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December 19, 2019

Via Electronic Mail

Safer Consumer Products Branch
California Department of Toxic Substances Control
P.O. Box 806
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Submitted via CalSAFER Comment Portal

Comments on DTSC Work Plan Implementation: Ortho-phthalates in Food Packaging

Dear Sir or Madam:

BASF Corporation[1] is pleased to submit these comments to the Safer Consumer Products Branch of the California Department of Toxic Substances Control (DTSC) regarding your proposal to evaluate food packaging containing ortho-phthalates for possible designation as Priority Products under the Safer Consumer Products Regulations (SCPR). We appreciate the opportunity to provide public comments on this process.

These comments are in response to the questions presented by DTSC in their "Work Plan Implementation: Phthalates in Food Packaging" background document regarding the use of ortho-phthalates in food packaging.[2] We particularly would like to address which alternatives are available and how they might be used in food packaging and other food contact applications.

Alternatives to ortho-Phthalates

What alternatives are being used as plasticizers in food packaging?

The background document states that "it is unclear what chemical alternatives for OPs are currently available and being used in specific food packaging applications." The FDA publication referenced in the DTSC document (Carlos, et al., 2018) is likely not an exhaustive review of plasticizers used in food contact applications; however, it is, to our knowledge, representative and useful.[3]

In addition to the ortho-phthalates DEHP, DINP, and DIDP, several other plasticizers were found in the FDA testing, including acetyl tributyl citrate (ATBC), di-2-ethylhexyl adipate (DEHA or DOA), diisononyl adipate (DINA), epoxidized soybean oil (ESBO), di-2-ethylhexyl

[1] BASF Corporation is a subsidiary of BASF SE and is a manufacturer of plasticizers including some ortho-phthalates as well as di-2-ethylhexyl terephthalate, adipates, trimellitates, and polymeric plasticizers.

[2] See Work Plan Implementation: Phthalates in Food Packaging, October 2019, available at https://dtsc.ca.gov/wp-content/uploads/sites/31/2019/10/Final-Public-Background-Document_FoPa_Ortho-phthalates.pdf.

[3] Carlos, de Jager, and Begley, "Investigation of the primary plasticizers present in polyvinyl chloride (PVC) products currently authorized as food contact materials," *Food Add. Contam.: Part A,* 2018, 35, 1214 – 1222.

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terephthalate (DEHT or DOTP), and diisononyl cyclohexane-1,2-dicarboxylate (DINCH). Table I summarizes the regulatory status and commercial availability of these products.

Table I. Non-ortho-phthalate plasticizers reported in Carlos, et al. 2018.

Plasticizer	FDA	EU EFSA	Availability (US, Canada) [1]	Comments[2]
ATBC CAS# 77-90-7	Prior sanctioned 21 CFR 181.27 21 CFR 175.105 21 CFR 175.300 21 CFR 176.170 21 CFR 176.180 21 CFR 177.1210 21 CFR 177.2600 21 CFR 178.3740	93760 SML = 60 mg/kg	Vertellus	Tubing and cap gaskets.
DEHA CAS# 103-23-1	21 CFR 175.105 21 CFR 177.1200 21 CFR 177.1210 21 CFR 177.2600 21 CFR 177.1400 21 CFR 178.3740	31920 SML = 18 mg/kg	BASF, Eastman, PolyOne, and imports	Food service and commerical wraps. Also used as a secondary plasticizer to improve low temperature performance.
DINA CAS# 33703-08-1	21 CFR 178.3740		BASF, ExxonMobil, PolyOne	Food service and commerical wraps. Also used as a secondary plasticizer to improve low temperature performance.
ESBO CAS# 8013-07-8	Prior sanctioned 21 CFR 181.27 21 CFR 172.723 21 CFR 175.105 21 CFR 175.300 21.CFR 177.1650 21 CFR 178.3910	88640 SML = 60 mg/kg (baby foods = 30 mg/kg)	Arkema, Galata Valtris	Cap gaskets for non-alcoholic bottled drinks and jarred foods.
DOTP CAS# 6422-86-2	FCN 1056 (Eastman, PVC) FCN 1473 (BASF, PVC) FCN 1778 (BASF nitrile rubber) 21 CFR 177.1210	92200 SML = 60 mg/kg	BASF, Eastman, and imports	Tubing and cap gaskets for bottled beer and jarred foods.
DINCH CAS# 474919-59-0, 166412-78-8		45705 SML = 60 mg/kg	Imported (BASF and others)	Reported in one imported cap gasket for jarred foods.

