: Case-Control Health Effect: Reproductive/Developmental-Premature thelarche (isolated breast development in girls aged 4-8 years)-Non-cancer	Children (2-18 years) Inclusion of PESS: Yes Female cases - Turkey, Antalya City, 29 girls (4-8 years old) with premature thelarche. controls - Turkey, Antalya City, 25 healthy girls (4-8 years old).	Mean± SEM concentrations (as ug/g creatinine) were significantly lower in controls vs cases for MOiNP and MCiOP, a marginally non-significant difference for sumDiNP, and a large but non-significant difference in MHiNP. MiNP levels were similarly low in both groups. However, the concentrations reported for individual metabolites was not consistent with the similar levels reported for the sum of DiNP/ The sum of individual metabolite means = 144.18 in controls vs. 15.66 in cases, while the sumDINP was 221.21 vs 220.81. No explanation was provided, and it is unclear whether there was a conversion or reporting error. MCiOP controls = 86.77 ug/g ± 65.48 vs. cases = 8.00 ug/g ± 1.39 (p=0.014); MHiNP controls =40.02 ug/g ± 20.20 vs. cases 4.97 ug/g ± 0.88 (p=0.021); MiNP controls = 1.94 ug/g ± SEM 1.02 vs cases = 0.51 ug/g ± 0.20 (p=0.278); MOiNP 15.45 ug/g ± 9.80 vs cases 2.18 ug/g ± 0.47. Sum DiNP controls 287.39 ug/g ± 47.19 vs. cases 284.60 ± 41.35 ug/g (p=0.051).	Analyses were limited to describing unadjusted differences in DiNP metabolites in cases vs controls. There were significantly higher concentrations reported for in controls vs cases for two of the four DiNP metabolites. However, as noted and shown above, the values reported for individual DiNP metabolites were not consistent with values reported for the sum of the metabolites.	Low	5512126

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Epidemiology Extraction Table:

Measured Effect/ Endpoints	Study Population	Exposure	Results	Overall Quality Determination	HERO ID
Allergic disease outcomes measured using a Danish modified version of the International Study of Asthma and Allergies in Childhood questionnaire. Asthma measures were self-reported asthma, wheeze, doctor-diagnosed asthma, and use of medicine for asthma/cold. Eczema measures were self-reported eczema, doctor-diagnosed eczema, and use of medicine for eczema. Rhinitis measure was self-reported rhinitis. Study Design: Cohort Health Effect: Lung/Respiratory-Asthma, Rhinitis, Wheeze-Non-cancer-Immune/Hematological-Eczema-Non-cancer	Children (2-18 years) Inclusion of PESS: Yes Female, Male Odense Child Cohort (OCC): 2010-2012, Denmark, n=552 mother-child pairs with third trimester urinary phthalate metabolite measures and information about age 5 asthma, eczema and rhinitis.	DiNP metabolites were mono-iso-nonyl phthalate MiNP, mean = 1.2 ng/mL, median = <LOD (maximum 135.5 ng/mL, 88.4% <LOD); mono-oxo-iso-nonyl phthalate MOiNP, mean = 5.0 ng/mL, median = 1.1 ng/mL (25th-75th percentile: 0.45-2.5 ng/mL), mono-hydroxy-iso-nonyl phthalate MHiNP, mean = 9.4 ng/mL, median = 1.6 ng/mL (25th- 5th percentile: 0.78-3.8 ng/mL), and mono-carboxy-iso-octyl phthalate MCiOP, mean = 13.3 ng/mL, median = 3.7 ng/mL (25th-75th percentile: 1.8-7.5 ng/mL). Metabolites were summed as a measure of DiNP, mean = 38.1 ng/mL, median = 8.5 ng/mL (25th-75th percentile: 4.3-18.3 ng/mL).	The authors reported no significant associations in multivariate logistic regression between relevant prenatal phthalate exposure and asthma, rhinitis and wheeze. The odds ratio from logistic regression of eczema when doubling the sum of DiNP metabolites was marginally significant at 1.24 (95% CI 1.00, 1.55). Comments: Table 6	Medium	7975862