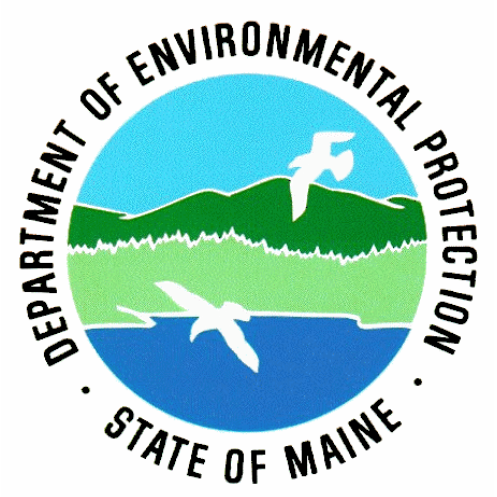

Toxic Chemicals in Food Packaging

Food Contact Chemicals of High Concern Criteria Documentation

Prepared by
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Food Packaging Chemicals of High Concern Listing Criteria

Summary

In June 2019, Maine's *Toxic Chemicals In Food Packaging* legislation [LD 1433, 128th Legislature] was signed into law, adding Chapter 26-B to the already established *Act To Protect the Environment and Public Health by Further Reducing Toxic Chemicals in Packaging* (32 MRSA §§1731-1747). Amendments included adding a tiered system of chemical listing for the purposes of assessing chemicals currently used in food packaging and pursuing safer alternatives.

These new sections of law require the Department to publish a list of no more than 10 food contact chemicals of high concern in order to gather information on their use in food packaging available in Maine (32 MRSA §1742). To be listed as a food contact chemical of high concern in this context the chemicals must meet the following criteria:

- present on Maine's Chemicals of Concern list published in accordance with Title 38, section 1693; or
- has been identified by an authoritative governmental entity as:
    - a carcinogen, reproductive or developmental toxicant or an endocrine disruptor;
    - persistent, bioaccumulative and toxic; or
    - very persistent and very bioaccumulative.

The Department must also determine that there is strong credible scientific evidence that the chemical is a reproductive or developmental toxicant, endocrine disruptor or human carcinogen; and
that there is strong credible scientific evidence that the chemical meets one or more of the following exposure based criteria:

- found through biomonitoring studies to be present in human blood, human breast milk, human urine, or other human bodily tissues or fluids;
- found through sampling and analysis to be present in a food or beverage product; or
- has been added to or is present in a food package.

After meeting the criteria for designation as a food contact chemical of high concern, the Department may elevate any of those substances to priority status if the food contact chemical meets the following additional exposure based criteria (32 MRSA §1743):

- has been found through biomonitoring to be present in human blood, including umbilical cord blood, breast milk, urine or other human bodily tissues or fluids;
- has been found through sampling and analysis to be present in a food or beverage product; or
- is present in a food package.

When priority food contact chemicals are identified, a manufacturer or distributor of a food package available for sale in the State that contains a chemical on this list, in an amount greater

than the de minimis, must report this use to the Department within 180 days. This information provides the Department with a clearer understanding of how people might be exposed to these chemicals through food packaging sold in Maine.

If the Department determines that more information is necessary to assess the potential for exposure or to better understand the availability of safer alternatives to the priority food contact chemical, additional information may be requested. Examples of additional information include the extent to which users of the food package are likely to be exposed to the chemical, the likelihood that the chemical will be released into the environment, the extent to which the chemical is known to be present in the environment or human body, or an alternative assessment meeting specific criteria.

This document provides chemical specific information about the toxicity and exposure criteria for substances proposed for listing as a food contact chemical of high concern based on the statutory mandate described above. This document represents the Department's findings based on a preliminary scientific literature search for references that meet the listing criteria and is not intended to be comprehensive.

Food Packaging Chemicals of High Concern Listing Criteria

Bisphenol structure

Because the bisphenol chemical structure of two phenols connected by carbon and hydrogen are so similar for bisphenol A, bisphenol B, bisphenol S, and bisphenol F, these four chemicals are listed together as one group of reportable substances.