[1] IHS Markit, Plasticizers, 2018.
[2] Uses as reported in Carlos, et al., 2018.
FCN Food contact notification
SML Specific migration limit; all additives limited to 60 mg/kg, but some substances have a lower SML.

These six plasticizers have been commercially available for a number of years and are well characterized with respect to health and safety:

1. Acetyl tributyl citrate (ATBC) – The plasticizer has been used in applications such as toys and food contact materials for many years. The most recent assessment of the toxicology data is in a review commissioned by the U.S. Consumer Product Safety Commission (CPSC).[4] TCO Certified includes it in their Acceptable Substances List

[4] https://www.cpsc.gov/s3fs-public/Toxicity%20Review%20of%20ATBC.pdf?AsgeTCxYY0_3F.wMkaokmHmiD5LWh.zO.

(ASL) based on a GreenScreen® Benchmark score of 3.[5] We don't have access to the GreenScreen® assessment by ToxServices; however, this appears to be a reasonable Benchmark score based on our review of the available data (see Table II). In Europe, under EFSA regulations, it is only subject to the general specific migration limit (SML) of 60 mg/kg.

2. Di-2-ethylhexyl adipate (DEHA or DOA) and diisononyl adipate (DINA) – DEHA, and to a lesser extent DINA, have been used for more than 20 years as plasticizers in vinyl commercial and food service film (typical consumer cling films are made with polypropylene). DEHA performs well in this application due to oxygen permeability of films plasticized with it.[6] Outside of this application, DEHA and DINA are not usually used as primary plasticizers but as secondary plasticizers in formulations to improve low temperature flexibility.[7] In this regard they are not replacements for ortho-phthalates such as DEHP and DINP but are specialty additives used to meet a particular technical requirement. In Europe, under EFSA regulations, DEHA is subject to a SML of 18 mg/kg.

   DEHA and DINA have been reviewed in assessments commissioned by US CPSC.[8] They also are included in the TCO Certified ASL with GreenScreen® Benchmark scores of 2.[9] We do not have access to the full assessment but consider this to be a conservative conclusion. DEHA has an almost complete dataset that shows overall low hazard (Table II). We assume it was assigned a moderate cancer classification since it is an EPA Class C carcinogen; however, it is IARC Class 3 (not classifiable), and the observed tumors are attributed to peroxisome proliferation (likely not relevant to humans) and were seen in mice but not in rats or dogs.

3. Di-2-ethylhexyl terephthalate (DOTP, DEHT) – DOTP is cleared by U.S. FDA for use in closures with sealing gaskets in food containers (21 CFR 177.1210), and through three Food Contact Notifications (FCN). The FCN's are manufacturer specific and are available from Eastman (No. 1056, vinyl repeat use applications) and BASF (1473, vinyl repeat use applications, and 1778, nitrile rubber repeat use applications).[10] In Europe, under EFSA regulations, it is only subject to the general specific migration limit (SML) of 60 mg/kg.

