MANUFACTURER REQUEST FOR RISK EVALUATION
DIISONONYL PHTHALATE (DINP)

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Office of Pollution Prevention and Toxics (OPPT)
Environmental Protection Agency
1200 Pennsylvania Ave., NW
Washington, DC 20460-0001

Background

The American Chemistry Council's High Phthalates Panel (ACC HPP) represents major manufacturers, importers, and users of DINP, DIDP, and other high molecular weight phthalates. Pursuant to Section 6(b)(4)(C)(ii) of the Toxic Substances Control Act (TSCA) and 40 C.F.R. Section 702.37, Evonik Corporation, ExxonMobil Chemical Company, and Teknor Apex ("the manufacturers"), through the ACC High Phthalates Panel, formally request that the Agency conduct a risk evaluation of diisononyl phthalate (DINP), represented by the two Chemical Abstracts Service Registry Numbers (CASRNs) 28553-12-0 and 68515-48-0. This document and Appendices A-C provide the information to be submitted as set forth in §702.37(b).[1]

Contact information of entity submitting the request

The High Phthalates Panel is comprised of companies that manufacture, compound, convert, or import certain high molecular weight phthalates.[2]

Substance identity

The chemical identity of DINP is provided in Appendix A. Tables 1-3 of Appendix A include reasonably known names of the chemical substance, including common or trade names and CASRNs. Structures for each CASRN are also provided in figures 1 and 2 of Appendix A. As noted previously, this substance is represented by two CASRNs. CASRN 28553-12-0 (DINP-2) is manufactured by esterification of phthalic anhydride with alcohol groups made from n-butene (predominantly C9 methyl octanols and dimethyl heptanols). It predominantly contains C_9H_{19} isomers as alkyl side chains. CASRN 68515-48-0 (DINP-1) is manufactured by esterification of phthalic anhydride with alcohol groups made from octene (>95% comprise roughly equal amounts of 3,4-, 3,5-, 3,6-, 4,5-, 4,6-, and 5,6- dimethyl heptan-1-ols). It contains a distribution of C_8H_{17} to $C_{10}H_{21}$ isomers, where C_9H_{19} alkyl chains are predominant (>70%). As discussed in Appendix A, a third type of DINP, DINP-3, was manufactured with alcohol groups from n-butene and iso-butene, resulting in higher proportions of branched methyl ethyl hexanols than other types of DINP. DINP-3 has not been in commercial production or use since 1995 and is not considered relevant to this request.

As described in Appendix A, reviewing agencies, including the European Chemicals Bureau/Chemicals Agency (ECHA), Australia NICNAS and Environment Canada/Health Canada, have considered the two CASRNs (specifically DINP-1 and DINP-2) to be toxicologically equivalent and have evaluated them as a single substance. Hence, this request is to evaluate the risk of both CASRNs as a single substance. For the purpose of this request, the term "DINP" refers to DINP-1 and/or DINP-2.

[1] Unless otherwise indicated, all section citations are to 40 C.F.R.
[2] See https://phthalates.americanchemistry.com/About-Us/

Conditions of use requested for evaluation

The Agency defines conditions of use as "circumstances, as determined by the Administrator, under which a chemical substance is intended, known, or reasonably foreseen to be manufactured, processed, distributed in commerce, used or disposed of." §702.33. The uses of DINP are summarized in Appendix B. Both European Union and American sources are cited, as DINP uses are essentially the same in both regions. The primary intended, known or reasonably foreseen use of DINP (>90%) is as a plasticizer to impart flexibility to polyvinyl chloride (PVC) in consumer and industrial applications.[3, 4, 5, 6, 7] These applications include wire and cable jacketing, building and construction (vinyl tiles, resilient flooring, PVC-backed carpeting, roofing, wall coverings, etc.), automotive (window glazing, doors, acrylic plastisol sealants in wheel wells, underbody coatings and paints), vinyl clothing (raincoats and boots, gloves, etc.), tool handles, flexible tubes, profiles, and hoses. Approximately 5% of DINP is used in non-PVC applications such as rubber polymers, inks and pigments, adhesives, sealants, and paints. This list of uses is consistent with those identified for DINP in existing European Union (EU) REACH registrations (see Appendix C of this request for links to EU REACH registration dossiers for DINP). These uses mirror those reported in the US EPA's 2016 Chemical Data Reporting (CDR) database for CAS numbers 28553-12-0 and 68515-48-0. According to the CDR data, CAS numbers 28553-12-0 and 68515-48-0 are reported for use in industrial, commercial, and consumer applications. Primary uses include incorporation into article, formulation, mixture, or reaction product as a plasticizer (for manufacturing of plastic materials and resins), use as an adhesive and sealant chemical, paint and coating manufacturing, synthetic rubber manufacturing, furniture and furnishings, floor coverings, fabric, textile and leather products, building and construction materials, electrical and electronic products, and automotive care products.

The manufacturers, through the ACC HPP, request that the following uses be evaluated under the risk evaluation of DINP:

- DINP Manufacturing
- DINP use as a general purpose plasticizer for PVC used in the following applications;
    - Building and construction – wire and cable jacketing, vinyl tiles, resilient flooring, PVC-backed carpeting, wall coverings, roofing, pool applications, etc.
    - Automotive – window glazing, wire and cable jacketing, underbody coatings, doors, acrylic plastisol sealants, windshield adhesive, etc.
    - Other consumer applications – vinyl clothing (raincoats, boots, gloves), tool handles, flexible tubes, hoses and profiles, etc.
    - Non-PVC applications – inks and pigments, adhesives, sealants, and paints.

[3] American Chemistry Council (ACC) (2018). Phthalates: High phthalates uses and applications. https://phthalates.americanchemistry.com/High-Uses-and-Applications.html

[4] IHS Markit. (2018). Chemical Economics Handbook: Plasticizers, pp. 42. 4 May 2018.

[5] European Plasticisers (2018). Plasticisers Information Center: Orthophthalates. https://www.plasticisers.org/plasticisers/orthophthalates/

[6] European Chemicals Bureau (2003). European Union Risk Assessment Report, 1,2-benzenedicarboxylic acid, di-C8-10-branched alkyl esters, C9-rich and di-"isononyl" phthalate (DINP) (68515-48-0 & 28553-12-0), pp.26-28. 2nd Priority List Volume 35 Report 046, https://echa.europa.eu/documents/10162/8fa0a07f-ec2a-4da6-bbe8-5b5e071b5c16.

[7] European Chemicals Agency (ECHA). 2013. Evaluation of new scientific evidence concerning DINP and DIDP in relation to entry 52 of Annex XVII to REACH Regulation (EC) No 1907/2006. August 2013, pp. 21-28. https://echa.europa.eu/documents/10162/31b4067e-de40-4044-93e8-9c9ff1960715.

- Use in PVC for children's toys and childcare articles – although DINP is currently restricted in children's toys and childcare articles,[8] the manufacturers, through the ACC HPP request that potential DINP exposure of children from toys and childcare articles be evaluated, consistent with the Agency's stated concerns in the USEPA 2012 Phthalate Action Plan.[9]

Information relevant to the risk evaluation of DINP

TSCA requires EPA to conduct risk evaluations to determine whether there is unreasonable risk to humans or the environment using the best available science and weight of the scientific evidence.[10] The definition of weight of the scientific evidence adopted by EPA states:

> "Weight of the scientific evidence means a systematic review method, applied in a manner suited to the nature of the evidence or decision, that uses a pre-established protocol to comprehensively, objectively, transparently, and consistently identify and evaluate each stream of evidence, including strengths, limitations, and relevance of each study and to integrate evidence as necessary and appropriate based upon strengths, limitations, and relevance."[11]

These scientific standards apply to manufacturer requests for risk evaluation and any request must include all the existing information relevant to the risk evaluation.[12] Specifically,

> "The request must also include a list of all the existing information that is relevant to whether the chemical substance, under the circumstances identified by the manufacturer(s), presents an unreasonable risk of injury to health or the environment. The list must be accompanied by an explanation as to why such information is adequate to permit EPA to complete a risk evaluation addressing the circumstances identified by the manufacturer(s), The request need not include copies of the information; citations are sufficient, if the information is publically [sic] available. The request must include or reference all available information on the health and environmental hazard(s) of the chemical substance, human and environmental exposure(s), and exposed population(s), as relevant to the circumstances identified in the request."[13]

To provide EPA with "all existing information that is relevant" to conduct the manufacturer requested risk evaluation, an extensive literature search was conducted. Appendix C details the protocol used to comprehensively, objectively, transparently, and consistently identify relevant information in several databases. The process used comports with the requirements specified by EPA for a weight of the

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[8] US Consumer Product Safety Commission (CPSC). Prohibition of Children's Toys and Child Care Articles Containing Specified Phthalates. 82 Fed. Reg. 49938, 49982 (Oct. 27, 2017), https://www.gpo.gov/fdsys/pkg/FR-2017-10-27/pdf/2017-23267.pdf, codified at 16 C.F.R. § 1307.3(b). "Children's toy" is defined as a consumer product designed or intended by the manufacturer for a child 12 years of age or younger for use by the child when the child plays" and "child care article" is defined as "a consumer product designed or intended by the manufacturer to facilitate sleep or the feeding of children age 3 and younger, or to help such children with sucking or teething." 16 C.F.R. § 1307.2.