Bisphenol A

CAS 80-05-7

Bisphenol A (BPA) has been commonly used in food packaging plastics for its ability to make the material particularly durable. Though there are a variety of uses for BPA in consumer products, the primary exposure source for most people is through food packaging.[1] In 2017, the European Chemicals Agency identified BPA as a Substance of Very High Concern based on its classification as a Reproductive Toxicant Category 1B.[2] Concern for the human health effects of BPA have also been affirmed by its designation as a Category 1 Endocrine Disruptor by the European Union[3,4] and by the U.S. EPA's notable concern for BPA's potential reproductive and developmental toxicity.[1] The U.S. National Toxicology Program also concluded that there is "some concern" for the potential effects of BPA on human health.[5] Because of this, many regulatory agencies have expressed concern for the scope of this chemical's use related to human health and environmental impacts.

Exposure concern is established by the U.S. CDC report that BPA was confirmed to be present in 93% of people tested.[6,7]

1. U.S. Environmental Protection Agency. (2010). *Bisphenol A Action Plan*. March 29, 2010.
2. European Chemicals Agency (ECHA). (2016). *Member State Committee Support Substance of Very High Concern Because of Its Toxic For Reproduction (Article 57 C) Properties*. Adopted 2 December 2016.
3. European Commission DG Environment. (2000). *Towards the establishment of a priority list of substances for further evaluation of their role in endocrine disruption. Final Report.* Annex 10. 10 November 2000.
4. European Chemicals Agency (ECHA). (2017). *Endocrine Disruptor Assessment for Bisphenol A* (concluded by France). Helsinki, 16 June 2017.
5. U.S. Department of Health and Human Services. National Toxicology Program (NTP) - Center for the Evaluation of Risks to Human Reproduction (CERHR). (2008). *NTP-CERHR Monograph on the Potential Human Reproductive and Development Effects of Bisphenol A.* NIH Publication No. 08-5994.
6. U.S. Centers for Disease Control and Prevention (CDC). National Health and Nutrition Examination Survey 2003–2004 Laboratory Files.
7. Calafat, AM, X Ye, Y-L Wong, JA Reidy, and LL Needham. (2008). "Exposure of the U.S. Population to Bisphenol A and 4-tertiary-Octylphenol: 2003-2004." *Environ Health Perspect* 2008:116:39-44.

Food Packaging Chemicals of High Concern Listing Criteria

Bisphenol B
CAS 77-40-7

Known to be used as a substitute for BPA in plastics and epoxy resin, the extent of bisphenol B (BPB) use in food packaging is unclear. With evidence of effects on reproductive system function,[1] BPB has been shown to mimic BPA in the human body due to its structural similarities.[2] BPB is classified as a Category 1 Endocrine Disruptor by the European Union, as referenced in the criteria for the chemical's inclusion on Maine's Chemicals of Concern list.[3,4]

BPB has been measured in women with illness related to sensitivity of endometriotic cells which resulted in increased disease growth.[5] Other studies have confirmed BPB's presence in food.[6]

References

1. Sera, et al. (2019). "Evidence for Bisphenol B Endocrine Properties: Scientific and Regulatory Perspectives." *Environmental Health Prospect* 2019 October; 127(10): 106001.
2. Ijaz, et al. (2020). "Exposure of BPA and its alternatives like BPB, BPF, and BPS impair subsequent reproductive potential in adult female Sprague Dawley rats." *Toxicol Mech Methods* 2020 Jan;30(1):60-72.
3. Maine Department of Environmental Protection Chemicals of Concern Listing Criteria. (2011). European Union Endocrine Disruptor Chemical Assessment.
4. Petersen, et al. (2007). *Revised Report to European Commission DG Environment*. *Study on enhancing the Endocrine Disrupter priority list with a focus on low production volume chemicals.* ENV.D.4/ETU/2005/0028r. p.242. May 2007.
5. Cobellis, et al. (2009). "Measurement of bisphenol A and bisphenol B levels in human blood sera from healthy and endometriotic women." *Biomed Chromatogr* 2009 Nov; 23(11):1186-90.
6. Grumetto, et al. (2008). "Determination of Bisphenol A and Bisphenol B Residues in Canned Peeled Tomatoes by Reversed-Phase Liquid Chromatography." *Journal of Agricultural and Food Chemistry* 2008 Nov:56(22); 10633-10637.

