BASF

We create chemistry

August 24, 2020

Toxics in Packaging Clearinghouse
c/o NERC, 139 Main ST., Suite 401
Brattleboro, VT 05301

Filed Electronically at: info@toxicsinpackaging.org

Re: Comments on Draft Model Legislation for Toxics in Packaging, July 9, 2020

Dear TPCH Program Manager:

BASF appreciates the opportunity to comment on the draft update to the Toxics in Packaging Clearinghouse Model Legislation referenced above.[1] BASF Corporation is a subsidiary of BASF SE and is a manufacturer of plasticizers including specialty ortho-phthalates, terephthalates (Palatinol® DOTP), cyclohexane-dicarboxylates (Hexamoll® DINCH), adipates, trimellitates, and polymeric plasticizers. The comments will focus on the proposal to regulate ortho-phthalates as a class and the importance of human biomonitoring data.

Ortho-Phthalates Should Not be Regulated as a Class

It is inappropriate to regulate ortho-phthalates as a class. The reproductive and developmental effects that have driven most of the regulatory action on some of these products depend upon the alcohol chain length; in addition, not all ortho-phthalates show the same adverse effects.[2] For example, the results of a U.S. EPA screening test for effects on fetal rat testosterone and subsequent anti-androgenic effects are summarized in the following table (Fuhr, et al., 2014).[3]

[1] TPCH Requests Comments on Updates to their Model Legislation for Toxics in Packaging, July 9, 2020 https://toxicsinpackaging.org/?wysija-page=1&controller=email&action=view&email_id=14&wysijap=subscriptions&user_id=225

[2] It should be noted that the reproductive and developmental effects depend upon the alcohol chain length and not all ortho-phthalates show the same adverse effects. See Fabjan, E.; Hulzebos, E.; Mennes, W.; Piersma, A. W. "A Category Approach for Reproductive Effects of Phthalates," *Crit. Rev. Tox.*, **2006**, *36*, 695-726.

[3] Furr, J. R.; Lambright, C. S.; Wilson, V. S.; Foster, P. M.; Gray, Jr., L. E. "A Short-Term In Vivo Screen Using Fetal Testosterone Product, a Key Event in the Phthalate Adverse Outcome Pathway, to Predict Disruption of Sexual Differentiation," *Toxicol. Sci.*, **2014**, *140*, 403-424.

BASF Corporation
11750 Katy Freeway
Suite 120
Houston, TX 77079

We create chemistry

Observed effect on rat fetal testis testosterone production

	Alcohol		
Plasticizers	**Carbon chain**	**C Backbone**	**Outcome**
DMP	1	1	Negative
DEP	2	2	Negative
DIBP	4	3	Positive
DBP	4	4	Positive
BBP	4/7	4	Positive
DPenP	5	5	Positive
DHexP	6	6	Positive
DEHP	8	6	Positive
DINP	9	6-9	Weak positive
DPHP	10	7	Negative
DIDP	10	7-9	Negative
Alternatives			
TOTM	8	6	Negative
Hexamoll® DINCH	9	7-9	Negative
DOTP/DEHT	8	6	Negative

The products that were inactive (negative) in these tests are not classified in Europe or other regions for fertility or developmental effects; however, the ones that are active (positive) are classified.

Authoritative government agencies also recognize the differences in the behavior of the various ortho-phthalates. U.S. CPSC lifted the restriction on diisodecyl phthalate (DIDP) and di-n-octyl phthalate (DNOP) in toys and childcare articles based on the absence of these effects.[4] The EU ECHA Risk Assessment Committee (RAC) recently concluded that "no classification for DINP [diisononyl phthalate] for either effects on sexual function and fertility, or for developmental toxicity is warranted."[5]

[4] https://www.federalregister.gov/documents/2017/10/27/2017-23267/prohibition-of-childrens-toys-and-child-care-articles-containing-specified-phthalates.

[5] https://echa.europa.eu/documents/10162/56980740-fcb6-6755-d7bb-bfe797c36ee7.

We create chemistry

Human Biomonitoring

Human biomonitoring (HBM) is an important and well-established tool for conducting exposure assessments that cover all exposure sources and routes, both on an individual and population level.[6] For example, US CPSC used HBM data in their risk assessments of ortho-phthalates.[7] The detection of substances or metabolites in HBM studies alone is not sufficient to classify a material as a "chemical of concern". HBM data have been used to understand the exposures to established chemicals of concern and will be important as alternative materials are developed and used as replacements.

As an example, human biomonitoring methods and data are currently available for four alternative plasticizers: DOTP,[8] DINCH,[9] DEHA,[10] and TOTM.[11] European exposure data are available for all four; U.S. CDC has published U.S. data for DOTP and DINCH. These methods are critical for risk assessments and determining general human exposure.

If you have any questions, please contact me at 346-252-4123 or patrick.harmon@basf.com.

Sincerely yours,

J P Harmon

Patrick Harmon, Ph.D.
Industry Manager Industrial Petrochemicals
BASF Corporation

---

6 Nehring, et al., "Metabolism and urinary excretion kinetics of di(2-ethylhexyl) adipate (DEHA) in four human volunteers after a single oral dose." *Tox Letters* 2020, **321**, 95 – 102.

7 See Footnote 4.

8 Lessmann, F; Schuetze, A; Weiss, T.; Langsch, A.; Otter, R.; Bruening, T.; Koch, H.M. Metabolism and Urinary Excretion Kinetics of Di-(2-Ethylhexyl)terephthalate (DEHTP) in Three Male Volunteers After Oral dosage. *Arch. Toxicol.* 2016, 90, 1659 – 1667; and Silva, M.J.; Wong, L-Y; Samandar, E.; Preau, J.L., Jr.; Jia, L.T.; Calafat, A.M. Exposure to Di-2-ethylhexyl Terephthalate in the U.S. General Population from the 2015–2016 National Health and Nutrition Examination Survey. Environ. Int. 2019, 123, 141 – 147.

9 Schuetze, et al. Additional oxidized and alkyl chain breakdown metabolites of the plasticizer DINCH in urine after oral dosage to human volunteers, *Arch Toxicol,* 2017, 91, 179-188.; and Silva, M. J.; Jia, T.; Samandar, E.; Preau, J. L.; Calafat, A. M. Environmental Exposure to the Plasticizer 1,2-Cyclohexane Dicarboxylic Acid, Diisononyl Ester (DINCH) in US Adults (2000 - 2012), *Environ. Res.*, 2013, 126, 159 - 163. http://dx.doi.org/10.1016/j.envres.2013.05.007.

10 Nehring, et al. Determination of human urinary metabolites of the plasticizer di(2-ethylhexyl) adipate (DEHA) by online-SPE-HPLC-MS/MS, *J Chromatography B* 2019, 1124, 239-246j.

11 Hoellerer, et al. Human metabolism and kinetics of tri-(2-ethylhexyl) trimellitate (TEHTM) after oral administration. *Arch Toxicol,* 2018, 92, 2793-2807.