[9] US EPA, Phthalates Action Plan (Mar. 14, 2012 revision), pp. 8 & 12, https://www.epa.gov/sites/production/files/2015-09/documents/phthalates_actionplan_revised_2012-03-14.pdf [hereafter "2012 Action Plan"].

[10] 15 U.S.C. 2625(h) and (i); defined at 40 C.F.R. Part 702.33

[11] 40 CFR Part 702.33

[12] 40 CFR Part 702

[13] Environmental Protection Agency; Procedures for Chemical Risk Evaluation Under the Amended Toxic Substances Control Act, 82 Fed. Reg. 33,749 (July 20, 2017)(codified at 40 C.F.R. Pt. 702.37).

scientific evidence review method and meets the requirements for submission of a manufacturer requested risk evaluation under 40 CFR Part 702.37.

Specifically, Appendix C contains bibliographic citations to publicly available information that is relevant to whether DINP, under the circumstances identified above, presents an unreasonable risk of injury to health or the environment. We note that DINP (and phthalates in general) has been the subject of considerable academic and regulatory interest for several decades. Thus, while the list in Appendix C is robust, it does not necessarily represent all existing hazard and exposure information on DINP. Nevertheless, it does include all the existing information that is relevant to whether DINP, under the conditions of use noted herein, presents an unreasonable risk of injury to health or the environment, including the following: information on the hazard and exposure potential of DINP, information on the persistence and bioaccumulation of DINP, information on potentially exposed or susceptible subpopulations relevant to the EPA risk evaluation, information on the potential for storage near significant sources of drinking water, and information on DINP production volumes. The manufacturers, through the ACC HPP, believe that having provided all the existing information listed above, such information is more than adequate for EPA to conduct a thorough risk evaluation addressing the conditions of use we have identified. Additionally, we note that the US EPA, under the Integrated Risk Information System (IRIS), had identified studies that it deemed relevant to a proposed toxicological review of DINP in 2014. A link to the draft materials collected by the Agency is provided in Appendix C. The following provides an overview of the information referenced in Appendix C.

Information relevant to the human health hazard potential of DINP –

In its 2012 Phthalates Action Plan and 2014 update to the TSCA Work Plan,[14] the Agency indicated that the critical endpoint of concern for DINP is developmental toxicity (hazard score of 2 – "moderate" assigned). In addition, in the 2012 Action Plan, the Agency indicated that it intended to consider results of risk evaluations being conducted by the US Consumer Product Safety Commission (CPSC), the FDA, and the Agency's IRIS program to inform the extent of any future TSCA Section 6 action addressing the listed phthalates, including DINP.[15]

The most relevant information sources, with respect to the reproductive/developmental hazard and risk assessment of DINP, are the recently completed regulatory risk evaluations from the European Union (2003, 2013 and 2018), US CPSC (1998, 2001 and 2017), Environment Canada and Health Canada (2015 and 2017) and the Australian National Industrial Chemicals Notification and Assessment Scheme (NICNAS) (2012). References to these risk evaluations are available on page 2 of Appendix C.

US CPSC –

In 2017, the CPSC concluded that DINP in isolation does not pose a risk to children, pregnant women or other susceptible individuals with an adequate margin of safety.[16] This supports a 2001 conclusion by the CPSC's Chronic Hazard Advisory Panel (CHAP) that "the risk to reproductive and developmental processes in humans due to DINP exposure is extremely low or non-existent",[17] following the draft (later

[14] 2012 Action Plan, note 9, pp. 1 & 4; TSCA Work Plan for Chemical Assessments: 2014 Update, p. 12, https://www.epa.gov/assessing-and-managing-chemicals-under-tsca/tsca-work-plan-chemical-assessments-2014-update [hereafter "2014 Work Plan"].

[15] 2012 Action Plan, note 9, pp. 10-11 ("Next Steps").

[16] CPSC Phthalate Rule, note 8, 82 Fed. Reg. at 49963.

[17] Consumer Product Safety Commission (CPSC). 2001. Report to the US Consumer Product Safety Commission by the Chronic Hazard Advisory Panel on DINP, cover letter and pages 53-58, Bethesda, MD: U.S. Consumer Product Safety Commission. https://cpsc.gov/s3fs-public/pdfs/dinp.pdf.

final) conclusion of the National Toxicology Program (NTP) Center for the Evaluation of Risks to Human Reproduction (CERHR) that there was "minimal risk" of developmental or reproductive effects from current exposure levels.[18] Subsequently, the US CPSC evaluated the cumulative risk of DINP exposure (combined with DIBP, BBP, DBP and DEHP) in women of reproductive age, using data from the National Health and Nutrition Examination Survey (NHANES).[19, 20] Using actual, experimental hazard data for DINP, and looking at the 95th percentile, the cumulative risk of the five phthalates was a hazard index (HI) of 0.4 or less for all biomonitoring data after 2008, well below the level of concern (HI>1.0).[21] For DINP itself, the risk was a hazard quotient (HQ) less than 0.2 at the 95th percentile, well below the level of concern (HQ>1.0).[22] Overall, these data provide adequate confidence that DINP poses no reproductive or developmental toxicity risk to the most susceptible populations, children or women of reproductive age.

European Union –

The European Union (EU) conducted a comprehensive risk assessment on DINP, published in 2003, covering the range of human health hazard endpoints.[23] Since 2003, the EU has published two additional detailed risk evaluations of DINP, including a hazard evaluation to determine whether there is sufficient evidence to classify DINP for reproductive/developmental effects.[24, 25] Both the 2003 and 2013 risk evaluations concluded that there was no need for further testing or risk mitigation with respect to exposure to DINP for workers and consumers.[26] The ECHA 2013 report evaluated the risk of exposure to DINP for children and adults from several uses including toys and childcare articles (e.g. school supplies), skinny vinyl leather pants (assuming these are worn 10 hours/day for 2 weeks per month by pregnant women), indoor air, house dust and food.[27] The EU report found no reproductive toxicity risk with DINP exposure in any of the uses evaluated.[28] In 2018, the European Chemicals Agency (ECHA) Risk Assessment Committee (RAC) concluded its 3-year evaluation of the animal and

[18] National Toxicology Program. 2003. NTP-CERHR Monograph on the Potential Human Reproductive and Developmental Effects of Di-isononyl Phthalate (DINP). NIH Publication No. 03-4484. NTP conclusions are summarized on pages 2 – 3 of the report. https://ntp.niehs.nih.gov/ntp/ohat/phthalates/dinp/dinp_monograph_final.pdf.

[19] Consumer Product Safety Commission. 2015. Estimated Phthalate Exposure and Risk to Pregnant Women and Women of Reproductive Age as Assessed Using Four NHANES Biomonitoring Data Sets (2005/2006, 2007/2008, 2009/2010, 2011/2012). https://www.cpsc.gov/s3fs-public/NHANES-Biomonitoring-analysis-for-Commission.pdf [hereafter "CPSC 2015"].

