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See attached document for comments.

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June 14, 2023

Submitted online and via email: ChemActionPlans@ecy.wa.gov

Comments: Draft Phthalates Action Plan

BASF appreciates the opportunity to comment on the Draft Phthalates Action Plan (PAP).[1] The following comments are submitted to address information and recommendations presented in the draft PAP; complementary comments may be found in our substantive submissions from January 28, 2022, and February 3, 2003, on the Safer Products for Washington proposal. Our comments are not exhaustive, i.e., they have not necessarily addressed every point of concern; however, they are representative and focus on the following topics:

- Phthalates should not be regulated as a class owing to the differences in structure, physical properties, and toxicological behavior across the range of products.
- The recommendation to encourage the avoidance of ortho-phthalate-containing building materials is misinformed, owing to the low toxicity and strong performance properities of the higher molecular weight products typically used in these applications.
- The draft PAP relies heavily on epidemiological studies that show associations (or not) but no clear evidence of causation. We recommend again reviewing the EU SCENIR (2015) report on DEHP in medical devices; their conclusions on various epidemiological studies ranged from "no association" to "weak association" to :inconsistent evidence" - hardly sufficient as a justification for regulatory action on specific ortho-phthalates or this whole class of chemicals.
- Some references report the detection of low levels (often described as "high") of ortho-phthalates in various consumer and other products. Any evaluation of these studies must also consider likely human exposure and potential risk relative to established NOAELs, TDIs, etc.
- The report also contains a number of errors such as incorrect citations, misrepresentation of the conclustions of some studies, and typographical errors.

Page 25: Black women: "… *phthalates that are used as fragrance in personal care products."* Phthalates (e.g., DMP or DEP) are not used as fragrances; however, they may be used as a carrier for the fragrance.

[1] BASF manufactures a number of plasticizers including DOTP, DINCH, high molecular weight ortho-phthalates, adipates, and trimelliates. BASF Corporation is a subsidiary of BASF SE.

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Page 26: Regulations – Washington State: The regulation in the link restricts ortho-phthalates, individually or in combination, to 0.1% or 1000 ppm and not 100 ppm (See RCW 70A.430.020(1)(c)).

p. 30 – Automotive products

Trim et al. (2017) presented testing results for a variety of automotive and other related products, which were described as “high” concentrations. Regrettably the values were reported in µg/kg or ppb, giving the impression that high levels were found. Some brake pads had 17,000 – 22,000 µg/kg, and serpentine belts had 950 – 1900 µg/kg; in mg/kg or ppm, these values are 17 – 22 mg/kg and 0.95 – 1.9 mg/kg (or 0.0017 – 0.0022% and 0.000095 – 0.00019%). It is unlikely that the respective phthalates were present in these products and most of the others as functional ingredients (i.e., intentionally added). Why they were detected is unknown; however, they may have been impurities in some of the materials or were analytical artifacts (i.e., misidentified or were present in lab equipment or sample containers).

It is misinformed to simply equate detection of an ortho-phthalate in a product with potential risk without considering the likely exposure and relative hazard.

One major use of ortho-phthalates is in interior automotive materials such as trim, floormats, and seats. OEM materials are subject to low fogging requirements (SAE J1756); typically these are only met when using linear C9 and higher molecular weight ortho-phthalates (i.e., linear C9 and branched or linear C10 and higher; cf. Wickson, 1993). These products have lower toxicity concerns, and lower exposure is expected due to their low vapor pressures. After-market replacement parts may or may not meet the low fogging requirements.

p. 51 – Phthalates in medical products

"The use of DEHP in PVC blood bags is one medical application for which alternatives do not yet meet performance standards. DEHP has a stabilizing effect on red blood cells and allows for longer stable storage of blood products. This benefit is critical for maintaining adequate blood supplies, despite the risk of high exposure during transfusion procedures."

Non-DEHP medical products have been and are available for a variety of applications, including for storage of blood storage products. The European Pharmocopaoeia was updated to now include alternatives to DEHP – DINCH, DOTP/DEHT, TOTM, and BTHC:

https://www.edqm.eu/en/news/ph-eur-revised-its-general-chapters-plasticised-pvc-materials

In addition, please refer to the two publications, Lagerberg et al. (2015) and Prowse et al. (2014) for more detailed examples. More information on these applications can be provided if needed.