Bisphenol S
CAS 80-09-1

Known to be used as an alternative to BPA, U.S. EPA's assessment of structurally similar bisphenols revealed evidence that bisphenol S (BPS) is moderately toxic for reproductive and developmental effects, in addition to the potential for estrogenic activity that may interfere with endocrine function.[1]

Widespread exposure to BPS is a concern as studies confirm its detection in humans throughout the world[2,3] and in several types of U.S. food samples[4]. Data from the National Health and Nutrition Examination Survey (NHANES) 2013-2014 reported high detection frequencies of BPS in urine from U.S. adults.[5]

A U.S. National Toxicology Program (NTP) study of alternatives to BPA concluded that there is widespread use of a suite of alternatives in the bisphenol structural family, particularly BPS, and given their similarities, NTP concluded that further testing and reconsideration for their use as alternatives in consumer products should be examined.[6]

1. United States Environmental Protection Agency (US EPA). (2014). *Bisphenol A Alternatives In Thermal Paper* (Final Report January 2014). U.S. Environmental Protection Agency, 2014.
2. Liao, et al. (2012). "Bisphenol S in Urine from the United States and Seven Asian Countries: Occurrence and Human Exposures." *Environ. Sci. Technol* 2012; 46, 12, 6860-6866.
3. Philips, et al. (2018). "Bisphenol and phthalate concentrations and its determinants among pregnant women in a population-based cohort in the Netherlands, 2004-5." *Environ Res* 2018; 161,562-572.
4. Liao, C., Kannan, K. (2013). "Concentrations and profiles of bisphenol A and other bisphenol analogues in foodstuffs from the United States and their implications for human exposure." *J Agr Food Chem* 2013; 61(19):4655-4662.
5. U.S. Center for Disease Control, National Health and Nutrition Examination Survey (NHANES) Examination Data 2013-2014.
6. U.S. Department of Health and Human Services, National Toxicology Program (NTP). (2017). *NTP Research Report on Biological Activity of Bisphenol A (BPA) Structural Analogues and Functional Alternatives.* October 2017. NTP Research Report 4. ISSN: 2473-4756.

Bisphenol F
CAS 620-92-8

Bisphenol F (BPF) was also included in U.S. EPA's assessment of structurally similar bisphenols used as alternatives to BPA, which revealed that BPF is moderately toxic for reproductive effects and an estimated high hazard toxicity for developmental effects.[1] EPA's assessment also concluded that data show BPF to exhibit androgenic and anti-androgenic activity.[1]

Other studies have found that BPF shows the propensity to have both estrogenic and anti-androgenic action, concluding that BPF may be as potent as BPS in its estrogenic activity.[2]

A study of a variety of commercially available food items found that of the bisphenol analogues measured, BPF was one of the more predominant chemicals.[3,4]

Found to be present in the U.S. civilian population, BPF was detected in over half of the urine samples analyzed as part of the NHANES 2013-2014 survey.[5]

