ENVIRONMENTAL DEFENSE FUND, BREAST CANCER PREVENTION PARTNERS, CLEAN WATER ACTION, CONSUMER REPORTS, ENDOCRINE SOCIETY, ENVIRONMENTAL WORKING GROUP, HEALTHY BABIES BRIGHT FUTURES, MARICEL MAFFINI, AND LINDA BIRNBAUM

January 27, 2022

Dr. Dennis Keefe, Director
Office of Food Additive Safety (HFS-200)
Center for Food Safety and Applied Nutrition
5100 Campus Drive
College Park, MD 20740-3835

Re: New food additive petition asking FDA to remove or restrict its approvals of bisphenol A (CASRN 80-05-7) pursuant to 21 USC § 348 with expedited review

Dear Dr. Keefe:

We submit this food additive petition to the Food and Drug Administration (FDA) requesting that the agency remove its approvals of the use of bisphenol A (CASRN 80-05-7) pursuant to 21 U.S.C. § 348 because recently published scientific studies show that the exposure from those food additive uses is not safe.[1]

We base our request on a substantial body of studies of the health effects of dietary BPA exposure published since 2013, which were recently evaluated in a comprehensive safety assessment of BPA released by the European Food Safety Authority (EFSA) on December 15, 2021, titled "Re-evaluation of the risks to public health related to the presence of bisphenol A (BPA) in foodstuffs."[2] The 17-member expert panel convened by EFSA ("EFSA Expert Panel") unanimously concluded that "there is a health concern from dietary BPA exposure for all age groups." The Panel considered published scientific studies and raw data, including those from the Consortium Linking Academic and Regulatory Insights on BPA Toxicity (CLARITY-BPA) managed by the US National Toxicology Program (NTP) in which FDA was a key partner.[3]

[1] As defined by FDA at 21 CFR § 170.3(s).
[2] EFSA Panel on Food Contact Materials, Enzyme and Processing Aids (CEP), Re-evaluation of the risks to public health related to the presence of bisphenol A (BPA) in foodstuffs, November 24, 2021 at https://connect.efsa.europa.eu/RM/s/publicconsultation2/a0l1v00000E8BRD/pc0109. (EFSA Expert Panel Report) The document is undergoing public consultation until February 22, 2022 but is sufficient to support the petition.
[3] NTP, CLARITY-BPA Program, accessed on January 23, 2022 at https://ntp.niehs.nih.gov/whatwestudy/topics/bpa/; NTP, CLARITY-BPA Study Data, accessed on January 23, 2022 at https://cebs.niehs.nih.gov/cebs/program/CLARITY-BPA; NTP CLARITY-BPA Core Study The CLARITY-BPA Core Study: A Perinatal and Chronic Extended-Dose-Range Study of Bisphenol A in Rats, NTP RR 9, September 2018, https://ntp.niehs.nih.gov/publications/reports/rr/rr09/index.html; and NTP, CLARITY BPA Compendium Report of Published Findings, NTP RR-18, October 2021, https://ntp.niehs.nih.gov/publications/reports/rr/rr18/index.html. See also EFSA Expert Panel Report at Section 1.3.3.

EFSA Expert Panel's safety assessment established a new tolerable daily intake (TDI) of 0.04 ng of BPA per kilogram of body weight per day (ng/kg bw/d) and identified the immune system as the "most sensitive health outcome category to BPA exposure."[4] The Panel also identified harm to the female and male reproductive systems at exposure levels significantly lower than FDA's most recent estimated daily intake of BPA from food contact uses.

In 2014, FDA estimated exposures to BPA for children less than 2 years old (<2) and the US population 2 years old and older (≥ 2).[5] The mean and 90th percentile estimated daily intake for the US population older than 2 years was 200 ng/kg bw/day and 500 ng/kg bw/day, respectively.[6]

Using FDA's own exposure estimates, the average American is exposed to more than 5,000 times the safe level of 0.04 ng BPA/kg bw/day set by the EFSA Expert Panel. Without a doubt, these values constitute a high health risk and support the conclusion that uses of BPA are not safe according to 21 CFR § 170.3(i).

Given the magnitude of the overexposure, we request an expedited review by FDA of the food additive petition because the proposed amendments to the agency's rule are intended to significantly increase the safety of the food supply. Not only will it dramatically decrease exposure to a toxin – BPA – in food that undermines the proper functioning of the immune and reproductive systems, but it will allow the immune system to more successfully respond to exposure to human pathogens in or on food.

We have submitted this food additive petition electronically.

If you have questions or comments, please contact Tom Neltner at tneltner@edf.org and Dr. Maricel Maffini at drmvma@gmail.com on all responses.

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[4] EFSA Expert Panel Report.

[5] FDA, Jason Aungst Memorandum to Michael Landa, Director, CFSAN, "2014 Updated safety assessment of Bisphenol A (BPA) for use in food contact applications." June 17, 2014. See https://www.fda.gov/media/90124/download. (FDA 2014 Exposure Assessment).

[6] Id. We only include the exposure estimate for the population 2 years and older because of uncertainties about estimates for infant and toddlers as expressed by FDA in its 2014 Memo: "Previous FDA exposure assessments estimated exposures [footnote 5 reference to a Memo dated 5/4/2011, Bailey/Hatwell/Mihalov to Twaroski, Updated exposure to Bisphenol A (BPA) from the consumption of infant formula, toddler food and adult (canned) food-new data on canned food and beverages] for infants and toddlers less than 2 years old with mean and 90th percentile estimates as follows (age, µg/kg-bw/d): 0-1 year, 0.3, 0.6; 1-2 years, 0.5, 1.1. In the current 2014 memorandum, the exposure assessment did not include updated values for these groups but did note that exposure is expected to decrease based on recent amendments to the food additive regulations that no longer authorize the use of polycarbonate resins in infant feeding bottles and spill-proof cups designed to help train babies and toddlers to drink from cups (77 FR 41899, July 17, 2012) and to no longer provide for the use of BPA-based epoxy resins as coatings in packaging for infant formula (78 FR 41840, July 12, 2013), as well as an increase in effective notifications for "BPA-free" materials including can coatings."

Sincerely,

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Appendix I
Responses to elements required by 21 CFR § 171.1

Per 21 CFR § 171.1, we provide responses to the requested elements of a food additive petition.

I.A. Name and Pertinent Information Concerning Food Additive

The identity of the food additive is as follows:

1. Name: 4,4′-(Propane-2,2-diyl)diphenol (preferred IUPAC name). Other names are Bisphenol A, BPA, p,p-Isopropylidenebisphenol, 2,2-Bis(4-hydroxyphenyl)propane or 4,4′-(Propane-2,2-diyl)diphenol. See below for other names that FDA has identified.
2. Chemical formula: $C_{15}H_{16}O_2$
3. Formula weight: 228.291
4. Chemical Abstract Service No.: 80-05-7
5. INS No.: Not applicable
6. UNI No.: 2924 2430

In its "Inventory of Food Contact Substances Listed in 21 CFR,"[7] FDA lists the following other names for Bisphenol A.

- BISPHENOL A
- BISPHENOL
- DIPHENYLOLPROPANE
- ISOPROPYLIDENEDIPHENOL, P,P'-
- DIMETHYLMETHYLENE-P,P'-DIPHENOL
- ISOPROPYLIDENEDIPHENOL
- 2,2-DI(4-HYDROXYPHENYL)PROPANE
- 2,2-BIS(4-HYDROXYPHENYL)PROPANE
- 4,4'-(1-METHYLETHYLIDENE)BIS(PHENOL)
- PHENOL, 4,4'-(1-METHYLETHYLIDENE)BIS-
- PHENOL, 4,4'-ISOPROPYLIDENEDI-

[7] FDA, Inventory of Food Contact Substances Listed in 21 CFR - Bisphenol A, accessed on December 29, 2021 at https://www.cfsanappsexternal.fda.gov/scripts/fdcc/?set=IndirectAdditives&id=BISPHENOLA&sort=Sortterm_ID&order=ASC&startrow=1&type=basic&search=bisphenol%20A.