[20] Consumer Product Safety Commission. 2017. Estimated Phthalate Exposure and Risk to Women of Reproductive Age as Assessed Using 2013 2014 NHANES Biomonitoring Data. https://www.cpsc.gov/s3fs-public/Estimated%20Phthalate%20Exposure%20and%20Risk%20to%20Women%20of%20Reproductive%20Age%20as%20Assessed%20Using%202013%202014%20NHANES%20Biomonitoring%20Data.pdf [hereafter "CPSC 2017"].

[21] CPSC 2015, note 19, p. 13 (Table 6); CPSC 2017, note 20, p. 4 (Table 5). Note – Case 2 represents read-across modeled data rather than actual toxicological data on DINP which forms the basis for Cases 1 and 3.

[22] CPSC 2015, note 19, p. 16 (Figure 7); CPSC 2017, note 20, p. 3 (Table 3).

[23] European Chemicals Bureau. 2003. European Union Risk Assessment Report on 1, 2-benzenedicarboxylic acid, di-C8-10-branched alkyl esters, C9-rich and di-"isononyl" phthalate (DINP). https://echa.europa.eu/documents/10162/83a55967-64a9-43cd-a0fa-d3f2d3c4938d [hereafter "ECB 2003"].

[24] European Chemicals Agency. 2013. Evaluation of new scientific evidence concerning DINP and DIDP in relation to entry 52 of Annex XVII to REACH Regulation (EC) No 1907/2006. August 2013. https://echa.europa.eu/documents/10162/31b4067e-de40-4044-93e8-9c9ff1960715 [hereafter ECHA 2013].

[25] European Chemicals Agency Committee for Risk Assessment. 2018. Opinion proposing harmonised classification and labelling at EU level of 1,2-Benzenedicarboxylic acid, di-C8-10-branched alkylesters, C9- rich; [1]di-"isononyl" phthalate; [2] [DINP]. CLH-O-0000001412-86-201/F. 9. March 2018. https://echa.europa.eu/documents/10162/56980740-fcb6-6755-d7bb-bfe797c36ee7 [hereafter "RAC 2018"].

[26] ECB 2003, note 23, pp. IX & 259; ECHA 2013, note 24, pp. 7-8.

[27] ECHA 2013, note 24, pp. 267-276.

[28] Id., Tables 4.90, 4.93, 4.99, 4.105, 4.111, and 4.116.

epidemiological data on DINP, announcing that "no classification for DINP for either effects on sexual function and fertility, or for developmental toxicity is warranted."[29]

Australia NICNAS –

In 2012, the Australian NICNAS published a detailed hazard and risk assessment of DINP exposure through the use of plastic toys and childcare articles.[30] For its assessment, NICNAS identified three critical health effects observed in rodents: repeated-dose toxicity (increased liver and kidney weights with histopathological findings in the liver), fertility-related parameters (reduced testicular testosterone and altered sexual differentiation) and developmental toxicity (reduced pup weight).[31] NICNAS concluded that the data indicated an adequate safety margin even in the reasonable worst-case scenario.[32] This report is the basis for the current lack of a restriction for DINP in children's toys and childcare articles in Australia.[33]

Environment Canada and Health Canada –

Environment Canada and Health Canada conducted a detailed risk evaluation of DINP.[34] The report identified several critical endpoints for the risk evaluation including carcinogenicity (hepatocellular tumors), non-cancer liver effects in male and female rats (with the lowest NOAEL of 15-18 mg/kg bw/d) and developmental effects in the male reproductive system (occurring at higher doses compared to liver lesions)).[35] [36] Several sources of DINP exposure for the general population were identified, including food, dust, contact with PVC articles, and mouthing PVC toys and articles.[37] Table 9-21 of the Canada report summarizes the margins of exposure (MOE) estimates for subpopulations with the highest exposures to DINP.[38] Using the lowest NOAEL identified (15 mg/kg bw/day based on non-cancer liver effects in rats), the report concluded that comparison of upper-bound estimate of exposure to DINP (from environmental media and food) for infants and children 6 months to 4 years of age resulted in MOEs ranging from 500 – 8333.[39] With infants 0-18 months of age mouthing plastic toys and articles containing DINP, an upper-bound MOE of 125 was determined.[40] Comparisons of upper-bound estimates from dermal exposure to DINP from various PVC items for infants 0-18 months of age

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[29] RAC 2018, note 25, p. 32.

[30] Australian Government National Industrial Chemicals Notification and Assessment Scheme. 2012. Diisononyl Phthalate. Priority Existing Chemical Assessment Report No. 35. September 2012. https://www.nicnas.gov.au/__data/assets/word_doc/0008/34838/PEC35-DINP.docx [hereafter "NICNAS 2012"].

[31] Id. pp. 52-53.

[32] Id., p. 55 (Table 8.2). Note that, unlike other reviewers, NICNAS did not base its no observed effect level on spongiosis hepatis, noting that it "is a spontaneous, chronic liver lesion of ageing" with "no comparable lesion type in humans." Id. at 48.

[33] Australia NICNAS Chemical Information Factsheet on DINP. https://www.nicnas.gov.au/chemical-information/factsheets/chemical-name/diisononyl-phthalate-dinp. See section on "Recommendations".

[34] Environment Canada and Health Canada State of the Science Report. 2015. Phthalate Substance Grouping: 1, 2-Benzenedicarboxylic acid, diisononyl ester 1, 2-Benzenedicarboxylic acid, di-C8-10-branched alkyl esters, C9-rich (Diisononyl Phthalate; DINP). http://ec.gc.ca/ese-ees/47F58AA5-57BE-4869-A128-587DEADCAAD8/SoS_Phthalates%20%28DINP%29_EN.pdf [hereafter "Canada 2015"]. See also Environment Canada and Health Canada. 2017. Draft Screening Assessment Phthalate Substance Grouping: Sections 9 and 10. http://www.ec.gc.ca/ese-ees/default.asp?lang=En&n=1E5B3C8F-1 [hereafter "Canada 2017"].

[35] Canada 2015, note 34, pp. iii-iv & 96.

[36] Canada discussed the carcinogenicity data, id. at 95-96, concluding: "There is uncertainty associated with the mode of induction of tumors. Postulated modes of action have been identified for some tumor-types, but they have not been fully elucidated." Id. at 100. Canada found the margins of exposures adequate with respect to tumors. Id. at 98-99.

[37] Id. pp. 97-98 (Table 9-21).

[38] Id.

[39] Id. p. 97, see Table 9-21.

[40] Id.

resulted in an upper-bound MOE of 1744.[41] For males aged 20+ years of age and children aged 6-11, the report estimated MOEs ranging from 577-625 using the 95th percentile of biomonitoring data.[42] Canada also evaluated the risk associated with in-utero developmental effects in pregnant women. Using NOAELs identified for decreased pup weights as well as decreased testicular testosterone and testicular pathology in male pups, MOEs ≥2173 were estimated.[43] Overall, Canada concluded that the MOEs were adequate to indicate no concern for risk with DINP exposure.[44]

Environment Canada/Health Canada also reviewed available epidemiological literature on the potential effects of DINP exposure in humans.[45] With respect to the potential for reproductive and developmental toxicity, all cross-sectional, case-control and cohort studies identified were scored for quality using a consistent evaluation metric that designates the each level of evidence for association as sufficient, limited, inadequate, or evidence suggesting no association.[46] Canada noted that the evaluation did not consider the biological plausibility of the relationship (i.e. no causal inference was established).[47] Overall, no sufficient evidence was established for an association with DINP exposure and any reproductive/developmental parameter in humans.[48] No associations were found for birth measures, gestational age, reproductive endpoints such as gynecomastia and time to pregnancy and male infant genitalia effects.[49] There was inadequate evidence for associations with DINP and female puberty and semen parameters (sperm volume, sperm motility etc.).[50] Canada concluded that there was limited evidence for associations of mono-isononyl phthalate (MINP),[51] a metabolite of DINP, with sex hormones in infants and adult males.[52] Regarding epidemiological data on other systemic effects, Canada concluded that there was inadequate evidence for an inverse association between DINP exposure and insulin-like growth factor I (IGF-1) and no associations were found between DINP and effects on cardiovascular function, allergic symptoms or oxidative stress.[53]

Regarding the use of DINP in non-PVC applications like coatings (paints), sealants and adhesives, Canada concluded that these “would not be considered to be of concern for human health” based on