1. United States Environmental Protection Agency (US EPA). (2014). *Bisphenol A Alternatives In Thermal Paper* (Final Report January 2014). U.S. Environmental Protection Agency, 2014.
2. Rochester, J.R. and Boden, A. L. (2015). "Bisphenol S and F: Systemic review and comparison of the hormonal activity of bisphenol A substitutes." *Environ. Health Prospect* 2015:123(7), 643-650.
3. Liao, C., Kannan, K. (2013). "Concentrations and profiles of bisphenol A and other bisphenol analogues in foodstuffs from the United States and their implications for human exposure." *J Agr Food Chem* 2013; 61(19):4655-4662.
4. Cacho, J., Campillo, N., Vinas, P., Hernandez-Cordoba, M. (2012). "Stir bar sorptive extraction coupled to gas chromatography-mass spectrometry for the determination of bisphenols in canned beverages and filling liquids of canned vegetables." *J Chromatogr A.* 2012; 1247:146-153.
5. U.S. Center for Disease Control, National Health and Nutrition Examination Survey (NHANES) Examination Data 2013-2014.

Food Packaging Chemicals of High Concern Listing Criteria

4-octyl phenol

CAS 1806-26-4

The chemical 4-octyl phenol is often used as an intermediate in manufacturing processes and is common in plastics which may become food packaging. This chemical has been listed on Maine's Chemicals of High Concern as a Category 1 Endocrine Disruptor based on classification by the European Union.[1]

4-octyl phenol has been detected in commonly available foods.[2]

1. European Commission DG Environment. (2002). *Endocrine Disruptors: Study On Gathering Information On 435 Substances With Insufficient Data* (Final report B4-3040/2001/325850/MAR/C2). p.119. 15 November 2002.
2. Cacho, J.I., Campillo, N., Vinas, P., Hernandez-Cordoba, M. (2012). "Determination of alkylphenols and phthalate esters in vegetables and migration studies from their packages by means of stir bar sorptive extraction coupled to gas chromatography–mass spectrometry." *Journal of Chromatography A* 1241, 21-27.

Octamethyl cyclotetrasiloxane (D4)

CAS 556-67-2

Used in as an intermediate for silicone polymers, octamethyl cyclotetrasiloxane (D4) met the criteria to be listed on Maine's Chemicals of High Concern due to its Category 1 Endocrine Disruptor classification by the European Union.[1,2] Suspected of damaging human fertility, D4 is also classified as a Category 2 Reproductive Toxicant by the European Union.[3]

Separate studies of European adults found D4 to be present in human blood.[4,5]

1. Maine Department of Environmental Protection Chemicals of Concern Listing Criteria. (2011). European Union Endocrine Disruptor Chemical Assessment.
2. Peterson, G., Rasmussen, D., Gustavson, K. (2007). *Revised Report to European Commission DG Environment*. *Study on enhancing the Endocrine Disrupter priority list with a focus on low production volume chemicals.* May 2007. ENV.D.4/ETU/2005/0028r.
3. European Union Regulation No 1272/2008 of the European Parliament and of the Council of 16 December 2008 on classification, labelling and packaging of substances and mixtures.
4. Hanssen, L., Warner, N., Braathen, T., Odland, J.O., Lund, E., Nieboer, E., Sandanger, T.M. (2013). "Plasma concentrations of cyclic volatile methylsiloxanes (cVMS) in pregnant and prostmenopausal Norwegian women and self-reported use of personal care products." *Environment International* 51, 82-87.
5. Fromme, H., Cequier, E., Kim, J.T., Hanssen, L., Hilger, B., Thomsen, C., Chang, Y.S., Volkel, W. (2015). "Persistent and emerging pollutants in the blood of German adults: Occurrence of dechloranes, polychlorinated naphthalenes, and siloxanes." *Environment International* 85, 292-298.

Toluene
CAS 108-88-3

Most commonly used in the production of polymers and as an ink solvent, toluene is listed on Maine's Chemicals of High Concern for its Category 1 Reproductive Toxicant classification by the Globally Harmonized System of Classification and Labelling.[1]

Biomonitoring studies human urine have revealed that the general population is exposed to toluene.[2-8]