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Page 59 – Building materials

Certain building materials are particularly important applications for high molecular weight ortho-phthalates, including specialty linear phthalates. For this reason, we disagree with the recommendations to support and encourage efforts to "avoid using phthalate-containing building materials," especially since the products most likely used have low toxicity and result in low exposure due to their low vapor pressure and water solubility.

For example, roofing membranes are an important market for plasticized vinyl. Owing to the need for low temperature flexibility and superior outdoor weather performance, specialty linear ortho-phthalates as well as DINP and DPHP are used. The following table shows some representative applications and the plasticizers typically used:[2]

Use	**Plasticizers**
Water-stop	DOTP, DINP
Caulks and sealants	Dibenzoates, DINP, DOTP, DINCH, DIDP
Pond and pool liners	DINP, DPHP, DIDP
Roofing membrane	DINP, DPHP, linear ortho-phthalates

Wire and Cable

Another key application for ortho-phthalates is for wire and cable insulation and jacketing. As noted in Godwin and Krauskopf (2008),[3] general purpose plasticizers such as DEHP may be used to meet 60 °C UL-rated PVC formulations; however, DEHP is not widely used for these applications in North America. As discussed in Godwin and Krauskopf, “flexible PVC products rated for 75 – 80 °C performance require less-volatile plasticizers such as DINP, DIDP, DPHP, or 711P types. Performance ratings for even higher temperatures (i.e., 90 and 105 °C) require the low volatility higher-molecular-weight phthalates and/or trimellitates. In all cases, the optimum plasticizer choice is a function of wall thickness and other factors influencing oven aging . . .” The following table, which was adapted from Godwin and Krauskopf, shows examples of plasticizers that meet various oven aging tests and the corresponding UL temperature ratings.

[2] Godwin and Krauskopf, “Monomeric Plasticizers” in *Handbook of Vinyl Formulating*, 2nd ed., Grossman, R. F., Ed., Wiley: New Jersey, 2008.

[3] Cf. Goodwin and Krauskopf.

Wall thickness (mil)	Test temperatures for 7-day aging, deg C			
	100 UL 60	113 UL 80, SAE-80	121 UL 90	136 UL 105
8	DIDP, DPHP	DUP	DUP	TOTM, TINTM
15	DIDP, DPHP	911P, DUP	DUP, DIDP/DTDP	DUP/TOTM
30	DINP, DOTP, DIDP, DPHP	DIDP	DIDP	DTDP/TINTM
60	DINP, DOTP, DIDP, DPHP	DIDP, DPHP	DIDP, DPHP	DUP, DTDP

It is important to note that in the building materials segment, including wire and cable, specific high molecular weight ortho-phthalates are used owing to the performance requirements of the application; the important performance criteria are, for example, low temperature flexibility, heat stability, and outdoor weathering stability – higher molecular weight ortho-phthalates excel in these areas and are difficult to replace. In addition, flexible PVC usually provides the most cost-effective and best-performing option.

Page 138, physical-chemical properties: Delete “may”; ortho-phthalates have clearly defined and well-known structure activity relationships.

The water solubility is a function of chain length of the respective alcohols; i.e., longer chains are less water soluble and have lower vapor pressures.

Page 138, Table 6: This table appears to have come from the 2010 CPSC report, as referenced; however, some of the values appear to be incorrect and do not make sense. For example, the vapor pressure values of DEHP and DnOP in the table are lower than for DINP and DIDP (see Cousins, Mackay, and Parkerton, 2003, for leading references and more details).

The correct chemical name for DEHT is bis(2-ethylhexyl) terephthalate, although it is often described as diethylhexyl terephthalate or dioctyl terephthalate (i.e., DEHT and DOTP acronyms). NSF International has published an oral risk assessment on terephthalic acid and its esters (Ball et al., 2012), which provides details on the other esters.

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Page 139: Engel et al. speculates about the potential for regrettable substitution and calls on government agencies to “eliminate phthalate use”. As noted in previous comments, recommendations for restrictions on phthalates as a class is misinformed and does not consider the differences in structure between the various members of that class and the impact on physical properties and toxicological behavior.