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[41] Id.
[42] Id.
[43] Id.
[44] Id. pp. iii-iv.
[45] Id. pp. 79-80 (section 9.2.2.4).In section 9.4 (Uncertainties in Evaluation of Risk to Human Health) of its report on DINP, Environment Canada/Health Canada notes that there are several uncertainties associated with the epidemiological literature on DINP and other phthalates. These include the fact that these studies are mostly observational in nature, posing a challenge with respect to measures of exposure and outcome, lack of evidence for causal inference, presence of confounding factors, inherent bias and poor reproducibility. Id. at 100-101.
[46] Id. p. 79.
[47] Id.
[48] Id. at 80.
[49] Id.
[50] Id.
[51] Note that MINP is recognized as a non-specific, insensitive biomarker of exposure to DINP. Calafat, A.M., L.-Y. Wong, M.J. Silva, E. Samandar, J.L. Preau, Jr., L.T. Jia et al.: Selecting adequate exposure biomarkers of diisononyl and diisodecyl phthalates: data from the 2005-2006 National Health and Nutrition Examination Survey. *Environmental Health Perspectives* 119(1): 50-55 (2011).
Silva Manori, J., A. Reidy John, L. Preau James, L. Needham Larry, and M. Calafat Antonia: Oxidative Metabolites of Diisononyl Phthalate as Biomarkers for Human Exposure Assessment. *Environmental Health Perspectives* 114(8): 1158-1161 (2006).
[52] Canada 2015, note 34, p. 80.
[53] Id. pp. 94-95 (section 9.2.2.6).

low dermal absorption of DINP in rats (4%), evidence that human skin is less permeable than rat skin to phthalate esters, low tissue distribution with no accumulation, and rapid excretion.[54]

Other Information –
With respect to other endpoints of potential concern for DINP exposure, the manufacturers, through the ACC HPP, note that DINP is listed as causing cancer under California's Proposition 65.[55] However, this determination is solely based on animal data, without consideration of human relevance.[56] The US CPSC provided a detailed analysis of the cancer potential of DINP in humans.[57] It identified three cancer effects from chronic dietary studies in rats and mice: increased incidences of renal tubular cell carcinoma in male rats, hepatocellular tumors in rats and mice of both sexes, and mononuclear cell leukemia (MNCL) in Fischer 344 rats.[58] The CPSC considered the renal tubule tumors to arise by an α2u-globulin mechanism that is unique to male rats.[59] CPSC concluded hepatocellular tumors arise by a peroxisome proliferation mode of action that is not easily inducible in humans.[60] CPSC noted MNCL is a neoplasm with high spontaneous rate in Fischer 344 rats that is considered of questionable relevance to humans.[61] Based on these considerations, CPSC concluded to not consider carcinogenicity in evaluating the potential risks of DINP exposure in humans.[62] This is in line with the conclusion of the Chronic Hazard Advisory Panel in 2001 that "humans do not currently receive DINP doses from DINP-containing consumer products that are plausibly associated with a significant increase in cancer risk".[63] Similar to the US CPSC conclusions, the European Union's 2013 risk evaluation of DINP considered the renal tumors in rats to stem from an α2u-globulin mode of action, not considered to be relevant for humans.[64] With respect to the liver tumors in rats and mice, the EU report emphasized the need for caution when interpreting the relevance of these tumors to humans.[65] The EU was unable to draw a definite conclusion on the relevance of the MNCL findings but concluded that it was not a driver for risk assessment.[66] As discussed above, Environment Canada/Health Canada found uncertainty regarding the relevance of animal tumors from DINP to humans, but in any event determined margins of exposure indicated no risk of concern.[67]

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[54] Id. p. 99.
[55] Office of Environmental Health Hazard Assessment. Chemical Listed Effective December 20, 2013 as Known to the State of California to Cause Cancer: Diisononyl Phthalate (DINP) (Dec. 12, 2013). https://oehha.ca.gov/proposition-65/crnr/chemical-listed-effective-december-20-2013-known-state-california-cause-cancer.
[56] See statement of Chairman Mack, Meeting of the Proposition 65 Carcinogen Identification Committee, December 5, 2013, transcript p. 98 ("The question is not whether or they're relevant to humans. That's not what the law says. The law says that the regulation, which comes from the Proposition 65, says does it cause cancer? It does not say does it cause cancer in humans?"). https://oehha.ca.gov/media/downloads/proposition-65/transcript/cic120513transcript.pdf
[57] M. Babich and C. Osterhout. 2010. Toxicity review of Diisononyl Phthalate (DINP). Consumer Product Safety Commission, pp. 58-84 (Section 8). https://www.cpsc.gov/s3fs-public/toxicityDINP.pdf.
[58] Id. p. 83
[59] Id. p. 81
[60] Id. pp. 80-81.
[61] Id. p. 82.
[62] Id. pp. 83-84.
[63] Consumer Product Safety Commission (CPSC). 2001. Report to the U.S. Consumer Product Safety Commission by the Chronic Hazard Advisory Panel on diisononyl phthalate (DINP), cover letter. Bethesda, MD: U.S. Consumer Product Safety Commission, https://cpsc.gov/s3fs-public/pdfs/dinp.pdf.
[64] ECHA 2013, note 24, p. 98 (section 4.4.8.1.5).
[65] Id.
[66] Id.
[67] See note 36.

Overall, although there is evidence that high dose DINP exposure can cause specific tumor lesions in rodents, the weight of the evidence does not support a carcinogenicity risk for humans, in line with the conclusions reached by several regulatory agencies.[68] References to all evaluations summarized above are provided in footnotes to this document and also available in Appendix C, which also gives citations for independent party/authoritative assessments by the US National Academy of Sciences and the World Health Organization International Programme on Chemical Safety.

Although an EPA IRIS evaluation of DINP has not been completed, all references identified by the EPA IRIS program through July 2014 for the hazard evaluation of DINP are provided in Appendix C.[69] To the best of our knowledge, no hazard or risk evaluation of DINP has been conducted by the FDA since the Phthalate Action Plan was issued. We have included a reference to a publicly available FDA investigation of levels of plasticizers (including DINP) present in PVC articles authorized as food contact materials in Appendix C (see Carlos et al. 2018).

Information relevant to the exposure potential of DINP –

According to the 2014 update to the TSCA Work Plan, DINP is assigned an exposure score of 3 (high), based its common use as a plasticizer in PVC with industrial, commercial, and consumer applications.[70] The US Centers for Disease Control and Prevention (CDC)'s National Health and Nutrition Examination Survey (NHANES) has reported urinary levels of DINP metabolites for the US population from 1999 to 2016.[71] [72] These data have served as the basis for recent risk evaluations of DINP by regulatory Agencies including the US CPSC and Environment Canada and Health Canada.[73] These values represent a snapshot of DINP exposure in the general population from various sources (industrial, commercial, and consumer) across a wide range of age, gender and race. The NHANES data however only provide biomonitoring information from ages 6 and above. The manufacturers, through the ACC HPP, note that the US CPSC Chronic Hazard Advisory Panel[74] utilized biomonitoring data from the Study for Future Families (SFF)[75] to estimate exposure to children from 2 to 36 months, as well as estimating prenatal and postnatal measurements from their mothers. However, the manufacturers,

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[68] As noted above, the California Office of Environmental Health Hazard Assessment has listed DINP under Proposition 65 as "known to the State to cause cancer", but in fact the Cancer Identification Committee made this recommendation on the basis of animal evidence without considering whether the animal tumors are relevant to humans. For a critique of the OEHHA hazard identification document, see https://oehha.ca.gov/media/downloads/proposition-65/crnr/comments/2exxonmobildinpcic.pdf

[69] See EPA, IRIS Toxicological Review of Diisononyl Phthalate (Dinp) (Preliminary Assessment Materials), https://cfpub.epa.gov/ncea/iris_drafts/recordisplay.cfm?deid=237476.

[70] 2014 Work Plan, note 14, p. 12.