1. Maine Department of Environmental Protection. (2015). *Maine CDC Chemical of High Concern Chemical-Specific Inclusion Criteria*. July 21, 2015.
2. Klaassen, C.D. (2008). "The Basic Science of Poisons." Casarett and Doull's Toxicology. 7th ed. New York, NY: McGraw-Hill, 2008., p. 1010.
3. U.S. Center for Disease Control (CDC). (2015). *Fourth National Report on Human Exposure to Environmental Chemicals. Blood Toluene (2001 – 2006).* Centers for Disease Control and Prevention, Atlanta, Ga.
4. Elliott, L., Longnecker, M. P., Kissling, G. E., London, S. J. (2006). "Volatile organic compounds and pulmonary function in the Third National Health and Nutrition Examination Survey, 1988-1994." *Environmental Health Perspectives* 114(8): 1210-1214.
5. Kim, S. R., Halden, R. U., Buckley, T. J. (2007). "Volatile organic compounds in human milk: Methods and measurements." *Environmental Science Technology* 41(5): 1662-1667.
6. Sexton, K., Adgate, J. L., Church, T. R., Ashley, D. L., Needham, L. L., Ramachandran, G., Fredrickson, A. L., Ryan, A. D. (2005). "Children's exposure to volatile organic compounds as determined by longitudinal measurements in blood." *Environmental Health Perspectives* 113(3): 342-348.
7. Sexton, K., Adgate, J. L., Fredrickson, A. L., Ryan, A. D., Needham, L. L., Ashley, D. L. (2006). "Using biologic markers in blood to assess exposure to multiple environmental chemicals for inner-city children 3 - 6 years of age." *Environmental Health Perspectives* 114(3): 453-459.
8. Woodruff, T.J., Zota, A.R., Schartz, J.M. (2011). "Environmental chemicals in pregnant women in the United States: NHANES 2003-2004." *Environmental Health Perspectives* 119:878-885.

Food Packaging Chemicals of High Concern Listing Criteria

Styrene
CAS 100-42-5

Styrene is commonly used as a monomer for various types of plastic material, including some that may become food packaging. Listed as one of Maine's Chemicals of High Concern, styrene is classified as a Category 1 Endocrine Disruptor by the European Union.[1,2] More recently, styrene has been classified by the International Agency for Research on Cancer as a Group 2A Carcinogen.[3]

Styrene has been found to be present in humans through several biomonitoring studies.[4,5,6,7]

1. Maine Department of Environmental Protection. (2015). *Maine CDC Chemical of High Concern Chemical-Specific Inclusion Criteria*. July 21, 2015.
2. European Commission DG Environment. (2000). *Towards the establishment of a priority list of substances for further evaluation of their role in endocrine disruption. Final Report.* Annex 10. 10 November 2000.
3. World Health Organization, International Agency for Research on Cancer (IARC). (2019). *IARC Monographs on The Definition of Carcinogenic Hazards to Humans, Vol. 60, 82, 121*.
4. U.S. Center for Disease Control (CDC). (2015). *Fourth National Report on Human Exposure to Environmental Chemicals. Blood Styrene (2001 – 2006).* Centers for Disease Control and Prevention. Atlanta, Ga.
5. Elliott, L., Longnecker, M. P., Kissling, G. E., London, S. J. (2006). "Volatile organic compounds and pulmonary function in the Third National Health and Nutrition Examination Survey, 1988-1994." *Environmental Health Perspectives* 114(8): 1210-1214.
6. Sexton, K., Adgate, J. L., Church, T. R., Ashley, D. L., Needham, L. L., Ramachandran, G., Fredrickson, A. L., Ryan, A. D. (2005). "Children's exposure to volatile organic compounds as determined by longitudinal measurements in blood." *Environmental Health Perspectives* 113(3): 342-348.
7. Sexton, K., Adgate, J. L., Fredrickson, A. L., Ryan, A. D., Needham, L. L., Ashley, D. L. (2006). "Using biologic markers in blood to assess exposure to multiple environmental chemicals for inner-city children 3 - 6 years of age." *Environmental Health Perspectives* 114(3): 453-459.