I.B. Directions, Recommendations, and Suggestions Regarding Proposed Use

We are asking FDA to revoke uses of BPA for adhesives and coatings and strictly limit migration of the substances into food from various plastic food contact articles. Below is a summary of our requested changes to the FDA's regulations. Appendix II provides specific proposed changes, edits, and additions.

1. Add new § 174.7 as a "General limitation of use 4,4'-Isopropylidenediphenol" with the following restriction on use of BPA:

   Except as specifically described in parts 175, 176, and 177, for any use of the 4,4'-Isopropylidenediphenol, CAS Reg. No. 80-05-7, as a constituent in a food contact article that may migrate into food, the substance is subject to a specific migration limit of 0.5 nanograms per kilogram of food. If the specific migration limit is below the limit of quantification (based on 95% confidence that the false negative rate is less than 5%) using the most sensitive method, the concentration must be below the limit of quantification.

2. Modify the following sections that currently allow the use of BPA in food contact articles:

   a. § 175.105 – Adhesives used as components of articles intended for use in packaging, transporting, or holding food.

      Proposed change: Remove the eight listings of BPA permitted for use in adhesives from paragraph (c)(5).

   b. § 175.300 – Resinous and polymeric coatings used as the food-contact surface of articles intended for use in producing, manufacturing, packing, processing, preparing, treating, packaging, transporting, or holding food.

      Proposed change: Remove the eight listings of BPA permitted for the following uses:
      - *Rosins esters*
      - *Phenolic resins*
      - *Epoxy resins*
      - *Glycidyl ethers*
      - *Melamine-formaldehyde*

      Proposed change: Remove paragraph (i) prohibiting use of epoxy resins in packaging for powdered and liquid infant formula since it is mooted.

   c. § 177.1440 – 4,4'-Isopropylidenediphenol-epichlorohydrin resins minimum molecular weight 10,000 used as articles or components of articles intended for use in producing, manufacturing, packing, processing, preparing, treating, packaging, transporting, or holding food.

Proposed change: Insert new paragraph (d) with the language limiting migration of BPA that is described in section 1, above, tailored to the resins covered by this section.

d. § 177.1580 – Polycarbonate resins used as articles or components of articles intended for use in producing, manufacturing, packing, processing, preparing, treating, packaging, transporting, or holding food.

Proposed change: Add new paragraph (e) with the language limiting migration of BPA that is described in section 1, above, tailored to the resins covered by this section.

e. § 177.1585 – Polyestercarbonate resins used as articles or components of articles intended for use in producing, manufacturing, packing, processing, preparing, treating, packaging, or holding food.

Proposed change: Add new paragraph (d) with the language limiting migration of BPA that is described in section 1, above, tailored to the resins covered by this section.

f. § 177.2280 – 4,4'-Isopropylidenediphenol-epichlorohydrin thermosetting epoxy resins used as articles or components of articles intended for repeated use in producing, manufacturing, packing, processing, preparing, treating, packaging, transporting, or holding food.

Proposed change: Insert new paragraph (e) with the language limiting migration of BPA that is described in section 1, above, tailored to the resins covered by this section.

g. § 177.2440 – Polyethersulfone resins used as articles or components of articles intended for repeated use in contact with food.

Proposed change: Remove listings of BPA permitted for use in paragraph (a)(2).

I.C. Data establishing that food additive will have intended physical or other technical effect.

We are asking FDA to revoke or limit the approved uses of BPA as described above. To the extent that BPA continues to be used (within the proposed limits), the existing intended physical or technical effects will remain.

I.D. Description of practicable methods to determine the amount of the food additive in the food

In 2019, Dr. Xu-Lian Cao and collaborators at Health Canada's Food Research Division of the Bureau of Chemical Safety published a study evaluating 159 composite food samples from the Canadian Total Diet Study using liquid chromatography and tandem mass spectrometry (LC-MS/MS).[8] They defined the method detection limit (MDL) as 10 times the signal-to-noise ratio for different food matrices (not pure standard) and established an MDL for BPA in eight types of food matrices.

Food matrix	Method Detection Limit (MDL) using LC-MS/MS
Infant formula	1,000 ng/kg
Fish	57,000 ng/kg
Meat	4,900 ng/kg
Fruit	640 ng/kg
Vegetable	1,500 ng/kg
Soup	2,700 ng/kg
Beverage	450 ng/kg
Water	38 ng/kg
ng/kg = nanograms of BPA per kilogram of food.	

Dr. Cao et al described the specific method as follows:

> A Waters Acquity Ultra Performance Liquid Chromatography (UPLC) system (Milford, MA, USA) coupled to a Waters Quattro Premier XE mass spectrometer (Milford, MA, USA) operated in electrospray ionisation (ESI) negative mode was used for analyses. Chromatographic separation of target bisphenol analytes was achieved at 22°C on an Acquity UPLC BEH Phenyl column from Waters (1.7 µm, 2.1 mm x 100 mm) attached to a Waters Van Guard BEH phenyl pre-column (1.7 µm, 2.1 × 5 mm). The mobile phase consisted of (A): Water and (B): Acetonitrile. The gradient programming was as follows: initial gradient 40% (B) (held for 2 min) to 90% (B) in 8 min, hold for 1 min and go back to 40% (B) in 1 min, hold for additional 1 min to equilibrate. The injection volume was 10 µL and the flow rate set at 0.20 mL/min.
>
> The MS/MS was operated in electrospray negative ionisation multiple reaction monitoring (MRM) mode. Source temperature, desolvation temperature, and desolvation gas flow were 120°C, 350°C, and 1000 L/hour, respectively. Extractor and capillary

[8] Xu-Liang Cao, Ivana Kosarac, Svetlana Popovic, Simon Zhou, Daryl Smith & Robert Dabeka (2019) LC-MS/MS analysis of bisphenol S and five other bisphenols in total diet food samples, Food Additives & Contaminants: Part A, 36:11, 1740-1747, DOI:10.1080/19440049.2019.1643042. https://doi.org/10.1080/19440049.2019.1643042.

> voltages were set at 4 V and 3 kV, respectively. Nitrogen was used as cone and desolvation gas and argon was used as collision gas with a flow of 0.20 mL/min.
>
> The calculation of concentrations of bisphenols in samples was based on the isotope dilution methodology, BPF-13C12 was used as the internal standard for BPE due to lack of its labelled standard. In the course of method development, matrix effect was observed and 2,4′-BPS- 13C12 was used as a performance standard to account for this, as well as for the uncertainty associated with injection reproducibility. The performance standard was added to the samples and calibration standards immediately prior to injection.[9]

We maintain that the LC-MS/MS as described by Dr. Cao et al. is a practicable method to determine the amount of BPA in the food.

[9] Id.

I.E. Full reports of investigations made with respect to the safety of the food additive

We adopt by reference two reports as investigations into the safety of BPA.

- **Investigation to establish a tolerable daily intake:** European Food Safety Authority (EFSA) Panel on Food Contact Materials, Enzyme and Processing Aids (CEP), Re-evaluation of the risks to public health related to the presence of bisphenol A (BPA) in foodstuffs, November 24, 2021, including Annexes A to M, at https://connect.efsa.europa.eu/RM/s/publicconsultation2/a0l1v00000E8BRD/pc0109. ("EFSA Expert Panel Report").

- **Investigation to establish an estimated daily intake:** FDA, Jason Aungst Memorandum to Michael Landa, Director, CFSAN, "2014 Updated safety assessment of Bisphenol A (BPA) for use in food contact applications." June 17, 2014. ("FDA 2014 Exposure Assessment").