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5 https://tcocertified.com/accepted-substance-list/

6 Sears, J. K. and Darby, J. R., *The Technology of Plasticizers* (John Wiley & Sons: New York), 1982, p. 443.

7 Grossman, R. F., ed., *Handbook of Vinyl Formulating*, 2nd Edition, Wiley Interscience, 2008.

8 https://www.cpsc.gov/s3fs-public/Toxicity%20Review%20of%20DEHA.pdf?TSiSSb20aUy68dV0qk1AllBUrIaPFSaE and https://www.cpsc.gov/s3fs-public/ToxicityReviewforDiisononylAdipate062019.pdf?vM1E2MpKwInTRd11A7yyAUAZq8gAn2Xl.

9 See Ref 5.

10 See FDA FCN database: https://www.fda.gov/food/packaging-food-contact-substances-fcs/inventory-effective-food-contact-substance-fcs-notifications,

DOTP has a full toxicological profile and no relevant hazards. It has been reviewed by EFSA,[11] ANSES under the EU RMOA process,[12] NSF International,[13] and more recently by US CPSC.[14] Three GreenScreen® profilers agreed on a consensus Benchmark score of 3_{DG}, with only a data gap for "endocrine activity". As noted in Harmon and Otter (2018), BASF has concluded there is no data gap for this end point based on in vitro data and in vivo data from various chronic and subchronic studies.[15] The two commercial U.S. made products are listed in the CleanGredients® database that is based on the US EPA Safer Choice criteria.

4. Diisononyl cyclohexane-1,2-dicarboxylate (DINCH) – DINCH (e.g., Hexamoll® DINCH from BASF) has broad global clearances for food contact applications outside the US (EFSA, Japan, China, Canada, Australia); however, it does not have a specific clearance by US FDA. Beyond food contact uses, it is used globally for applications with close human contact, such as those involving toys, medical devices, and indoor products.

   The BASF product has an extensive toxicological database and has been assessed by EFSA,[16] US CPSC,[17] Australia (NICNAS),[18] NSF International,[19] and ANSES under the RMOA process.[20] A GreenScreen® profiler raised concerns about endocrine activity (thyroid effects) and assigned a classification of moderate (overall Benchmark score is

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[11] European Chemicals Agency (ECHA), "Guidance on Information Requirements and Chemical Safey Assessment, Chapter R.7a: Endpoint Specific Guidance, Version 4.1," October 2015. [Online]. Available: http;//echa.europa.eu/documents/10162/13632/information_requirements_r7a_en.pdf. [Accessed 21 August 2016].

[12] ANSES, "Risk Management Options Analysis (RMOA) - Diethylhexyl Terephthalate," January 2016. [Online]. Available: https://www.echa.europa.eu/documents/10162/dd0220b0-1187-4c2b-8991-51ddbbc9d462. [Accessed 18 May 2016].

[13] Ball, G. L.; McLellan, C. J.; Bhat, V. S. "Toxicological Review and Oral Risk Assessment of Terephthalic Acid and Its Esters: a Category Approach," *Crit. Rev. Tox*., 2012, 42, 28-67. DOI: 10.3109/10408444.2011.623149.

[14] https://www.cpsc.gov/s3fs-public/Toxicity%20Review%20of%20DEHT.pdf?FObpuBBqgypVtw7gIEGMFXHN5H7vbeEz.

[15] Harmon, J. P. and Otter, R. "Green Chemistry and the Search for New Plasticizers," *ACS Sustainable Chem. Eng.* **2018**, 6, 2078 – 2085.

[16] European Food Safety Authority (EFSA), "Opinion of the Scientific Panel on Food Additives, Flavorings, Processing Aids and Materials in Contact with Food (SFC). The EFSA Journal 395 to 401:1-221," 2006. [Online]. Available: http://echa.europa.eu/documents/10162/13632/information_requirements_r7a_en.pdf. [Accessed 20 June 2016].

[17] https://www.cpsc.gov/s3fs-public/Toxicity%20Review%20of%20DINX.pdf?n_tDo9yqCvnxEdDVuINE7tQba9lrg_XQ.