Food Packaging Chemicals of High Concern Listing Criteria

Benzene
CAS 71-43-2

Benzene has been known to be used in plastics, detergents, and dyes which may find their way into the materials used for food packaging. Classified as a known human carcinogen by the U.S. Department of Health and Human Services[1], a Group 1 Carcinogen by the International Agency for Research of Cancer[2], and Category 1A Carcinogen the European Union,[3] benzene has been shown to cause harm thorough many routes of exposure.[4]

Concern for exposure through our food supply is confirmed by the U.S. Food and Drug Administration's Total Diet Study, which measured benzene in an assortment of commonly available food.[5] Exposure to benzene in the general population is prevalent as has been confirmed through numerous biomonitoring studies.[6-13]

1. U.S. Department of Health and Human Services, Agency Toxic Substance and Disease Registry. (2007). *Toxicological Profile for Benzene* August 2007.
2. World Health Organization, International Agency for Research on Cancer. (1987). IARC Monographs on the Evaluation of Carcinogenic Risks to Humans, Supplement No 7: Overall Evaluations of Carcinogenicity: An Updating of IARC Monographs Volumes 1 to 42.
3. European Commission, Joint Research Centre, Institute for Health and Consumer Protection. (2008). *European Union Risk Assessment Report: Benzene Final Risk Assessment.*
4. U.S. Environmental Protection Agency, National Center for Environmental Assessment. (April 1998). Carcinogenic Effects of Benzene: an update. EPA/600/p-97/1001F.
5. U.S. Food and Drug Administration Total Diet Study. Market Baskets 1991-3 through 2003-4.
6. U.S. Center for Disease Control and Prevention. (2015). *Fourth National Report on Human Exposure to Environmental Chemicals. Blood Benzene (2001-2006).* Centers for Disease Control and Prevention, Atlanta, Ga.
7. Elliott, L., Longnecker, M. P., Kissling, G. E., London, S. J. (2006). "Volatile organic compounds and pulmonary function in the Third National Health and Nutrition Examination Survey, 1988-1994." *Environmental Health Perspectives* 114(8): 1210-1214.
8. Kim, S. R., Halden, R. U., Buckley, T. J. (2007). "Volatile organic compounds in human milk: Methods and measurements." *Environmental Science Technology* 41(5): 1662-1667.
9. Lin, Y. S., Egeghy, P. P., Rappaport, S. M. (2008). "Relationships between levels of volatile organic compounds in air and blood from the general population." *Journal of Exposure Science and Environmental Epidemiology* 18: 421-429.
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11. Sexton, K., Adgate, J. L., Church, T. R., Ashley, D. L., Needham, L. L., Ramachandran, G., Fredrickson, A. L., Ryan, A. D. (2005). "Children's exposure to volatile organic compounds as determined by longitudinal measurements in blood." *Environmental Health Perspectives* 113(3): 342-348.
12. Sexton, K., Adgate, J. L., Fredrickson, A. L., Ryan, A. D., Needham, L. L., Ashley, D. L. (2006). "Using biologic markers in blood to assess exposure to multiple environmental chemicals for inner-city children 3 - 6 years of age." *Environmental Health Perspectives* 114(3): 453-459.
13. Woodruff, T.J., Zota, A.R., Schartz, J.M. (2011). "Environmental chemicals in pregnant women in the United States: NHANES 2003-2004." *Environmental Health Perspectives* 119:878-885.

Methylenedianiline

CAS 101-77-9

Used as an intermediary in the manufacture of rubber, a curing agent in resin, and as a dye, methylenedianiline (MDA) is classified as a Group 1B Carcinogen by the U.S. National Toxicology Program (NTP)[1] and a Category 2B Carcinogen by the International Agency for the Research of Cancer[2].

This chemical has more recently been added to the European Union Substances of Very High Concern list with a Category 2 Carcinogen classification.[3]

A recent study showed concern for the use of MDA in food contact material due to evidence of its potential migration into food.[4]

1. U.S. Department of Health and Human Services, National Toxicology Program. (January 2005). Eleventh Report on Carcinogens: 4,4'-Methylenedianiline (101-7-9).