1. Investigation to establish a tolerable daily intake.

We base our request on a substantial body of studies of the health effects of dietary BPA exposure published since 2013, which were recently evaluated in a comprehensive safety assessment of BPA released by the European Food Safety Authority (EFSA) on December 15, 2021, titled "Re-evaluation of the risks to public health related to the presence of bisphenol A (BPA) in foodstuffs."[10] The Panel considered published scientific studies and raw data, including those from the Consortium Linking Academic and Regulatory Insights on BPA Toxicity (CLARITY-BPA) managed by the US National Toxicology Program (NTP) in which FDA was a key partner.[11]

The EFSA Expert Panel Report is a comprehensive risk assessment of BPA building on its 2015 comprehensive review of BPA.[12] The agency describes the timeline[13] to develop the EFSA Expert Panel Report as follows:

- **2016:** New data confirm EFSA's previous conclusion that BPA might affect the immune system in animals, but the evidence was too limited to draw any conclusions for human health.[14]

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[10] EFSA Expert Panel Report.
[11] NTP, CLARITY-BPA Program, accessed on January 23, 2022 at https://ntp.niehs.nih.gov/whatwestudy/topics/bpa/; NTP, CLARITY-BPA Study Data, accessed on January 23, 2022 at https://cebs.niehs.nih.gov/cebs/program/CLARITY-BPA; NTP CLARITY-BPA Core Study The CLARITY-BPA Core Study: A Perinatal and Chronic Extended-Dose-Range Study of Bisphenol A in Rats, NTP RR 9, September 2018, https://ntp.niehs.nih.gov/publications/reports/rr/rr09/index.html; and NTP, CLARITY BPA Compendium Report of Published Findings, NTP RR- 18, October 2021, https://ntp.niehs.nih.gov/publications/reports/rr/rr18/index.html. See also EFSA Expert Panel Report at Section 1.3.3.
[12] EFSA, Bisphenol A, accessed on January 16, 2021 at https://www.efsa.europa.eu/en/topics/topic/bisphenol.
[13] Id.
[14] EFSA, Bisphenol A: new immune system evidence useful but limited, October 13, 2016 at https://www.efsa.europa.eu/en/press/news/161013.

- **2017:** EFSA's experts endorsed a scientific protocol for the re-evaluation of BPA hazards following a public consultation. The protocol was a detailed plan that defines upfront the scope, methodology and information needs before the assessment starts in 2018. Experts from Denmark, France, Germany, the Netherlands, Norway, Sweden, and Switzerland were appointed by their governments to take part in the protocol working group as well as four independent scientists appointed by EFSA.
- **2018:** A new EFSA working group of scientific experts started evaluating recent toxicological data on BPA with an updated assessment scheduled for 2022.[15]
- **2019:** Before being applied to the new BPA re-evaluation, the study appraisal methodology described in the 2017 BPA hazard assessment protocol was tested on a selection of studies. The testing phase, its outcome, and the resulting refinement of the 2017 methodology was described in a scientific report.[16]
- **November 2021:** EFSA's scientific opinion on the re-evaluation of the risks to public health related to the presence of BPA in foodstuffs was unanimously endorsed by the CEP Panel.

We summarize the EFSA Expert Panel Report below.

a. Hazard Assessment

EFSA's Expert Panel organized the assessed health outcomes into categories, clusters, and endpoints to facilitate the appraising of evidence. It recognized eight health outcome categories (HOC):

1. General toxicity;
2. Immunotoxicity;
3. Metabolic effects;
4. Cardiotoxicity;
5. Neurotoxicity and developmental neurotoxicity;
6. Reproductive and developmental toxicity;
7. Carcinogenicity and mammary gland proliferative effects; and
8. Genotoxicity.

Except for genotoxicity, each HOC was comprised of clusters that included:

> Several toxicologically relevant endpoints that are physiologically or toxicologically related, and that in concert shed light on the likelihood of an effect of BPA exposure in that cluster. The endpoints are measures of an individual parameter that is adverse in itself, i.e., an apical endpoint, or may be involved in the development of an adverse condition, i.e., an intermediate endpoint.[17]

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[15] EFSA, BPA update: working group to start reviewing new studies, September 4, 2019 at https://www.efsa.europa.eu/en/press/news/180904.
[16] EFSA, Testing the study appraisal methodology from the 2017 Bisphenol A (BPA) hazard assessment protocol, November 11, 2019 at https://www.efsa.europa.eu/en/supporting/pub/en-1732.
[17] Id.

For example, the general toxicity HOC included two clusters: liver toxicity and kidney toxicity. The liver toxicity cluster comprised three endpoints: ALT [alanine transaminase], AST [aspartate transaminase] and gamma-glutamyl transpeptidase. The kidney toxicity cluster included one endpoint, hyperuricemia.

EFSA Expert Panel members evaluated the studies based on their expertise and according to EFSA's BPA hazard assessment protocol,[18] and identified nine health outcome clusters as "likely" to be associated with BPA toxicity (Table 1).

Table 1: Summary of EFSA Expert Panel's conclusions on BPA hazard identification

Health outcome category (HOC)	**HOC cluster/endpoint**	**Species where relevant effect was identified**	**Likelihood of BPA toxicity**	**Exposure period[1]**
General toxicity	Body weight; liver, kidney, lung, thyroid, parathyroid, pituitary gland, adrenal gland and bone marrow effects, and effects on hematological parameters	Animals	As likely as not	
Immunotoxicity	Asthma/Allergy	Human	As likely as not	Pregnancy and childhood
	Innate immunity	Animals	As likely as not	
	Cellular immunity	Animals	Likely	
	Humoral immunity	Animals	As likely as not	
	Inflammation	Animals	As likely as not	
	Allergic lung inflammation	Animals	Likely	
Metabolic effects	Obesity	Human	As likely as not	
	Cardiometabolic effects	Human	Not likely	
	Thyroid effects	Human	Not likely	
	Type-2 diabetes	Human	As likely as not	

[18] EFSA (European Food Safety Authority), Gundert-Remy U, Bodin J, Bosetti C, FitzGerald R, Hanberg A, Hass U, Hooijmans C, Rooney AA, Rousselle C, van Loveren H, Wölfle D, Barizzone F, Croera C, Putzu C and Castoldi A, 2017a. Bisphenol A (BPA) hazard assessment protocol. EFSA Supporting Publications 2017;14(12):1354E, 75 pp. https://doi.org/10.2903/sp.efsa.2017.EN-1354

	Gestational diabetes mellitus	Human	Not likely	
	Obesity	Animals	As likely as not	
	Fat deposition in the liver	Animals	As likely as not	
	Glucose regulation	Animals	As likely as not	
	Blood lipids	Animals	As likely as not	
	Uric acid	Animals	Likely	Adult
	Type 1 diabetes	Animals	As likely as not	
	Other metabolic hormones	Animals	Not likely	
	Thyroid hormones	Animals	Not likely	
Neurotoxicity and developmental neurotoxicity	Neurodevelopment	Human	Not likely	
	Neuromorphology	Animals	Likely	Developmental and growth phase/young age
	Nervous system functionality	Animals	Likely	Adult
	Behavior	Animals	Likely	All exposure periods
Reproductive and developmental toxicity	Fetal and postnatal growth	Human	Not likely	
	Prematurity	Human	Not likely	
	Pre-eclampsia	Human	As likely as not	
	Male fertility	Human	Not likely	
	Female fertility	Human	As likely as not	
	Developmental toxicity	Animals	As likely as not	
	Female reproductive toxicity	Animals	Likely	Developmental, developmental and adult, growth phase/young age, adult
	Male reproductive toxicity	Animals	Likely	Developmental, developmental and adult, growth phase/young age, adult
Cardiotoxicity	Heart weight	Animals	Not likely	
	Heart lesions	Animals	Not likely	

	Cardiac structural changes	Animals	Not likely	
	Cardiac function	Animals	Not likely	
	Blood pressure and atherosclerotic lesions	Animals	Not likely	
Carcinogenicity and mammary gland proliferative effects	Mammary gland weight	Animals	Not likely	
	Mammary gland histology	Animals	As likely as not	
	Prostate histology	Animals	As likely as not	
	Uterus weight	Animals	As likely as not	
	Uterus histology	Animals	Likely	Developmental
Genotoxicity	Genotoxic hazard (e.g., bacterial mutation, DNA strand breaks, etc.)	In vitro, animals	Unlikely to very unlikely	

[1] EFSA identified the following life stages:

- Developmental exposure (pre-natal and/or postnatal until weaning);
- Developmental and adult exposure (pre-natal and post-natal in pups until adulthood);
- Growth phase/young age exposure;
- Adult exposure (after puberty); and
- Indirect (germline) exposure.

b. Hazard Characterization

The EFSA Expert Panel used benchmark dose (BMD) analysis for dose-response modelling for each published report of the endpoints assigned a "likely" level of BPA toxicity association. Each BMD was then converted to human equivalent doses (HED). The table below, extracted from the Report, provides the lower and upper confidence limits for each BMD converted to HED.