[71] Data through the 2013-2014 NHANES cycle are presented in CDC's formal exposure report, which presents absolute and creatinine-adjusted values at various percentiles and according to various subpopulations. CDC 2018. Fourth National Report on Human Exposure to Environmental Chemicals. Updated Tables, March 2018, Volume One. pp. 493-502. https://www.cdc.gov/exposurereport/pdf/FourthReport_UpdatedTables_Volume1_Mar2018.pdf. [hereafter "NHANES 2005-2014"]

[72] Raw data for the 2015-2016 NHANES cycle are provided at https://wwwn.cdc.gov/nchs/nhanes/search/datapage.aspx?Component=Laboratory&CycleBeginYear=2015 [hereafter "NHANES 2015-16"]. These datasets need to be accessed using a SAS software viewer.

[73] CPSC 2015, note 19; CPSC 2017, note 20; Canada 2015, note 34.

[74] Chronic Hazard Advisory Panel (CHAP) on Phthalates. 2014. Chronic Hazard Advisory Panel on Phthalates and Phthalate Alternatives Final Report (2014). https://www.cpsc.gov/s3fs-public/CHAP-REPORT-With-Appendices.pdf. [hereafter "CHAP 2014"].

[75] Swan, S; Calafat, A; Kruse, R; Lasley, B; Redmon, B; Sparks, A; Wang, C. Final Report: Study of Phthalates in Pregnant Woman and Children (Study for Future Families (SFF)). EPA Grant Number: R829436. https://cfpub.epa.gov/ncer_abstracts/index.cfm/fuseaction/display.highlight/abstract/1950 https://www.cpsc.gov/s3fs-public/SFF-Biomonitoring-Data.pdf

through the ACC HPP, advise that the SFF data be interpreted with caution as there are several limitations associated with its use. First, the SFF data only track DINP exposures from 1999-2005 and likely do not reflect current exposures to DINP. Second, the SFF dataset for DINP is relatively small. For example, the number of samples available for prenatal women and infants (0-37 months) were 18 and 67, respectively.[76] More recent summary data on mono (carboxy-isooctyl) phthalate (MCiOP) DINP metabolite collected in The Infant Development and the Environment Study (TIDES) have been published.[77, 78] According to the study authors, TIDES is a prospective cohort study of phthalate metabolites in urine samples of pregnant women over 18 years old and <13 weeks pregnant, recruited from 2010-2012 and collected in the first, second and third trimesters.[79] Mean urinary concentrations of MCiOP (ng/mL) for each trimester have been published for a limited dataset (N = 167-168).[80] Mean values were well below the 90th percentile for all age groups 20 years and older and all females (regardless of age) reported for the US population from NHANES, suggesting that the NHANES data is an appropriate surrogate for estimating potential prenatal exposures to DINP. The limited size of the TIDES dataset indicates that it is likely less representative than that in the NHANES database, which contains similar data for MCiOP for a larger subset of US females 12-19 years and >20 years, for a broader time frame.[81]

Some data on urinary levels of DINP metabolites are also available for occupational workers and are referenced in Appendix C. For example, in one study of US workers recruited from 2003-2005, creatinine-adjusted DINP metabolite, MCiOP, levels ranged from 0.42-80 µg/g for PVC film workers and from 1.11-13.4 µg/g in PVC compounding workers.[82] The range of values for PVC compounding workers was less than the 90th percentile of creatinine-adjusted urine concentrations of MCiOP for adults 20-59 years and older, reported by NHANES for 2005-2006 (n = 1040).[83] The highest geometric mean value for PVC film workers (25.2 µg/g) was between the 90th and 95th percentile of creatinine-adjusted urine concentrations of MCiOP for the same NHANES dataset.[84] Since biomonitoring values in workers are not likely to be derived solely from exposure in the work place, but rather to be a result of aggregate exposures,[85] it can be inferred that the higher percentile ranges of the NHANES dataset

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[76] CHAP 2014, note 74, p. 45 (Table 2.7).

[77] Swan, S.H., S. Sathyanarayana, E.S. Barrett, et al.: First trimester phthalate exposure and anogenital distance in newborns. *Human Reproduction* 30(4): 963-972 (2015). https://academic.oup.com/humrep/article/30/4/963/613595.

[78] Martino-Andrade AJ, Liu F, Sathyanarayana S, Barrett ES, Redmon J, Nguyen RH, Levine H, Swan SH; TIDES Study Team. Timing of prenatal phthalate exposure in relation to genital endpoints in male newborns. Andrology. 2016 Jul;4(4):585-93. doi: 10.1111/andr.12180. Epub 2016 Apr 7. https://www.ncbi.nlm.nih.gov/pubmed/27062102

[79] Id. p. 588 (Methods).

[80] Id. p. 588 (Table 1).

[81] Geometric means and selected percentiles of urine concentrations of MCiOP (in µg/L) for the US population for the 2005/2006 to 2013/2014 NHANES cycles are provided in NHANES 2005-2014, note 71. Raw data are available for NHANES 2015-16, note 72.

[82] Hines, C.J., N.B. Hopf, J.A. Deddens, M.J. Silva, and A.M. Calafat: Occupational exposure to diisononyl phthalate (DiNP) in polyvinyl chloride processing operations. *International Archives of Occupational and Environmental Health* 85(3): 317-325 (2012).

[83] Calafat, A.M., L.-Y. Wong, M.J. Silva, E. Samandar, J.L. Preau, Jr., L.T. Jia et al.: Selecting adequate exposure biomarkers of diisononyl and diisodecyl phthalates: data from the 2005-2006 National Health and Nutrition Examination Survey. *Environmental Health Perspectives* 119(1): 50-55 (2011).

[84] See NHANES 2005-2014, note 71, pp. 501-502 for urinary MCiOP (in µg/g creatinine) for the 2005/2006 to 2013/2014 NHANES cycles.

[85] CDC defines “environmental chemical” as a chemical compound that could be present in air, water, food, soil, dust, or other environmental media (e.g. consumer products). CDC also indicates that the urine levels of environmental chemicals measured in NHANES reflect the amount of the chemical that actually gets into the body by all routes of exposure, including ingestion, inhalation, and dermal absorption. NHANES 2005-2014, note 71, p. 1.

can be used as an upper bound estimate or worst-case estimate of exposures to DINP across the population, including occupational workers.

One use that the manufacturers, through the ACC HPP, are requesting for risk evaluation is the use of DINP in children's toys, including those that can be placed in the mouth, and childcare articles. Several phthalate migration and PVC toy mouthing studies in infants are available and have been reviewed by other regulatory agencies. For example, the US CPSC conducted an assessment to identify the types and migration of plasticizers used in component parts of various children's toys and childcare articles on the market after 2008.[86] The CPSC identified 129 component parts from 63 samples, 38 of which were composed of PVC.[87] DINP was only found in 1 item (not mouthable); the majority of the items contained other plasticizers such as di-2-ethylhexyl terephthalate (DOTP) and 1, 2-cyclohexanedicarboxylic acid, di-isononyl ester (DINCH).[88] One mouthing study assessed DINP migration rates from 24 toys, including an assessment of mouthing activity in children, detailed characterization of the objects mouthed and estimation of exposure.[89] The study concluded that oral exposure to DINP from mouthing soft plastic toys is not likely to present a health hazard to children. Tables 4.65, 4.67 and Section 4.6.2.1.3 of the 2013 EU risk assessment of DINP provide a detailed review of published estimates of children's oral exposure to DINP in toys and estimates of toy mouthing times in young children.[90]

All documents discussed above are referenced in Appendix C of this request for the Agency's review.

Information relevant to the persistence and bioaccumulation of DINP –
According to the Agency's 2012 Phthalates Action Plan and 2014 TSCA Work Plan, DINP exhibits low toxicity to aquatic organisms and is ranked low for persistence and bioaccumulation.[91]

The most relevant and thorough ecological hazard and risk evaluations of DINP are available in the EU's 2003 risk assessment and Canada's 2015 State of the Science Report on DINP.[92] In the Canadian 2015 report, water is considered to be one of the primary receiving media for DINP with environmental exposure.[93] However, based on the low water solubility, low vapor pressure and high partitioning potential into organic carbon, DINP, if released into water, is expected to partition to sediment and the suspended particulate fraction of surface water.[94] DINP released into the soil is predicted to remain within the soil compartment and is not expected to leach through soil into ground water.[95] Canada concludes that DINP is readily biodegradable, has low bioaccumulation and biomagnification potential and is not expected to persist in the environment.[96]

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[86] US CPSC (2010). Phthalates and Phthalate Substitutes in Children's Toys. https://www.cpsc.gov/s3fs-public/phthallab.pdf
[87] Id. p. 4.
[88] Id.
[89] Babich, M.A., S.-B. Chen, M.A. Greene, C.T. Kiss, W.K. Porter, T.P. Smith et al.: Risk assessment of oral exposure to diisononyl phthalate from children's products. *Regulatory Toxicology and Pharmacology* 40(2): 151-167 (2004).
[90] ECHA 2013, note 24.
[91] 2012 Action Plan, note 9, pp. 5-6; 2014 Work Plan, note 14, p. 12.
[92] ECB 2003, note 6, pp. 29-117 & 259; Canada 2015, note 34, pp. 15-43.
[93] Canada 2015, note 34, p. 40.
[94] Id. pp. 19-20.
[95] Id.
[96] Id. p. 28.