2. World Health Organization, International Agency for the Research of Cancer (IARC) (1987). Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans. Vol. 39, Sup 7.

3. European Chemicals Agency. (2008). Member State Committee Support Document for Identification of 4,4'-Diaminodiaphenylmethane (MDA) as a Substance of Very High Concern (SVHC): Substance name: EC number: 202-974-4, CAS number: 101-77-9. Adopted on 1 October 2008.

4. Geueke, B. and Muncke J. (2017). "Substances of very high concern in food contact materials: Migration and regulatory background." *Packaging Technology and Science*.

Food Packaging Chemicals of High Concern Listing Criteria

Paraben Structure

Propyl paraben CAS 94-13-3
Butyl paraben CAS 94-26-8
Methyl paraben CAS 99-76-3
Ethyl paraben CAS 120-47-8

Often used in food packaging as an antimicrobial, structurally related parabens may be used simultaneously to create a specific product characteristic. Due to similarities in their chemical structure, uses and biologically similar health effects, these four parabens are listed as a chemical family. All four listed parabens show evidence of estrogenic activity that can interfere with normal development, earning them a classification as Category 1 Endocrine Disruptors by the European Union.[1]

1. European Commission DG Environment. (2002). *Endocrine disruptors: study on gathering information on 435 substances with insufficient data.* Final report B4-3040/2001/325850/MAR/C2.

Propyl paraben

CAS 94-13-3

Propyl paraben further meets the listing exposure criteria through biomonitoring results that confirm its presence in humans.[1,2,3,4]

1. U.S. Center for Disease Control (CDC). (2015). *Fourth National Report on Human Exposure to Environmental Chemicals. Urinary nPropyl paraben (2005 – 2010).* Centers for Disease Control and Prevention. Atlanta, Ga.

2. Calafat, A.M., Ye, X., Wong, L.Y., Bishop. A.M., Needham. L.L. (2010). "Urinary concentrations of four parabens in the U.S. population: NHANES 2005-2006." *Environmental Health Perspectives* 118 (5):679- 85.

3. Ye, X., Kuklenyik, Z., Bishop, A. M., Needham, L. L., Calafat, A. M. (2006). "Quantification of the urinary concentrations of parabens in humans by on-line solid phase extraction-high performance liquid chromatography-isotope dilution tandem mass spectrometry." *Journal of Chromatography B* 844: 53-59.

4. Ye, X., Bishop, A.M., Needham, L.L., Calafat, A.M. (2008). "Automated on-line column-switching HPLC-MS/MS method with peak focusing for measuring parabens, triclosan, and other environmental phenols in human milk." *Analytica Chimica Acta* 622:150-156.

Butyl paraben
CAS 94-26-8

Butyl paraben has been identified through biomonitoring studies as present in humans.[1,2,3]

1. U.S. Center for Disease Control (CDC). (2015). *Fourth National Report on Human Exposure to Environmental Chemicals. Urinary Butyl paraben (2005 – 2010).* Centers for Disease Control and Prevention. Atlanta, Ga.

2. Calafat, A.M., Ye, X., Wong, L.Y., Bishop, A.M., Needham, L.L. (2010). "Urinary concentrations of four parabens in the U.S. population: NHANES 2005-2006." *Environmental Health Perspectives* 118 (5):679- 85.

3. Ye, X., Kuklenyik, Z., Bishop, A. M., Needham, L. L., Calafat, A. M. (2006). "Quantification of the urinary concentrations of parabens in humans by on-line solid phase extraction-high performance liquid chromatography-isotope dilution tandem mass spectrometry." *Journal of Chromatography* B 844: 53-59.

Methyl paraben
CAS 99-76-3

The presence of methyl paraben in humans has been confirmed through several biomonitoring studies.[1,2,3]

1. U.S. Center for Disease Control. (2015). *Fourth National Report on Human Exposure to Environmental Chemicals. Urinary Methyl paraben (2005 – 2010).* Centers for Disease Control and Prevention. Atlanta, Ga.