Table 20: Overview of BMD confidence intervals used for the identification of the Reference Point[(c)] to derive a HBGV.

Reference	Endpoint	Species	BMR	Group	Administered doses		Administered doses converted to HED[(b)]	
					BMDL (µg/kg bw per day)	BMDU	BMDL (ng/kg bw per day)	BMDU
Immunotoxicity								
Luo et al. (2016) [RefID 4679]	Th17 cells	Mouse	20%	F PND21	0.06	0.74	**0.93**	11.5
		Mouse	20%	F PND42	0.17	1.79	2.64	27.7
		Mouse	20%	M PND21	0.30	3.39	4.65	52.5
		Mouse	20%	M PND42	0.35	3.38	5.43	52.4
Ogo et al. (2018) [RefID 11201]	Neutrophils in epididymis: Caput/corpus	Rat	20%		6.8	90.4	1126	14970
Metabolic effects								
Ma et al. (2018) [RefID 12637]	Hepatic uric acid	Mouse	20%		1.59	399	24.6	6185
Neurotoxicity and developmental neurotoxicity								
Johnson et al. (2016) [RefID 3241]	Sniffing incorrect holes on day 7 (learning and memory)	Rat	50%	F	10.1	2160	1673	357696
		Rat	50%	M	1.47	1520	243	251712
Chen Z et al. (2018) [RefID 11734]	Platform duration (learning and memory)	Rat	50%		10700	2.4e+7	1.77e+6	4.02e+9
	Relative expression NR2 in V1 (learning and memory)	Rat	20%		7.96	842	1318	139435
Xu XH et al. (2015) [RefID 8232]	Time in open arms (Anxiety/emotionality)	Mouse	50%	M	497	80400	7704	1.25e+06
Liu ZH et al. (2014) [RefID 10411]	Dendritic spine density	Rat	20%		16800	70100	2.78e+06	1.16e+07
Chen Z et al. (2018) [RefID 11734]	Dendritic spine density	Rat	20%		4.24	2350	702	389160
Reproductive and developmental toxicity								
Camacho et al. (2019) [RefID 11370] [(e)]	Ovary weight	Rat	5%		0.63	25,000	104	4.14e+06
Camacho et al. (2019) [RefID 11370] [(e)]	Incidence of follicle cysts (ovary histology)	Rat	10%		5.53	3680	916	6.09e+05
Hu et al. (2018) [RefID 11119]	Ratio of primordial and total follicles	Mouse	5%		0.96	349	14.9	5410
Camacho et al. (2019) [RefID 11370] [(e)]	Incidence of exfoliated germ cells (epididymis histology)	Rat	10%		2260	27500	3.74e+05	4.55e+06
Wang HF et al. (2016) [RefID 7618]	Viability (effects on sperm)	Mouse	20%		26.1	2460	405	38130
	Motility (effects on sperm)	Mouse	20%		3.41	74.8	53	1159

BMDL: lower confidence limit of the benchmark dose; BMDU: upper confidence limit of the benchmark dose; BMR: benchmark response; F: female; M: male; PND: post-natal day.
(a): All fitted models' Akaike information criterion (AIC) values are larger than null model's AIC – 2.
(b) For the calculation of the BMDL/BMDU values expressed as HED, a HEDF of 0.0155 was used for studies in mice and a HEDF of 0.1656 for studies in rats. The lowest BMDL value is shown in bold.
(c) The confidence intervals are shown as administered and as the corresponding human equivalent dose (HED).
(e): Full reference: NTP Clarity Report (2018)/Camacho et al. (2019).

For context, nine BMDLs converted to HED are below the 90th percentile 500 ng/kg bw/day EDI that FDA established in 2014[19] for populations two years or older (sorted greatest exceedance to least):

- Th17 cells endpoint in Luo et al. (2016)[20] for female mouse post-natal day 21 (PND21) with a BMDL of 0.93 ng/kg bw/day – 537 times lower than FDA's EDI;
- Th17 cells endpoint in Luo et al. (2016)[21] for female mouse post-natal day 42 (PND42) with a BMDL of 2.64 ng/kg bw/day – 189 times lower than FDA's EDI;
- Th17 cells endpoint in Luo et al. (2016)[22] for male mouse PND21 with a BMDL of 4.65 ng/kg bw/day – 108 times lower than FDA's EDI;
- Th17 cells endpoint in Luo et al. (2016)[23] for male mouse PND42 with a BMDL of 5.43 ng/kg bw/day – 92 times lower than FDA's EDI;
- Ratio of primordial and total ovarian follicles in Hu et al. (2018)[24] for mouse with a BMDL of 14.9 ng/kg bw/day – 34 times lower than FDA's EDI;

[19] FDA, Jason Aungst Memorandum to Michael Landa, Director, CFSAN, "2014 Updated safety assessment of Bisphenol A (BPA) for use in food contact applications." June 17, 2014. See https://www.fda.gov/media/90124/download. (FDA 2014 Exposure Assessment).
[20] Luo Q, Gao RF, Peng C, Yi J, Liu LL, Yang SM, Li DT, Hu JB, Luo T, Mei M, Song Y, Wu CD, Xiao XQ and Li QF, 2017. Bisphenol A promotes hepatic lipid deposition involving Kupffer cells M1 polarization in male mice. Journal of Endocrinology 234(2), 143–154. doi:10.1530/JOE-17-0028.
[21] Id.
[22] Id.
[23] Id.
[24] Hu Y, Yuan DZ, Wu Y, Yu LL, Xu LZ, Yue LM, Liu L, Xu WM, Qiao XY, Zeng RJ, Yang ZL, Yin WY, Ma YX and Nie Y, 2018. Bisphenol A initiates excessive premature activation of primordial follicles in mouse ovaries via the PTEN signaling pathway. Reproductive Sciences, 25(4), 609–620. doi:10.1177/1933719117734700.

- Sperm motility endpoint in Wang HF et al. (2016)[25] for mouse with a BMDL of 53 ng/kg bw/day – 9.4 times lower than FDA's EDI;
- Ovary weight endpoint in Camacho et al. (2019)[26] for rat with BMDL of 104 ng/kg bw/day – 4.8 times lower than FDA's EDI;
- Sniffing incorrect holes on day 7 endpoint (learning and memory) in Johnson et al. (2016)[27] for male rats with BMDL of 243 ng/kg bw/day – 2.1 times lower than FDA's EDI; and
- Sperm viability endpoint in Wang HF et al. (2016)[28] for mouse with a BMDL of 53 – 1.2 times lower than FDA's EDI.

c. Rationale for the selection of the benchmark response

EFSA Expert Panel selected Th17 cells as the most appropriate BMD to calculate the TDI. It stated:

> An adverse outcome pathway for BPA leading to allergic responses that can be modelled to establish a BMD is currently not available. What can be stated is that **T helper cells are key players in the immune-inflammatory chain of molecular events leading to amplification or suppression of specific immune elements, orienting the immune response towards effective resolution or chronic disease, and, according to an equilibrium in which these same cells and through the production of specific cytokines, restrict each other's own activity.** Functionally, T helper 17 cells play a role in host defence against extracellular pathogens by mediating the recruitment of inflammatory cells to infected tissues. **Aberrant regulation of Th17 cells plays a significant role in the pathogenesis of multiple inflammatory and autoimmune disorders.** The most notable role of IL-17 produced by Th17 cells is its involvement in inducing and mediating proinflammatory responses, associated with allergic responses. IL-17 induces the production of many other cytokines (such as IL-6, G-CSF, GM-CSF, IL-1β, TGF-β, TNF-α), chemokines (including IL-8, GRO-α, and MCP-1), and prostaglandins (e.g., PGE2) from many cell types (fibroblasts, endothelial cells, epithelial cells, keratinocytes, and macrophages). **As such, numerous studies have shown that Th17 cells and their cytokines are also associated with the development of asthma** (Doe et al., 2010). IL-17A is considered an important cytokine to induce the inflammatory response asthma. In the pathogenesis of asthma, Th17/IL-17A can induce

[25] Wang HF, Liu M, Li N, Luo T, Zheng LP and Zeng XH, 2016. Bisphenol A impairs mature sperm functions by a CatSper-relevant mechanism. Toxicological Sciences, 152(1), 145–154. doi:10.1093/toxsci/kfw070.
[26] Camacho L, Lewis SM, Vanlandingham MM, Olson GR, Davis KJ, Patton R, Twaddle NC, Doerge DR, Churchwell MI, Bryant MS, Mclellen FM, Woodling K, Felton RP, Maisha MP, Juliar BE, Gamboa da Costa G and Delclos KB, 2019. NTP CLARITY-BPA report (2018). A two-year toxicology study of bisphenol A (BPA) in Sprague-Dawley rats: CLARITY-BPA core study results. Food and Chemical Toxicology, 132. 110728
[27] Johnson SA, Javurek AB, Painter MS, Ellersieck MR, Welsh TH, Camacho L, Lewis SM, Vanlandingham MM, Ferguson SA and Rosenfeld CS, 2016. Effects of developmental exposure to bisphenol A on spatial navigational learning and memory in rats: A CLARITY-BPA study. Hormones and Behavior, 80, 139–148. doi:10.1016/j.yhbeh.2015.09.005.
[28] Wang HF, Liu M, Li N, Luo T, Zheng LP and Zeng XH, 2016. Bisphenol A impairs mature sperm functions by a CatSper-relevant mechanism. Toxicological Sciences, 152(1), 145–154. doi:10.1093/toxsci/kfw070.

the accumulation of inflammatory cells in the airway and participate in the process of asthma. In addition, the activation of Th17 cells and the secretion of IL-**17 can increase the immune response of Th2 cells, thereby aggravating the severity of allergic asthma**.

BPA exposure led to a dose-related increment of Th17 cells in mice. This effect was consistent with effects on cellular immunity based on Th17 cells and associated cytokines (IL-17, IL-21 and IL-23), as well as with effects of BPA in the cluster of allergic lung inflammation.

When using the benchmark approach, for dose-response analysis, a BMR [benchmark response] needs to be selected. The EFSA guidance (EFSA Scientific Committee, 2017a) recommends a BMR of 5% as default. However, deviating from this default is possible, based on toxicological or statistical considerations. For Th17 cells, there is currently insufficient information available on the normal variability of this measure, either in the mouse strain used in the study, or other strains. In humans, a study published in 2016 reported a retrospective analysis on lymphocyte subpopulations, analysed over few years in an outpatient laboratory in Northeast Italy (Sorrenti et al., 2016) to provide reference ranges. In Caucasian patients (mean age 42 ± 8.5 years), mean values ± SD of Th17 in peripheral blood are 221.6 ± 90.2 cells/μL (10.5 ± 4.4%). Registered cases of lymphocyte associated diseases (immunodeficiencies and lymphoproliferative disorders) were excluded from the study, as well as samples with values of total erythrocytes, total leukocytes, total lymphocytes, and major lymphocyte populations (T cells, Th, Tc and B lymphocytes) outside the normal range according to guidelines.

Furthermore, the CEP Panel notes that the increment of Th17 cells is an intermediate endpoint, and some reserve capacity will exist. While considering that in the human population, for individuals a 20% increase may not necessarily imply an adverse condition for that person, given the pivotal role of Th17 cells in lung allergy, the CEP Panel considered that if the population at large showed a 20% increment in Th17 cells, individuals that are in the higher segment of the normal range, will be put out of the normal range, and as a consequence numbers of lung allergy cases would be expected to go up.

In conclusion, **while the effect of BPA exposure on Th17 cells is clear,** considering the standard deviation in the outcomes of the animal study (see the Table in Section 2.1.1 of Annex I), the CEP Panel considered 20% would be in line with the variability noted in the animal study and the wider normality range in humans, and **considered it as adverse and took it as the BMR.**[29] *[Emphasis added]*.

[29] EFSA Expert Panel Report.

d. Calculation of a TDI of 0.04 ng/kg bw/day

Based on the BMDL of 0.93 ng BPA/kg bw/day, the EFSA Expert Panel applied an uncertainty factor of 2.5 for inter-species toxicodynamic difference and of 10 for intra-human variability in toxicokinetics and toxicodynamics and established a tolerable daily intake of 0.04 ng/kg bw/day.

2. Investigation to establish an estimated daily intake.

The most recent FDA-estimated daily intake on BPA we found was in a June 17, 2014 memo from Dr. Jason Aungst of the Division of Food Contact Notifications to the Director of the Center for Food Safety and Applied Nutrition titled "2014 Updated safety assessment of Bisphenol A (BPA) for use in food contact applications." [30] Regarding exposure, Dr. Aungst said:

> Chemists from the Division of Food Contact Notifications and the Division of Biotechnology and GRAS Notice Review collaborated to provide an updated exposure assessment (Attachment 1).[31] The exposure assessment was conducted using a probabilistic approach in evaluating exposures and resulted in an **updated estimate of 0.2 µg/kg-bw/d (mean) and 0.5 µg/kg-bw/d (90th percentile) for the adult US population aged 2 years and older**.
>
> Previous FDA exposure assessments estimated exposures[32] for infants and toddlers less than 2 years old with mean and 90th percentile estimates as follows (age, µg/kg-bw/d): 0-1 year, 0.3, 0.6; 1-2 years, 0.5, 1.1. In the current 2014 memorandum, the exposure assessment did not include updated values for these groups but did note that exposure is expected to decrease based on recent amendments to the food additive regulations that no longer authorize the use of polycarbonate resins in infant feeding bottles and spill-proof cups designed to help train babies and toddlers to drink from cups (77 FR 41899, July 17, 2012) and to no longer provide for the use of BPA-based epoxy resins as coatings in packaging for infant formula (78 FR 41840, July 12, 2013), as well as an increase in effective notifications for "BPA-free" materials including can coatings.[33] *[Emphasis added]*.

The memo also established an EDI based on the 90th percentile of:

- 1100 ng/kg bw/day for people younger than two years; and
- 500 ng/kg bw/day for people two years and older.

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[30] FDA 2014 Exposure Assessment.
[31] Id. Footnote 4 Memorandum dated 3/18/2014, Hatwell/Mihalov to Aungst, Updated exposure assessment for Bisphenol A (BPA) from the consumption of adult (canned) food – new data on canned food and beverages.
[32] Id. Footnote 5 Memorandum dated 5/4/ 2011, Bailey/Hatwell/Mihalov to Twaroski, Updated exposure to Bisphenol A (BPA) from the consumption of infant formula, toddler food and adult (canned) food-new data on canned food and beverages.
[33] Id.

The exposure assessment appears to have considered migration of BPA into food from two uses: in metal can lining and in the manufacture of polycarbonate plastic baby bottles. The 2014 analysis indicates that the EDI may actually be lower due to three factors:

- Abandonment of polycarbonate resins in infant feeding bottles and spill-proof cups designed to help train babies and toddlers to drink from cups;
- Abandonment of BPA-based epoxy resins as coatings in packaging for infant formula; and
- Market switch to "BPA-free" materials.