Page 143. “*Phthalates are regulated under several laws in Washington state. CSPA restricts the use of six phthalates in children’s products at concentrations* ***greater than 100 ppm*** *individually or combined. CSPA also requires manufacturer reporting for six additional phthalates when used in children’s products, for a total of 12 phthalates listed with a reporting requirement.”*

Please clarify what is the valid limit value?

RCW 70A.430.020 Prohibition on the manufacturing and sale of children's products containing lead, cadmium, **or phthalates.**

(c) Phthalates, individually or in combination, at more than 0.10 percent by weight (one thousand parts per million). ➔ **1000 ppm, the limit in US CPSIA and CPSA limit cited on page 32 of pdf.** Also see comment above.

Page 145:

“Phthalates as a chemical class can cause reproductive toxicity and developmental toxicity to the reproductive and nervous systems…”

> Not all – only those in the active cluster; this sentence should read "some phthalates" … (cf. Fabjan, 2006; CHAP, 2014)

“*There is broad consensus that phthalates are endocrine disrupting chemicals…”*

> Disagree: not phthalates in general, but only specific ones.

“*In studies of people, exposure to phthalates in the womb has been linked to brain and behavioral outcomes for children and respiratory symptoms after birth. When exposure occurs later in life, phthalates have adverse effects on semen quality and sperm count in men and on pregnancy outcomes in women. Risk and severity of uterine fibroids in women have been connected to phthalate exposure. Phthalates are also associated with metabolic effects like diabetes, gestational diabetes, insulin resistance, and obesity. In laboratory experiments in animals, phthalates cause liver and kidney toxicity.”*

> This whole paragraph is dealing with epidemiologic associations where no causal relationship can be proven.

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Page 146:

"U.S. EPA cited toxic effects on fetal development of the reproductive system as a critical health effect for the development of their 2012 action plan (US EPA, 2012)."

This sentence needs to be aligned with the EPA statement, which was more specific (EPA, 2012): "The most sensitive health outcomes following exposures of *some phthalates in animal studies* are the phthalate syndrome effects …"

"The CHAP report focused on male developmental toxicity."

- ⇨ Male developmental **toxicity in animals.**

Canada:

"*The key phthalate health hazards identified by ECCC are consistent with other studies: effects on the…"*

Should be more specific, i.e. The key phthalate health hazards identified by ECCC are consistent with other **animal** studies: effects on the ….

Page 147:

"Authoritative reports identify phthalates as endocrine disruptors." This is too generic and should be more clear; i.e., identify **specific** phthalates

"Phthalates possess some limited estrogenic activity, and there is strong evidence that they act as antagonists of androgen receptors (Begum & Carpenter, 2021)." See correct reference to the final version:

Begum, T. F., & Carpenter, D. **(2022).** Health effects associated with phthalate activity on nuclear receptors. *Reviews on Environmental Health*, *37*(4), 567–583. https://doi.org/10.1515/REVEH-2020-0162

"Most of the phthalates with side chains *of 4 to 10 carbons* (e.g., DBP, DiBP, DEHP, BBP, DCHP, and DINP) that have been tested have anti-androgenic properties in laboratory animals, although the potency varies (Lioy et al., 2015; NAS, 2017)."

- ⇨ Disagree: it is only with alcohol side chains of 4-9 carbons or 3 – 6 carbon backbone (Fabjan 2006).
- ⇨ This is an error in both NAS 2017 and Lioy et al. (2015). NAS 2017 states that it is "ester side chains containing 4 – 10 carbon atoms," and Lioy et al. says that it is "*three to eight*

carbon atoms in the backbone of the alkyl side chain." NAS 2017 cited studies (Gray 2000 and Furr 2014) confirming anti-androgenic *activity* only for C4-C9 side chains.[4]

Page 149:

"*A review of epidemiological evidence concluded…"* What specific evidence? Epidemiology reports only associations with no causal relation and no evidence. There is a danger of random associations, and the scientific basis may be questionable.

"The human epidemiology evidence for effects on male reproduction is strongest for DEHP (Swan et al., 2015); however, DIDP has been linked to cryptorchidism and hypospadias, and DINP has effects on AGD and semen parameters, although results are inconsistent (Radke et al., 2018)."

"DIDP has been linked to cryptorchidism and hypospadias, …"

Please add reference for this claim. Swan and Radke do not link DIDP with these effects.