[18] National Industrial Chemicals Notification and Assessment Scheme (NICNAS), "Public Report: 1,2-Cyclohexanedicarboxylic Acid, 1,2-Diisononyl Ester ("Hexamoll DINCH"), File No: EX/170 (STD/1259)," 2012. [Online]. Available: https://www.nicnas.gov.au/__data/assets/word_doc/0003/6699/EX170FR.docx. [Accessed 21 June 2016].

[19] Bhat, V. S.; Durham, J. L.; Ball, G. L.; English, J. C. "Derivation of An Oral Reference Dose (RfD) for the Non-Phthalate Alternative Plasticizer 1,2-Cyclohexane Dicarboxylic Aicd, Di-Isononyl Ester (DINCH)," *J. Toxicol. Environ. Health B: Crit. Rev*., 2014, 17, 63-94. http://dx.doi.org/10.1080/10937404.2013.876288.

[20] ANSES, "Analysis of the Most Appropriate Risk Management Option (RMOA) - 1,2 Cyclohexanedicarboxylic Acid, Diisononyl Ester (DINCH)," January 2016. [Online]. Available: https://www.echa.europa.eu/documents/10162/fc77bffd-e7ec-4846-b080-11de2564e582. [Accessed 21 March 2016].

2); however, BASF disagrees with this conclusion (see Harmon and Otter, 2018 for more details).

5. Epoxidized soybean oil (ESBO) – ESBO is cleared under various 21 CFR sections and is listed as prior sanctioned. Many PVC formulations incorporate ESBO at around 2–5 parts per hundred parts of PVC resin. ESBO is used for plasticization and heat stabilization; this is due to the observed synergism with mixed-metal stabilizers that provides resistance to heat and sunlight.[21] In the Carlos, et al., 2018, study, it was found in several cap gaskets for jarred foods.

   The toxicological profile shown in Table II indicates an overall low hazard concern. It also has been reviewed by EFSA[22] and US CPSC.[23] The TCO Certified ASL reports a Benchmark score of 3; however, we do not have access to the full assessment.

Table II – Hazard Summary Plasticizers in Food Contact

Endpoint	DOTP	ATBC	DEHA	DINA	ESBO	DINCH
Assessment by:	NSF	BASF	BASF	BASF	BASF	NSF
Data source	BASF	REACH dossier, SDS, CPSC				BASF
Cancer	L	L	M, EPA C, IARC 3	*Read across*	L	L
Mutagenicity	*L*	L	L	L	L	L
Reproductive	L	L	L	*Read across*	L	L
Developmental	L, rat and rabbit	No full pre-natal	L, rat and rabbit	*Read across*	L	L, rat and rabbit
Endocrine Activity	dg	dg	dg	dg	dg	M
Acute Toxicity	L	L	L	L	L	L
Systemic Toxicity	L	L	L	L	L	L
Neurotoxicity	L	dg	*L*	*L*	*L*	L
Skin Sensitization	L	L	L	*QSAR*	L	L
Respiratory Sensitization	*L*	*L*	*L*	*L*	*L*	*L*
Skin Irritation	L	L	L	L	M	M
Eye Irritation	L	L	L	L	L	L
Aquatic Toxicty	L	M	L	L	L	L
Chronic Aquatic Toxicity	L	L	L	*Read across*	dg	L
Persistence	vL	M	*L*	L	L	M
Bioaccumlation	L	L	L	*Read across*	dg	L

[21] Malveda, M., et al., *Plasticizers*, IHS Markit, 2018.

[22] EFSA (European Food Safety Authority) (2006). Opinion of the scientific panel on food additives, flavourings, processing aids and materials in contact with food related to exposure of adults to epoxidised soybean oil used in food contact materials. ESFA Journal 332,1-9.

[23] https://www.cpsc.gov/s3fs-public/ToxicityReviewforEpoxidizedSoybeanOil062019.pdf?LVXyPPxn8xq7shrxW2dBtF_lqU9rGPy_.