It is not clear that FDA's EDI accounts for five other FDA-approved uses of BPA:

- Adhesives used as components of articles intended for use in packaging, transporting, or holding food at § 175.105.
- 4,4'-Isopropylidenediphenol-epichlorohydrin resins minimum molecular weight 10,000 used as articles or components of articles intended for use in producing, manufacturing, packing, processing, preparing, treating, packaging, transporting, or holding food at § 177.1440.
- Polyestercarbonate resins used as articles or components of articles intended for use in producing, manufacturing, packing, processing, preparing, treating, packaging, or holding food at § 177.1585.
- 4,4'-Isopropylidenediphenol-epichlorohydrin thermosetting epoxy resins used as articles or components of articles intended for repeated use in producing, manufacturing, packing, processing, preparing, treating, packaging, transporting, or holding food at § 177.2280.
- Polyethersulfone resins used as articles or components of articles intended for repeated use in contact with food at § 1775.2440.

Similarly, FDA's EDI does not appear to have accounted for the uses that the agency authorized through its Food Contact Substance Notification (FCN) program. Between 2004 and 2017, the agency authorized twelve FCNs for BPA:

FCN No.	Food Contact Substance	Manufacturer/ Supplier	Effective Date
362	Siloxanes and silicones, di-methyl, 3-(4-hydroxy-3-methoxyphenyl)propyl group-terminated, **polymers with bisphenol A**, carbonic dichloride and 4-(1-methyl-1-phenylethyl)phenol (CAS Reg. No. 202483-49-6; also known as siloxane-modified polycarbonate) where the siloxane-modified portion of the FCS is approximately 22 percent by weight of the FCS.	SHPP US LLC	Jan 7, 2004
363	Siloxanes and silicones, di-methyl, 3-(4-hydroxy-3-methoxy-3-methoxyphenyl)propyl group-terminated, **polymers with bisphenol A**, carbonic dichloride and 4-(1-methyl-1-phenylethyl)phenol (CAS Reg. No. 202483-49-6; also known as siloxane-modified polycarbonate)	SHPP US LLC	Jan 7, 2004

	where the siloxane-modified portion of the FCS is approximately 7 percent by weight of the FCS.		
404	4,4'-[Isopropylidenebis(p-phenyleneoxy)]diphthalic dianhydride/4,4'-diaminodiphenyl sulfone copolymer (CAS Reg. No. 77699-82-2).	SHPP US LLC	May 13, 2004
463	1,3-Benzenedicarbonyl dichloride, polymer with 1,4-benzenedicarbonyl dichloride, 1,3-benzenediol, carbonic dichloride and **4,4'-(1-methylethylidene)bisphenol**, 4-(1-methyl-1-phenylethyl)phenyl ester (CAS Reg. No. 235420-85-6).	SHPP US LLC	Feb 12, 2005
517	Polysulfone-polyphenylene sulfone block copolymer CAS name: [1,1'-Biphenyl]-4,4'-diol, polymer with **4,4'-(1-methylethylidene)bis[phenol]** and 1,1'-sulfonylbis[4-chlorobenzene] (CAS Reg. No. 27757-21-7).	Solvay Specialty Polymers USA, LLC	Aug 31, 2005
624	Poly[(bis(isoindol-2-yl-1,3-dione)-1,3-phenylene)-**4,4'-(1-methylethylidene)bisphenol**].	SHPP US LLC	Sep 16, 2006
702	Carbonic dichloride, polymer with 4,4'-cyclohexylidenebis[2-methylphenol] and **4,4'-(1-methylethylidene)bis[phenol],** bis[4-(1-methyl-1-phenylethyl)phenyl] ester (CAS Reg. No. 411234-34-9).	SHPP US LLC	May 19, 2007
737	Poly[bis(isoindol-2-yl-1,3-dione)-1,3-phenylene-**4,4'-(1-methylethylidene)bisphenol**].	SHPP US LLC	Sep 5, 2007
1092	1,3-benzenedicarbonyl dichloride, polymer with 1,4-benzenedicarbonyl dichloride, carbonic dichloride and **4,4'-(1-methylethylidene)bis[phenol]** (polyester carbonate resins) (CAS Reg. No. 71519-80-7). The resins are produced by the condensation of 4,4'-isopropylidenediphenol, carbonyl chloride, terephthaloyl chloride, and isophthaloyl chloride such that the finished resins are composed of 45 to 85 mole percent ester, of which up to 55 mole percent is the terephthaloyl isomer. The resins are manufactured using a phthaloyl chloride/carbonyl chloride mole ratio of (0.81 to 5.7)/1 and isophthaloyl chloride/terephthaloyl chloride mole ratio of 0.81/1 or greater. The manufacturing process may include optional adjuvant substances authorized for the resins.	SABIC Innovative Plastics	Aug 10, 2011
1115	Carbonic dichloride, polymer with **4,4'-(1-methylethylidene)bis[phenol]**, 4-(1-methyl-1-phenylethyl)phenyl ester (polycarbonate resins) (CAS Reg. No. 11211-39-3). The resins are produced by the condensation of **4,4'-(isopropylidenediphenol)** and carbonyl chloride. The manufacturing process may include optional adjuvant substances authorized in the production of the resins.	SABIC Innovative Plastics	Nov 12, 2011

1387	A mixture of 2-ethylhexyl acrylate (CAS Reg. No. 103-11-7), acrylic acid (CAS Reg. No. 79-10-7), methacrylic acid (CAS Reg. No. 79-41-4), methyl methacrylate (CAS Reg. No. 80-62-6) and styrene (CAS Reg. No. 100-42-5).	Sherwin-Williams Company	Jul 8, 2014
1751	Carbonic dichloride, polymer with 2,3-dihydro-3,3-bis(4-hydroxyphenyl)-2-phenyl-1-H-isoindol-1-one and **4,4-(1-methylethylidene)bis[phenol],** bis[4-(1-methyl-1-phenylethyl)phenyl] ester (CAS Reg. No. 503834-43-3).	SHPP US LLC	Jul 7, 2017

Finally, FDA appears to have only considered migration from final food packaging and ignored migration from food contact articles used in food processing, manufacturing, and service (such as restaurants).

Because of the various ambiguities, we assume that FDA's 2014 90th percentile EDI for the population 2 years and older is unlikely to be more than an order of magnitude higher or lower if the agency were to update it.

3. Consideration of the cumulative effect of the substance in the diet, taking into account any chemically- or pharmacologically-related substance or substances in such diet.

Because the 90th percentile EDI for BPA already exceeds the TDI by four orders of magnitude, there is no need to consider the "cumulative effect of the substance in the diet, taking into account any chemically or pharmacologically related substance or substances in such diet" to conclude that FDA's approved food-contact uses are not safe pursuant to 21 CFR § 170.3(i) and 21 U.S.C. § 348.

If FDA determines that our proposed TDI is inappropriate or the EDI does not actually exceed the TDI, then it must consider the cumulative effect all substances in the diet that are:

- Chemically-related to BPA; and
- Pharmacologically-related to BPA because they affect the:
  - Immune system;
  - Metabolic system;
  - Neurodevelopment; and
  - Male and female reproduction and development.

I.F. Proposed tolerances for the food additive

In 2015, EFSA established a temporary TDI (*t*-TDI) of 4,000 ng/kg bw/day – 20% more protective than the one set by FDA.[34] Based on the *t*-TDI, the European Commission established a specific migration limit of 50,000 ng of BPA per kg of food (ng/kg). This limit is based on "a conventional exposure assumption that 1 kg of food is consumed daily by a person of 60 kg body weight and that all exposure comes from food contact materials."[35]

Since the revised TDI of 0.04 ng/kg bw/day is 100,000 times lower than the *t*-TDI, the revised specific migration limit should be proportionally lower. We calculate that the revised specific migration limit for BPA should be 0.5 ng/kg.

Therefore, we propose a specific migration limit, which is effectively the tolerance, for BPA in food of 0.5 ng/kg.

[34] European Commission Regulation (EU) 2018/213 of 12 February 2018 on the use of bisphenol A in varnishes and coatings intended to come into contact with food and amending Regulation (EU) No 10/2011 as regards the use of that substance in plastic food contact materials, Official Journal of the European Union, 14.2.2018, https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32018R0213&from=EN,
[35] Id.