Page 149:

"Three recent reviews conclude that phthalates have the potential to disrupt neurodevelopment and alter neurobehavior (Engel et al., 2021; Radke, 2020; Eales, 2022). Engel et al. (2021) concluded that the combined evidence from human and animal studies is sufficient to call for policy actions to reduce phthalate exposure to pregnant women and children and protect against harm to neurodevelopment and neurobehavior (Engel et al., 2021). "

Radke et al. (2020): "Conclusions and implications of key findings: Overall, there is not a clear pattern of association between prenatal phthalate exposures and neurodevelopment. There are several possible reasons for the observed null associations related to exposure misclassification, periods of heightened susceptibility, sex-specific effects, and the effects of phthalate mixtures. Until these limitations are adequately addressed in the epidemiology literature, these findings should not be interpreted as evidence that there are no neurodevelopmental effects of phthalate exposure."

"*Another recent review of human health effects of phthalates concludes that there is robust evidence that phthalates can affect some neurodevelopmental outcomes but that there is a lack of clarity around susceptibility factors and the developmental stage when exposure has the greatest impact remains unclear (Eales et al., 2022)"*

The publication by Eales et al., 2022, reports*:* The overview "**found robust evidence for an association** between phthalates/metabolites …" This is different from the conclusion of robust evidence for neurodevelopmental outcomes. Further, results from environmental epidemiology

[4] Furr et al. (2014) notes that "some C3 and C7 PEs reduce fetal T Prod and alter male rat reproductive development."

are not suitable to provide evidence for a causal relation. Recommend to carefully revisit Section 5.2 of Eales et al. on limitations.

Page 150:

"A third-party reviewed hazard assessment, Greenscreen, categorized DIDP as a high hazard for developmental toxicity." Add proper citation to enable the reader to understand the basis for this Greenscreen claim

DIDP is listed under CA Proposition 65 for potential developmental toxicity; however, it is not classified under EU REACH for any hazard end point, and US CPSC removed the restriction for use in children's products owing to the lack of anti-androgenic effects observed with certain other ortho-phthalates and since the Margin of Exposure (MOE) was sufficiently high when comparing the low exposures and critical NOAEL.

"In laboratory animal studies that exposed pregnant females to DINP during pregnancy and lactation, the most pronounced effects noted were skeletal malformations and kidney abnormalities in offspring (CRE & ACC, 2003)"

Disagree: This is a very selective reading and false citation of the letter by CRE & ACC to EPA; the effects in the Waterman studies do not support what is stated here. Please refer to US CPSC CHAP, which concluded that any developmental risk to humans from DINP is "extremely low or non-existent".

"Phthalates can affect reproductive health in both males and females. Authoritative bodies in the U.S. and other countries share a consensus that phthalates are reproductive toxicants based primarily on the toxicological effects in animals. There is also a body of supporting evidence for these effects in…"

- ⇨ Needs to be specified/corrected to "**some specific phthalates**" as structure activity relations are common knowledge and internationally accepted.

Female reproductive toxicity and preterm birth.

Care needs to be taken in evaluating these epidemiological studies that report associations but no causal relations – findings may be random. There are too many limitations to conclude anything meaningful.

Page 152:

"A *systematic review of male reproductive outcomes for a subset of phthalates concluded that there is moderate to robust evidence of an association between DBP, BBP, DEHP, and DINP and adverse effects on semen quality parameters (Radke et al., 2018) and moderate evidence of DEHP, DINP and DIDP with reduced testosterone in adult men."*

This is what Radke et al. (2019) stated in the abstract:

Conclusions and implications of key findings: Overall, despite some inconsistencies across phthalates in the specific outcomes associated with exposure, these results support that phthalate exposure at levels seen in human populations **may** have male reproductive effects, particularly DEHP and DBP. The relative strength of the evidence reflects differing levels of toxicity as well as differences in the range of exposures studied and the number of available studies.

Please note: associations need to be considered with some care and are not a proof for a causal link. The basic issue is that there is a lot of cross referencing and citing each other to get confirmation for own hypotheses – which is dangerous as there is a risk of bias.

In addition, neither Radke et al. (2018) nor Radke et al. (2019) appear to have discussed DIDP.