A detailed risk characterization of DINP in surface water and sediments, through each life cycle step (including manufacture, processing in PVC and non-PVC, uses in adhesives, sealants, inks, paints, etc.) is provided in Tables 3.47 and 3.48 of the EU 2003 risk assessment of DINP.[97] In each case, a no risk conclusion was reached for the aquatic and benthic ecosystem.

Test results and robust summaries pertaining to DINP's persistence and bioaccumulation are referenced in Appendix C under the data sets submitted to the European Chemicals Agency.

Potentially exposed or susceptible subpopulations relevant to the EPA risk evaluation –
The Agency has indicated that it considers children and the developing fetus as the susceptible subpopulations for which the health risks of DINP should be assessed.[98] The CDC report of NHANES data for urinary metabolites of DINP (reported as geometric means and selected percentiles) is stratified by gender (males and females), race/ethnicity (Mexican American; Non-Hispanic Black; Non-Hispanic White) and age group (6-11 years, 12-19 years and ≥20 years).[99] Additional refinements can be made by directly accessing the NHANES database to obtain relevant information on DINP exposures in the subpopulation that the Agency considers to be most susceptible, children and women of childbearing age. As earlier mentioned, NHANES does not include data on infants or children <6 years of age. The SFF data, with a smaller subset (n = 67) of infants (2-37 months) may be considered as a surrogate, with caution, as noted previously.[100] With respect to women of childbearing age, the TIDES dataset provides information on over 400 pregnant women in the first trimester, but only within a limited exposure window (2010-2012).[101]

With respect to evaluation of DINP exposure from mouthing toys and childcare articles (the worst-case exposure scenario for children), several assessments of mouthing frequency and migration rate from mouthing toys are published. These are summarized in the exposure section.

Potential for storage of chemical substance near significant sources of drinking water, including storage facility location and nearby drinking water source(s) –
DINP is used primarily as a plasticizer in finished flexible PVC products. As the conditions of use in Appendix B (Production and Use) involve the end use products into which DINP is incorporated, none include storage of DINP next to significant sources of drinking water or otherwise. Any significant storage of the chemical is likely restricted to DINP manufacturing sites and storage terminals for DINP. As stated previously, a detailed evaluation of the fate and behavior of DINP in environmental media, including water, has been conducted by Environment Canada and Health Canada.[102] According to the level III fugacity model referenced in the report, as a result of its low volatility (vapor pressure – 6.8 x 10-6 to 2.9 x 10-3 Pa at 25 ºC) and low water solubility (4.1 x 10-5 to 0.2 mg/L at 22 to 25 ºC), DINP released into water is likely to distribute primarily into the sediment compartment (79-89%), with <20% remaining in the water column.[103] DINP distribution to air from water was considered to be minimal (0-0.1%).[104] The model predicts that DINP released into soil will strongly sorb to organic matter in the soil

[97] ECB 2003, note 6, pp. 115-116.
[98] 2012 Action Plan, note 9, p. 8.
[99] NHANES 2005-2014, note 71, pp. 493-502.
[100] See note 75 and associated text.
[101] See notes 77 and 78 and associated text.
[102] Canada 2015, note 34. See notes 93 to 96 and associated text.
[103] Id. pp. 19-20.
[104] Id.

and 100% remain in the soil compartment, due to its low water solubility and high partition coefficient.[105] The model prediction of low mobility for DINP means that it is unlikely to leach through soil to groundwater or a surface source of drinking water.

According to the Canadian report, DINP is rapidly biodegraded in aerobic aqueous environments, with 68% of the parent substance removed within 1 day and 90-100% removed within 5-28 days.[106] The DINP half-life under aerobic aqueous conditions has been estimated to be 7-40 days.[107] Overall, the physico/chemical properties of DINP (low water solubility and high partition coefficient/high hydrophobicity) are such that it is rapidly degraded in water and primarily partitions to suspended particulate fraction of surface waters in the event of spillage into water. In the event of spillage into a water body that serves as a source of drinking water, since DINP tends to sorb to sediment particles, treatment with flocculants and filters would separate out the DINP prior to distribution in the drinking water system. In the event of soil spillage, the high partition coefficient and low mobility of DINP suggests that it is primarily adsorbed to soil and unlikely to migrate to ground water. Therefore, should there be a spill of DINP into water or soil, the potential for significant contamination of sources of drinking water is very low.

In that respect, the manufacturers, through the ACC HPP, are aware of the following:

All manufacturing and storage locations have developed Spill Prevention Control & Countermeasure (SPCC) plans prepared in accordance with requirements and guidelines set forth in 40 CFR 112. The purpose of this SPCC Plan is to establish procedures and methods in accordance with best management practices to prevent and control the discharge of pollutants resulting from a spill event into navigable waters.

DINP production volume –
DINP production volumes for 2012-2015 for both DINP CASRNs, as reported in the Agency's Chemical Data Reporting database, are provided in Appendix B of this request. No significant changes in production volume were observed for the reported years.

Addendum

As noted above, the manufacturers, through the ACC HPP, believe that, to the best of our knowledge, we have provided the Agency with all the existing information that is relevant to whether DINP, under the conditions of use identified herein, presents an unreasonable risk of injury to health or the environment. As all of the information is publicly available, HERO database or bibliographic citations are provided, rather than actual copies of the information. The manufacturers, through the ACC HPP, commit to provide to the Agency any referenced information upon request.

[105] Id.
[106] Id. p. 22.
[107] Id.

Certification

I certify, on behalf of the American Chemistry Council High Phthalates Panel, that to the best of my knowledge and belief:

The ACC HPP represents major companies that manufacture, compound, convert, or import DINP, the chemical substance identified for risk evaluation.

All information provided in the notice is complete and accurate as of the date of the request.

On behalf of the ACC HPP, I have either identified or am submitting all information in my possession and control as ACC HPP manager, and a description of all other data known to or reasonably ascertainable by me as required for this request under this part. I am aware it is unlawful to knowingly submit incomplete, false and/or misleading information in this request and there are significant criminal penalties for such unlawful conduct, including the possibility of fine and imprisonment.

Sincerely,

Eileen Conneely

Eileen Conneely
on behalf of the American Chemistry Council
High Phthalates Panel

Certification

I certify that to the best of my knowledge and belief:

Evonik Corporation imports the chemical substance identified for risk evaluation.

All information provided in the notice is complete and accurate as of the date of the request.

I have either identified or am submitting all information in my possession, control, and a description of all other data known to or reasonably ascertainable by me as required for this request under this part. I am aware it is unlawful to knowingly submit incomplete, false and/or misleading information in this request and there are significant criminal penalties for such unlawful conduct, including the possibility of fine and imprisonment.

Sincerely,

Tiana Rosamilia

Tiana Rosamilia
on behalf of Evonik Corporation

Certification

I certify that to the best of my knowledge and belief:

ExxonMobil Chemical Company manufactures the chemical substance identified for risk evaluation.

All information provided in the notice is complete and accurate as of the date of the request.

I have either identified or am submitting all information in my possession, control, and a description of all other data known to or reasonably ascertainable by me as required for this request under this part. I am aware it is unlawful to knowingly submit incomplete, false and/or misleading information in this request and there are significant criminal penalties for such unlawful conduct, including the possibility of fine and imprisonment.

Sincerely,

M. David Adenuga

M. David Adenuga
on behalf of ExxonMobil Chemical Company

Certification

I certify that to the best of my knowledge and belief:

Teknor Apex manufactures the chemical substance identified for risk evaluation.