I.G. Full information on each proposed change to the original regulation

We are asking FDA to revoke uses of BPA for adhesives and coatings and strictly limit migration of the substances into food from various plastic food contact articles. Below is a summary of our requested changes to the FDA's regulations. Appendix II provides specific proposed changes, edits, and additions.

1. Add new § 174.7 as a "General limitation of use 4,4'-Isopropylidenediphenol" with the following restriction on use of BPA:

   Except as specifically described in parts 175, 176, and 177, for any use of the 4,4'-Isopropylidenediphenol, CAS Reg. No. 80-05-7, as a constituent in a food contact article that may migrate into food, the substance is subject to a specific migration limit of 0.5 nanograms per kilogram of food. If the specific migration limit is below the limit of quantification (based on 95% confidence that the false negative rate is less than 5%) using the most sensitive method, the concentration must be below the limit of quantification.

   Rationale: The new § 174.7 would establish a condition of use for BPA in a regulation issued pursuant to 21 U.S.C. § 348 that would apply to any use of BPA in food contact articles. We maintain that it is important to establish this condition of use for BPA to apply to current and future:
   - *Effective Food Contact Substance Notifications (FCN) including the 12 described in Section E.2 above;*
   - *Generally Recognized as Safe (GRAS) safety determinations, whether or not FDA has been notified of the determination; and*
   - *Food contact articles that contain pre- or post-consumer recycled materials that may have BPA.*

   In Section I.D, we described LC-MS/MS as a practicable method to determine the amount of the BPA in food at the ng/kg levels. However, its limit of quantitation is not sufficient to measure BPA at the proposed specific migration limit. We anticipate that more sensitive laboratory methods will be developed. Therefore, we provide an option for companies to demonstrate compliance by having a concentration in the food that is less than the limit of quantification for BPA using the most sensitive method then existing. We define the limit of quantification using the example in FDA's most recent guidance on validation of chemical methods.[36]

2. Modify the following sections that currently allow the use of BPA in food contact articles:

[36] FDA, Memorandum from its Regulatory Science Steering Committee to the Foods Program Government Board regarding Guidelines for the Validation of Chemical Methods for the FDA Foods Program, 3rd Edition, October 17, 2019, on page 24. See https://www.fda.gov/food/laboratory-methods-food/foods-program-methods-validation-processes-and-guidelines.

a. § 175.105 – Adhesives used as components of articles intended for use in packaging, transporting, or holding food.

Proposed change: Remove the eight listings of BPA permitted for use in adhesives from paragraph (c)(5).

Rationale: Removing the listings of BPA will prevent the substance being used in adhesives. We maintain that: 1) it is very difficult to prevent migration from an adhesive; and 2) adhesives with BPA are likely to contaminate food contact articles with pre- or post-consumer recycled materials that may have BPA. There are many non-BPA approved alternative adhesives in § 175.105.

b. § 175.300 – Resinous and polymeric coatings used as the food-contact surface of articles intended for use in producing, manufacturing, packing, processing, preparing, treating, packaging, transporting, or holding food.

Proposed change: Remove the eight listings of BPA permitted for the following uses:

- *Rosins esters*
- *Phenolic resins*
- *Epoxy resins*
- *Glycidyl ethers*
- *Melamine-formaldehyde*

Proposed change: Remove paragraph (i) prohibiting use of epoxy resins in packaging for powdered and liquid infant formula.

Rationale: Removing the listings of BPA will prevent the substance being used in resinous and polymeric coatings. We maintain that: 1) it is very difficult to prevent migration from a coating; and 2) coatings with BPA are likely to contaminate food contact articles with pre- or post-consumer recycled materials that may have BPA. There are many non-BPA approved alternative coatings in § 175.300 and in FCNs. The paragraph (i) banning use of BPA in powdered and liquid infant formula is not needed since the proposed change would prohibit the use in all packaging.

c. § 177.1440 – 4,4'-Isopropylidenediphenol-epichlorohydrin resins minimum molecular weight 10,000 used as articles or components of articles intended for use in producing, manufacturing, packing, processing, preparing, treating, packaging, transporting, or holding food.

Proposed change: Insert new paragraph (d) with the language limiting migration of BPA that is described in section 1, above, tailored to the resins covered by this section.

Rationale: BPA could continue to be used in 4,4'-Isopropylidenediphenol-epichlorohydrin resins, but the use must meet the 0.5 ng/kg specific migration limit consistent with proposed § 174.7.

d. § 177.1580 – Polycarbonate resins used as articles or components of articles intended for use in producing, manufacturing, packing, processing, preparing, treating, packaging, transporting, or holding food.

Proposed change: Add new paragraph (e) with the language limiting migration of BPA that described in section 1, abov,e tailored to the resins covered by this section.

Rationale: BPA could continue to be used in polycarbonate resins, but the use must meet the 0.5 ng/kg specific migration limit consistent with proposed § 174.7.

e. § 177.1585 – Polyestercarbonate resins used as articles or components of articles intended for use in producing, manufacturing, packing, processing, preparing, treating, packaging, or holding food.

Proposed change: Add new paragraph (d) with the language limiting migration of BPA that is described in section 1, above, tailored to the resins covered by this section.

Rationale: BPA could continue to be used in polyestercarbonate resins, but the use must meet the 0.5 ng/kg specific migration limit consistent with proposed § 174.7.

f. § 177.2280 – 4,4'-Isopropylidenediphenol-epichlorohydrin thermosetting epoxy resins used as articles or components of articles intended for repeated use in producing, manufacturing, packing, processing, preparing, treating, packaging, transporting, or holding food.

Proposed change: Insert new paragraph (e) with the language limiting migration of BPA that is described in section 1, above, tailored to the resins covered by this section.

Rationale: BPA could continue to be used in 4,4'-Isopropylidenediphenol-epichlorohydrin thermosetting epoxy resins, but the use must meet the 0.5 ng/kg specific migration limit consistent with proposed § 174.7.

g. § 177.2440 – Polyethersulfone resins used as articles or components of articles intended for repeated use in contact with food.

Proposed change: Remove listings of BPA permitted for use in paragraph (a)(2).

Rationale: BPA could be removed as one of two options to produce polyethersulfone resins.

I.H. Environmental review component

This food additive petition is categorically excluded from the need to prepare an Environmental Assessment under 21 CFR § 25.32(m) as an "action to prohibit or otherwise restrict or reduce the use of a substance in food, food packaging, or cosmetics." We have identified no extraordinary circumstances as defined at 21 CFR § 25.21 for the action requested in this petition which would require the submission of an Environmental Assessment.

If the manufacturer determined that these additives were also insufficient and no additives were "generally recognized as safe" without FDA review, the manufacturers would submit a food additive petition for agency review. In this review, the agency would consider compliance with the National Environmental Policy Act.

Determining whether a specific additive is an acceptable substitute involves a detailed analysis of each use. However, we identified the following alternatives.

- *Sec. 175.105 Adhesives:* FDA has approved more than 1200 chemicals other than BPA that it has approved for use in adhesives.
- *Sec. 175.300 Resinous and polymeric coatings:* FDA has approved more than 600 chemicals other than BPA that it has approved for use in resinous and polymeric coatings. In addition, FDA has already removed its approval for the use of BPA in epoxy resins as coatings in packaging for infant formula, demonstrating that sufficient FDA-approved or authorized alternatives are available to food manufacturers.[37] Also, in 2014, the agency noted an increase in effective notifications for "BPA-free" materials including can coatings.[38]
- *Sec. 177.2440 Polyethersulfone resins:* FDA has approved two formulations of the resin. We are only asking for the formulation involving BPA to be revoked, leaving another formulation

For the other resin uses, we ask that FDA limit to 0.5 ng/kg the amount of the BPA allowed to migrate into food.
In addition, FDA has already removed its approval for the use of BPA in polycarbonate resins in infant feeding bottles and spill-proof cups designed to help train babies and toddlers to drink from cups.[39] Therefore, food manufacturers have already demonstrated they have alternatives for BPA in these uses and can extend them to other broader uses of the same material.