Page 152:

"DINP is listed as a carcinogen in California based on neoplastic lesions in liver and mononuclear cell leukemias observed in laboratory rodent studies. EPA recently stated that based on a technical review, the available literature provides evidence that DINP can be reasonably anticipated to cause cancer in humans (CRE & ACC, 2003)."

Correct, but it would be fair to present the complete content of the CRE & ACC document where the EPA ideas were challenged:

> **Kidney:**
>
> CPSC CHAP concluded that the kidney tumors occurred through a rodent-specific mechanism that is unlikely to have relevance to human risk. [CPSC 2001]
>
> **MNCL:**
>
> The CPSC CHAP concluded that **MNCL** was likely to be strain-specific to F-344 rats, with great variance in the rates of spontaneous occurrence in controls, and therefore was "of questionable relevance to humans." [CPSC 2001 at 122] Overall, the **CHAP found that DINP is not plausibly associated with a significant increase in cancer risk in humans.** [CPSC 2001]

Ahern (2019, 2022) ➔ associations, but no causal relations shown. And note, DBP is not genotoxic.

Page 153:

"*Phthalates may increase the risk of type 2 diabetes, gestational diabetes, and insulin resistance in people. In laboratory animals some phthalates can alter glucose balance and impair glucose uptake. Phthalates are associated with glucose homeostasis disruption in people (T. Huang et al., 2014) and they can interact with receptors that may play a role in the development of type 2 diabetes and obesity (Begum & Carpenter, 2021)."*

- ⇨ The major source for human exposure to phthalates is food. Therefore, in case food intake is increased phthalate intake will be increased.
- ⇨ These associations may be a random finding.

The whole chapter “other health effects of concern” is populated with environmental epidemiology studies that report associations but no causal relations.

Page 157:

“Both the liver and kidney are targets of phthalate toxicity in rodents. EPA’s 2022 Technical Review of DINP concluded that DINP produces chronic liver and kidney toxicity in rats. Thus, DINP can reasonably be anticipated to cause serious or irreversible chronic health effects in humans at moderately low to low doses. These include developmental effects, kidney toxicity, and liver toxicity (US EPA, 2022a).”

Reference? Shouldn’t this be: https://www.govinfo.gov/content/pkg/FR-2022-08-08/pdf/2022-16908.pdf#page=1

Further, and again, the EPA proposal is based on historical EPA documents that have not been supported by others; i.e. CPSC CHAP.

Page 158:

Cumulative effects

Add reference: Cumulative Risk Assessment Under the Toxic Substances Control Act | US EPA

Assessment started some weeks ago

Page 163:

Is dust a relevant source of PAE exposure?

Please add the following references and use in the discussion:

Becker K et al. (2004). DEHP metabolites in urine of children and DEHP in house dust. International Journal of Hygiene and Environmental Health 207:409-417. DOI: https://doi.org/10.1078/1438-4639-00309.

Fromme H et al. (2013). Phthalates in German daycare centers: Occurrence in air and dust and the excretion of their metabolites by children (LUPE 3). *Environment international* **61**:64-72. DOI: https://doi.org/10.1016/j.envint.2013.09.006.

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Additional References

Ball GL, McLellan CJ, Bhat VS. 2012. Toxicological review and oral risk assessment of terephthalic acid (TPA) and its esters: A category approach. Crit Rev Toxicol. 42(1): 28–67.

Cousins IT, Mackay D, Parkerton TF. 2003. Physical-chemical properties and evaluative fate modelling of phthalate esters, in Handb Environ Chem: Phthalate Esters, Staples CA, Ed. Springer: Berlin, pp. 57 – 85.

Lagerberg et al. 2015. In Vitro evaluation of the quality of red blood cells collected and stored in systems completely free of DEHP plasticized materials. Transfusion. 55, 522 - 531. https://doi.org/10.1111/trf.12870

Prowse et al. 2014. Commercially available blood storage containers. Int J of Transfusion Medicine (Vox Sanguinis). 106, 1 - 13. https://doi.org/10.1111/vox.12084

Wickson EJ, Ed. 1993. Handbook of PVC formulating. John Wiley & Sons: New York. See Wickson, EJ, Formulation development, pp. 1 – 7; and Krauskopf, LG, Monomeric plasticizers, pp. 212 – 216, for more details.

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