All information provided in the notice is complete and accurate as of the date of the request.

I have either identified or am submitting all information in my possession, control, and a description of all other data known to or reasonably ascertainable by me as required for this request under this part. I am aware it is unlawful to knowingly submit incomplete, false and/or misleading information in this request and there are significant criminal penalties for such unlawful conduct, including the possibility of fine and imprisonment.

Sincerely,

Thomas Hmiel

Thomas Hmiel
on behalf of Teknor Apex

APPENDIX A – SUBSTANCE IDENTITY INFORMATION
DIISONONYL PHTHALATE (DINP)

Name and substance identifiers

The substance “di-isononyl phthalate” is described by two CAS numbers based on the composition of the alkyl side chains.

Table 1: Substance Identity

CAS Number	Systematic Name	EPA Registry Name	Molecular formula	Molecular weight range (g/mol)
28553-12-0*	1,2-benzenedicarboxylic acid, 1,2-diisononyl ester	Diisononyl phthalate	$C_{26}H_{42}O_4$	418.62
68515-48-0	1,2-Benzenedicarboxylic acid, di-C_{8-10}-branched alkyl esters, C_9-rich	Di(C_8-C_{10}, C_9 rich) branched alkyl phthalates	$C_{26}H_{42}O_4$	418.1**

* EPA Substance Registry Service on DINP

** European REACH dossier registration for CAS Number 68515-48-0

Structure

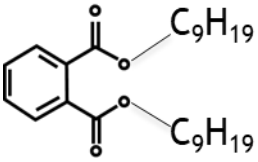

Figure 1: CAS Number – 28553-12-0

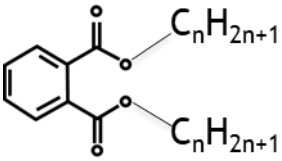

Figure 2: CAS Number – 685153-48-0, n = 8, 9, or 10

Table 2: Other Names Used (European Chemicals Agency [ECHA] REACH information)

CAS Number EINECS Number	Regulatory Process Names	Trade Names	IUPAC Names
28553-12-0 249-079-5*****	○ Di-"isononyl" phthalate ○ di-"isononyl" phthalate ○ Di-“isononyl” phthalate (DINP)	○ 1,2-Benzenedicarboxylic acid, diisononyl ester (9CI) ○ Di-"isononyl" phthalate ○ Diisononyl phthalate ○ DINP ○ DIPLAST NS ○ DIWP ○ Isononyl alcohol, phthalate (2:1) (8CI) ○ PALATINOL N ○ Phthalic acid, diisononyl ester (7CI, 8CI)	○ 1,2-Benzenedicarboxylic acid, 1,2-diisononyl ester ○ 1,2-Benzenedicarboxylic acid, di-C8-10 branched alkyl esters, C9 rich ○ 1,2-bis(7-methyloctyl) benzene-1,2-dicarboxylate ○ bis(7-methyloctyl) benzene-1,2-dicarboxylate ○ bis(7-methyloctyl) phthalate ○ di-"isononyl" phthalate ○ di-"isononyl" phthalate ○ Di-Isononyl-Phthalate ○ Di-isononylphthalate ○ diisononyl phthalate

		○ Phthalsaeure-di-isononylester ○ VESTINOL 9	○ DINP
68515-48-0 271-090-9**	○ 1,2-Benzenedicarboxylic acid, di-C8-10-branched alkyl esters, C9-rich ○ 1,2-Benzenedicarboxylic acid, di-C8-10-branched alkyl esters, C9-rich	○ Esterex P55 ○ Jayflex DINP	○ 1,2-Benzenedicarboxylic acid, di-C8-10-branched alkyl esters, C9-rich

*****ECHA substance information – https://echa.europa.eu/substance-information/-/substanceinfo/100.044.602
**ECHA substance information – https://echa.europa.eu/substance-information/-/substanceinfo/100.064.608

Table 3: Other Names Used (US NLM TOXNET data)

CAS Number	Synonyms
28553-12-0*****	Baylectrol 4200; 1,2-Benzenedicarboxylic acid, diisononyl ester; CCRIS 6195; Diisononyl phthalate; DINP; DINP2; DINP3; ENJ 2065; HSDB 4491; Isononyl alcohol, phthalate (2:1); Jayflex DINP; Palatinol N; Palatinol DN; Phthalic acid, diisononyl ester; Phthalisocizer DINP; Sansocizer DINP; Vestinol NN; Vinylcizer 90; Witamol 150; JAY-DINP; Vestinol 9; UNII-4010KIX4CK;
68515-48-0******	CCRIS 7927; Di(isononyl) phthalate branched; Di(C8-10, C9 rich) branched alkyl phthalates

*****https://chem.nlm.nih.gov/chemidplus/rn/28553-12-0
**https://chem.nlm.nih.gov/chemidplus/rn/68515-48-0
N/A – No number identified.

Considerations for Evaluating both CAS Numbers as a Single Substance[1, 2, 3, 4, 5]

Substance identity of DINP is described in the US EPA's preliminary materials for the IRIS toxicological review of DINP.[6] Three different DINP formulations (DINP-1, DINP-2 and DINP-3) have been produced in commercial quantities depending on the alcohol feedstock used in their manufacture (see figure 1.1 and Table 1.2, page 10 – 11 of footnote 6 & Page 1-2 of IRIS scoping document for DINP in footnote 7).

DINP-1, represented by CAS number 68515-48-0 (Figure 2), is a complex substance that contains alcohol groups manufactured from octene, by the "Polygas" process. It contains a distribution of C_8H_{17} to $C_{10}H_{21}$ isomers, where C_9H_{19} alkyl chains are predominant (>70%). In Figure 2 above, "n" = 8-10, predominantly 9.

DINP-2, represented by CAS number 28553-12-0 (Figure 1), contains alcohol groups manufactured from n-butene, resulting predominantly in C_9 methyl octanols and dimethyl heptanols. It predominantly contains C_9H_{19} isomers as alkyl side chains.

DINP-3, also represented by CAS number 28553-12-0, contained alcohol groups manufactured from n- and iso-butene. DINP-3 contained higher proportions of branched methyl ethyl hexanols than other formulations. Production of DINP-3 has ceased since 1995 and is no longer in commercial use.

The term "DINP" is used as a common name to describe both CAS numbers representing DINP-1 and DINP-2 in Table 1. Although the isomeric compositions of both substances may differ, both substances are considered to be commercially interchangeable. Several toxicological reviews have been conducted on DINP by the European Chemicals Agency (ECHA) and the United States Consumer Product Safety Commission (CPSC). In all cases, both substances are considered to be toxicologically equivalent and evaluated as a single substance.[7, 8, 9]

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[1] ECHA (2018): RAC Opinion proposing harmonized classification and labeling at EU level of DINP – https://echa.europa.eu/documents/10162/56980740-fcb6-6755-d7bb-bfe797c36ee7

[2] ECHA (2013): Evaluation of new scientific evidence concerning DINP and DIDP – https://echa.europa.eu/documents/10162/31b4067e-de40-4044-93e8-9c9ff1960715

[3] Babich and Osterhout (2010): Toxicity Review of Diisononyl Phthalate (DINP) – https://www.cpsc.gov/s3fs-public/ToxicityReviewOfDINP.pdf

[4] See US EPA IRIS scoping information document for DINP – https://cfpub.epa.gov/ncea/iris_drafts/recordisplay.cfm?deid=237476

[5] European Chemicals Bureau. 2003. European Union Risk Assessment Report on 1,2-benzenedicarboxylic acid, di-C8-10-branched alkyl esters, C9-rich and di-"isononyl" phthalate (DINP). https://echa.europa.eu/documents/10162/83a55967-64a9-43cd-a0fa-d3f2d3c4938d.

[6] U.S. EPA. 2014. IRIS Toxicological Review of Diisononyl Phthalate (Dinp) (Preliminary Assessment Materials). https://cfpub.epa.gov/ncea/iris_drafts/recordisplay.cfm?deid=237476.

[7] See Notes 1, 2 and 3.