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Additional alternatives

A few other FCN's have been filed for plasticizers in food contact applications over the past 10 years and are summarized in Table III below:

Table III – Hazard and FCN Summary for Additional Plasticizers

Endpoint	Tri-2-ethylhexyl trimellitate (TOTM)	Castor Oil based	Pentaerythritol tetrapentanoate	Epoxided soya, 2EH esters
CAS No.	3319-31-1	736150-63-3	15834-04-5	68082-34-8
Assessment by:	BASF	BASF	BASF	BASF
FCN/ 21CFR / EFSA*	FCN 1771 (BASF), 50% in vinyl, all food types.	FCN 1126 (Danisco), 50% in vinyl, non-fatty foods, <15% alcohol. EFSA SML = 60 mg/kg (55910)	FCN 1967 (Perstorp), 31% in vinyl, all food types.	FCN 1417 (Galata), 15% in vinyl, aqueous and dry non-fatty foods, <15% alcohol.
Data source	REACH dossier, SDS, other			
Cancer	dg	dg	dg	dg
Mutagenicity	*Low*	Negative	Negative	*L*
Reproductive	Moderate, OECD 421	Low, OECD 416	dg	*Read across*
Developmental	Low, OECD 414	Low, OECD 414	*Read across*	dg
Endocrine Activity	dg	dg	dg	dg
Acute Toxicity	Low	Low	*Read across*	*Read across*
Systemic Toxicity	Low	OECD 408	Negative	*Read across*
Neurotoxicity	*Low*	*Low*	dg	dg
Skin Sensitization	Low	Non-sensitizing	*QSAR, Read across*	*Read across*
Respiratory Sensitization	*Low*	*Low*	dg	dg
Skin Irritation	Low	Not irritating	*QSAR, Read across*	*Read across*
Eye Irritation	Low	Not irritating	dg	*Read across*
Aquatic Toxicty	Low	Low	*Read across*	Low
Chronic Aquatic Toxicity	Low	Low	dg	dg
Persistence	Moderate	Readily biodegradable	Readily biodegradable	Readily biodegradable
Bioaccumlation	Moderate	Moderate	*Read across*	*Low, QSAR*

* All FCNs restricted to repeat-use applications.

To our knowledge and based on the Carlos, et al. results, these four have limited use in food contact applications, particularly for food packaging. Some also have limited toxicological data; however, FDA data requirements depend on the expected migration into food, and monomeric plasticizers show negligible migration in aqueous and low alcohol foods (i.e., minimal data are required for these uses).

The TCO Certified ASL includes tri-2-ethylhexyl trimellitate (TOTM) based on a Benchmark 2 score by one profiler. We do not have access to the full assessment; however, this appears to be a reasonable conclusion. In addition, TOTM was negative in the rat fetal testosterone screen by EPA (Furr, et al.), which suggest the absence of anti-androgenic effects seen with some ortho-phthalates.[24] TOTM also was recently reviewed by CPSC.[25]

The castor oil-based plasticizer (COMGHA) has been reviewed by EFSA and CPSC.[26] There do not appear to be any publicly available assessments for the two other plasticizers, but information is available in the respective REACH dossiers.[27]

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[24] 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.

[25] https://www.cpsc.gov/s3fs-public/Toxicity%20Review%20of%20TOTM.pdf?Yjo0hEI05eJsEziyutApCzEobdUITWhX.

[26] https://www.cpsc.gov/s3fs-public/ToxicityReviewforCOMGHA062019.pdf?72HODKVckDhmujTYsOFVPcKfu.vwCMpr.

[27] https://echa.europa.eu/web/guest/information-on-chemicals/registered-substances.

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Human Biomonitoring

Human biomonitoring methods and data are available for four of the plasticizers discussed in this document, DOTP,[28] DINCH,[29] DEHA,[30] and TOTM.[31] 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,

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[28] 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.

[29] 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.

[30] 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.

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