2. Calafat, A.M., Ye, X., Wong, L.Y., Bishop, A.M., Needham, L.L. (2010). "Urinary concentrations of four parabens in the U.S. population: NHANES 2005-2006." *Environmental Health Perspectives* 118 (5):679- 85.

3. Ye, X., Kuklenyik, Z., Bishop, A. M., Needham, L. L., Calafat, A. M. (2006). "Quantification of the urinary concentrations of parabens in humans by on-line solid phase extraction-high performance liquid chromatography-isotope dilution tandem mass spectrometry." *Journal of Chromatography B* 844: 53-59.

Ethyl paraben
CAS 120-47-8

Exposure criteria for this substance has been met through biomonitoring studies that confirm the presence of ethyl paraben in humans.[1,2,3]

1. U.S. Center for Disease Control. (2015). *Fourth National Report on Human Exposure to Environmental Chemicals. Urinary Ethyl paraben (2005 – 2010).* Centers for Disease Control and Prevention. Atlanta, Ga.

2. Calafat, A.M., Ye, X., Wong, L.Y., Bishop, A.M., Needham, L.L. (2010). "Urinary concentrations of four parabens in the U.S. population: NHANES 2005-2006." *Environmental Health Perspectives* 118 (5):679- 85.

3. Ye, X., Kuklenyik, Z., Bishop, A. M., Needham, L. L., Calafat, A. M. (2006). "Quantification of the urinary concentrations of parabens in humans by on-line solid phase extraction-high performance liquid chromatography-isotope dilution tandem mass spectrometry." *Journal of Chromatography B* 844: 53-59.

Benzophenone
CAS 119-61-9

The chemical benzophenone is commonly used as an additive in plastics, coatings, adhesives, as a curing agent in ink, a flavor ingredient in foods, and ultraviolet light blocking agent for packaging materials.[1,2] An evaluation of available scientific literature led the International Agency for Research on Cancer to concluded that there is sufficient evidence to categorize benzophenone as possibly carcinogenic to humans, classifying it as a Group 2B Carcinogen.[2] Though considerable effect has been measured in the kidneys, the liver has been identified has the primary target organ of benzophenone toxicity.[1]

Benzophenone has been measured in food items ranging from frozen food to dairy products, baked goods and candy.[1,2] Known to migrate easily through polypropylene film, benzophenone may also migrate to food from paperboard and secondary packaging.[2]

Based on evidence from animal studies that benzophenone causes cancer, the U.S. FDA has recently amended its regulations to no longer provide for the use of benzophenone as a plasticizer in rubber articles in contact with food that are intended for repeated use.[3] While this change may help to reduce cumulative exposure to consumers, it is important to note that the FDA rule revision is specific to food articles intended for repeated use, not single use food packaging as is the focus of Maine's listing of benzophenone as a food contact chemical of high concern.

1. U.S. Department of Health and Human Services, National Toxicology Program. (2000). *NTP Technical Report on the Toxicity Studies of Benzophenone (CAS No. 119-61-9). National Toxicology Program Toxicity Report Series Number 61.* NIH Pub No. 00-3943.

2. International Agency for Research on Cancer (IARC). (2013). *Some Chemicals Present in Industrial and Consumer Products, Food and Drinking-Water, Volume 101.* IARC Monographs on The Evaluation of Carcinogenic Risks to Humans. Lyons, France – 2013.

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Nonylphenol
CAS 25154-52-3

Among its many manufacturing uses, nonylphenol (NP) is commonly used as a stabilizer and intermediary in plastics production. NP is classified as a Category 1 Endocrine Disruptor by the European Union.[1] The European Chemicals Agency has also classified NP as a Category 2 Reproductive Hazard due to its suspected damage to fertility.[2]

Several biomonitoring studies confirm widespread human exposure to nonylphenol.[3,4,5]

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