[8] Australian Government National Industrial Chemicals Notification and Assessment Scheme. 2012. Diisononyl Phthalate. Priority Existing Chemical Assessment Report No. 35. September 2012. https://www.nicnas.gov.au/__data/assets/word_doc/0008/34838/PEC35-DINP.docx [hereafter "NICNAS 2012"].

[9] Environment Canada and Health Canada State of the Science Report. 2015. Phthalate Substance Grouping: 1, 2-Benzenedicarboxylic acid, diisononyl ester 1, 2-Benzenedicarboxylic acid, di-C8-10-branched alkyl esters, C9-rich (Diisononyl Phthalate; DINP). http://ec.gc.ca/ese-ees/47F58AA5-57BE-4869-A128-587DEADCAAD8/SoS_Phthalates%20%28DINP%29_EN.pdf [hereafter "Canada 2015"].

APPENDIX B – PRODUCTION AND USE
DIISONONYL PHTHALATE (DINP)

Production volume

According to the 2015 US EPA Chemical Data Reporting (CDR) database[1], between 100 and 500 million pounds of DINP was imported or manufactured in the United States as follows (note that this volume has remained constant since 2012):

Table 1: US DINP Production volumes for 2012 to 2015, by CAS Number

Reporting Year		2012	2013	2014	2015
Total Aggregate Production Volume (lbs.)	CASRN 28553-12-0	100 – 250 million	100 – 250 million	100 – 250 million	100 – 250 million
	CASRN 68515-48-0	100 – 250 million	100 – 250 million	100 – 250 million	100 – 250 million

Uses

For the purpose of this document, the term DINP represents Chemical Abstract Service Registry Numbers (CASRNs) 28553-12-0 and 68515-48-0. The uses of DINP are summarized below. The primary intended, known or reasonably foreseen use of DINP (>90%) is as a plasticizer to impart flexibility to polyvinyl chloride (PVC) in consumer and industrial applications.[2, 3, 4, 5, 6] These applications include wire and cable jacketing, building and construction (vinyl tiles, resilient flooring, PVC-backed carpeting, roofing, wall coverings etc.), automotive (window glazing, doors, acrylic plastisol sealants in wheel wells, underbody coatings and paints), vinyl clothing (raincoats and boots, gloves etc.), tool handles, flexible tubes, profiles, and hoses. Approximately 5% of DINP is used in non-PVC applications such as rubbers, inks and pigments, adhesives, sealants, paints, lacquers and lubricants.

USEPA's 2016 Chemical Data Reporting (CDR) database indicates that CAS numbers 28553-12-0 and 68515-48-0 are used in industrial, commercial and industrial applications.[7] Primary uses include incorporation into article, formulation, mixture, or reaction product as a plasticizer (for manufacturing of

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[1] US EPA Chemical Data Access Tool (CDAT). https://chemview.epa.gov/chemview. Last accessed – December 12, 2018.

[2] American Chemistry Council (ACC) (2018). Phthalates: High phthalates uses and applications. https://phthalates.americanchemistry.com/High-Uses-and-Applications.html

[3] IHS Markit. (2018). Chemical Economics Handbook: Plasticizers, pp. 42. 4 May 2018.

[4] European Plasticisers (2018). Plasticisers Information Center: Orthophthalates. https://www.plasticisers.org/plasticisers/orthophthalates/

[5] European Chemicals Bureau (2003). European Union Risk Assessment Report, 1,2-benzenedicarboxylic acid, di-C8-10-branched alkyl esters, C9-rich and di-"isononyl" phthalate (DINP) (68515-48-0 & 28553-12-0), pp.26-28. 2nd Priority List Volume 35 Report 046, https://echa.europa.eu/documents/10162/8fa0a07f-ec2a-4da6-bbe8-5b5e071b5c16.

[6] European Chemicals Agency (ECHA). 2013. Evaluation of new scientific evidence concerning DINP and DIDP in relation to entry 52 of Annex XVII to REACH Regulation (EC) No 1907/2006. August 2013, pp. 21-28. https://echa.europa.eu/documents/10162/31b4067e-de40-4044-93e8-9c9ff1960715.

[7] CDR defines "industrial use" as use at a site at which one or more chemicals or mixtures are manufactured (including imported) or processed. "Commercial use" means the use of a chemical or a mixture containing a chemical (including as part of an article) in a commercial enterprise providing saleable goods or services. "Consumer use" means the use of a chemical or a mixture containing a chemical (including as part of an article, such as furniture or clothing) when sold to or made available to consumers for their use. – Public database 2016 chemical data reporting (Data last updated 12/9/2018). Washington, DC: US Environmental Protection Agency, Office of Pollution Prevention and Toxics.

plastic materials and resins), adhesive and sealant chemical, paint and coating manufacturing, synthetic rubber manufacturing, furniture and furnishings, floor coverings, fabric, textile and leather products, building and construction materials, electrical and electronic products and automotive care products.

The most recent assessment of United States (US) consumption of DINP (Figure 1) indicates that the principal applications are in electrical jacketing for wire and cable insulation, film and sheet (e.g. roofing, pool liners, wall coverings etc.), coated fabrics and plastisol dips.

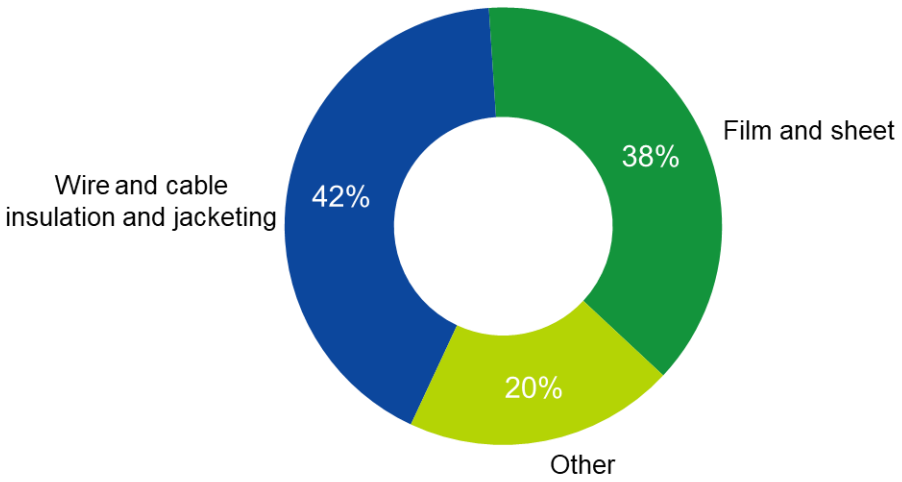

Figure 1: US Consumption of diisononyl phthalate (percent) – 2017 (Source – IHS Markit. Plasticizers. 4 May 2018).

Existing regulations restricting use

DINP has not been used in the manufacturing of children's toys and childcare articles intended to be placed in the mouth since 2009. In 2008, the United States congress passed the Consumer Product Safety Improvement Act (CPSIA) that placed an interim restriction on the use of DINP in childcare articles and in children's toys that can be placed in a child's mouth at concentrations no greater than 0.1%.[8] On the 27th of October 2017, the US Consumer Product Safety Commission (CPSC) published a final ruling in the Federal Register (82 FR 49938) that maintains this restriction and expands it to include all children's toys.[9]

Intended uses requested for evaluation

- DINP Manufacturing
- DINP use as a general purpose plasticizer for PVC used in the following applications;
  - *Building and construction* – wire and cable jacketing, vinyl tiles, resilient flooring, PVC-backed carpeting, wall coverings, roofing, etc.
  - *Automotive* – wire and cable jacketing, underbody coatings, doors, acrylic plastisol sealants, etc.

[8] Consumer Product Safety Act of 2008 – https://www.cpsc.gov/s3fs-public/pdfs/blk_pdf_cpsia.pdf

[9] US Consumer Product Safety Commission (CPSC) (2017). Prohibition of Children's Toys and Child Care Articles Containing Specified Phthalates. https://www.gpo.gov/fdsys/pkg/FR-2017-10-27/pdf/2017-23267.pdf

- *Other consumer applications* – vinyl clothing (raincoats, boots, gloves), tool handles, flexible tubes, hoses and profiles, etc.
- *Non-PVC applications* – inks and pigments, adhesives, sealants, and paints.
- *Use in PVC for children's toys and childcare articles*