[37] FDA, Indirect Food Additives: Adhesives and Components of Coatings, Final Rule, 78 *Federal Register* 41840, July 12, 2013, https://www.federalregister.gov/documents/2013/07/12/2013-16684/indirect-food-additives-adhesives-and-components-of-coatings.
[38] FDA 2014 Exposure Assessment.
[39] FDA, Indirect Food Additives: Polymers, Final Rule, 77 *Federal Register* 41899, July 17, 2012, https://www.federalregister.gov/documents/2012/07/17/2012-17366/indirect-food-additives-polymers.

Appendix II
Proposed Changes to FDA Approvals

PART 174 -- INDIRECT FOOD ADDITIVES: GENERAL

NEW Sec. 174.7- General limitation on use of 4,4'-Isopropylidenediphenol

Except as specifically described in parts 175, 176, and 177, for any use of the 4,4'-Isopropylidenediphenol, CAS Reg. No. 80-05-7, as a constituent in a food contact article that may migrate into food, the substance is subject to a specific migration limit of 0.5 nanograms per kilogram of food. If the specific migration limit is below the limit of quantification (based on 95% confidence that the false negative rate is less than 5%) using the most sensitive method, the concentration must be below the limit of quantification.

PART 175 -- INDIRECT FOOD ADDITIVES: ADHESIVES AND COMPONENTS OF COATINGS

SUBPART B - SUBSTANCES FOR USE ONLY AS COMPONENTS OF ADHESIVES

MODIFY EXISTING Sec. 175.105 Adhesives as follows:

(a) Adhesives may be safely used as components of articles intended for use in packaging, transporting, or holding food in accordance with the following prescribed conditions
. . .

(c) Subject to any limitation prescribed in this section and in any other regulation promulgated under section 409 of the Act which prescribes safe conditions of use for substances that may be employed as constituents of adhesives, the optional substances used in the formulation of adhesives may include the following:

. . .

(5) Substances permitted for use in adhesives by other regulations in this subchapter and substances named in this subparagraph: *Provided, however,* that any substance named in this paragraph and covered by a specific regulation in this subchapter, must meet any specifications in such regulation.

Substances	Limitations
~~Epichlorohydrin-4,4'-isopropylidenediphenol resin~~	
~~Epichlorohydrin-4,4'-sec-butylidenediphenol resin~~	
~~4,4'-Isopropylidenediphenol~~	
~~4,4'-Isopropylidenediphenol, polybutylated mixture~~	~~For use as preservative only.~~
~~Propylene glycol and p-p'-isopropylidenediphenol diether~~	

~~Rosin (wood, gum, and tall oil rosin), rosin dimers, decarboxylated rosin (including rosin oil, disproportionated rosin, and these substances as modified by one or more of the following reactants:~~	
~~4,4'-Isopropylidenediphenol-epichlorohydrin (epoxy)~~	
~~4,4'-Isopropylidenediphenol-formaldehyde~~	

SUBPART C - SUBSTANCES FOR USE AS COMPONENTS OF COATINGS

MODIFY EXISTING Sec. 175.300 Resinous and polymeric coatings as follows:

Resinous and polymeric coatings may be safely used as the food-contact surface of articles intended for use in producing, manufacturing, packing, processing, preparing, treating, packaging, transporting, or holding food, in accordance with the following prescribed conditions:
. . .

(b) The coatings are formulated from optional substances that may include:
. . .

(3) Any substance employed in the production of resinous and polymeric coatings that is the subject of a regulation in subchapter B of this chapter and conforms with any specification in such regulation. Substances named in this paragraph (b)(3) and further identified as required:
. . .

(v) Rosins and rosin derivatives, with or without modification by polymerization, isomerization, incidental decarboxylation, and/or hydrogenation, as follows:
. . .

(*b*) Rosin esters formed by reacting rosin (paragraph (b)(3)(v)(*a*) of this section) with:
. . .
~~4,4'-Isopropylidenediphenol-epichlorohydrin (epoxy).~~
. . .

(vi) Phenolic resins as the basic polymer formed by reaction of phenols with formaldehyde:
. . .

(a) Phenolic resins formed by reaction of formaldehyde with:
. . .
~~4,4'-Isopropylidenediphenol.~~
. . .

(viii) Epoxy resins, catalysts, and adjuncts:

(*a*) Epoxy resins, as the basic polymer:

. . .

(Alkoxy C10-C16)-2,3-epoxypropane, in which the alkyl groups are even numbered and consist of a maximum of 1 percent C10 carbon atoms and a minimum of 48 percent C12 carbon atoms and a minimum of 18 percent C14 carbon atoms, for use only in coatings that are intended for contact with dry bulk foods at room temperature.

. . .

~~4,4'-Isopropylidenediphenol-formaldehyde.~~

. . .

Glycidyl ethers formed by reacting phenolnovolak resins with epichlorohydrin.

. . .

~~4,4'-Isopropylidenediphenol-epichlorohydrin.~~

~~4,4'-Isopropylidenediphenol-epichlorohydrin reacted with one or more of the drying oils or fatty acids listed in paragraph (b)(3)(i) of this section.~~

~~4,4'-Isopropylidenediphenol-epichlorohydrin chemically treated with one or more of the following substances:~~

. . .

~~4,4'-Isopropylidenediphenol-formaldehyde.~~

. . .

Melamine-formaldehyde.

~~2,2'-[(1-methylethylidene)bis[4,1-phenyleneoxy[1-(butoxymethyl)-2,1-ethanediyl]oxymethylene>bisoxirane, CAS Reg. No. 71033-08-4, for use only in coatings intended for contact with bulk dry foods at temperatures below 100 deg.F.~~

. . .

~~(i) Epoxy resins derived by the reaction of 4,4'-isopropylidenediphenol and epichlorohydrin, as described in paragraph (b)(3)(viii)(*a*) of this section, may be used in accordance with this section except as coatings in packaging for powdered and liquid infant formula.~~

PART 177 -- INDIRECT FOOD ADDITIVES: POLYMERS

SUBPART B - SUBSTANCES FOR USE AS BASIC COMPONENTS OF SINGLE AND REPEATED USE FOOD CONTACT SURFACES

MODIFY EXISTING Sec. 177.1440 4,4'-Isopropylidenediphenol-epichlorohydrin resins minimum molecular weight 10,000.

4,4'-Isopropylidenediphenol-epichlorohydrin resins having a minimum molecular weight of 10,000 may be safely used as articles or components of articles intended for use in producing, manufacturing, packing, processing, preparing, treating, packaging, transporting, or holding food in accordance with the following prescribed conditions:

(a) 4,4'-Isopropylidenediphenol-epichlorohydrin resins consist of basic resins produced by the condensation of equimolar amounts of 4,4'-isopropylidenediphenol and epichlorohydrin terminated with phenol, to which may have been added certain optional adjuvant substances required in the production of the resins.

(b) The optional adjuvant substances required in the production of the resins may include substances generally recognized as safe in food, substances used in accordance with a prior sanction or approval, and the following:

List of substances	Limitations
Butyl alcohol	Not to exceed 300 p.p.m. as residual solvent in finished resin.
Ethyl alcohol	
Toluene	Not to exceed 1,000 p.p.m. as residual solvent in finished resin.

(c) 4,4'-Isopropylidenediphenol-epichlorohydrin resins shall meet the following nonvolatile extractives limitations:

(1) Maximum extractable nonvolatile fraction of 2 parts per million when extracted with distilled water at 70 deg.C for 2 hours, using a volume-to-surface ratio of 2 milliliters per square inch.

(2) Maximum extractable nonvolatile fraction of 3 parts per million when extracted with *n*- heptane at 70 deg.C for 2 hours, using a volume-to-surface ratio of 2 milliliters per square inch.

(3) Maximum extractable nonvolatile fraction of 6 parts per million when extracted with 10 percent (by volume) ethyl alcohol in distilled water at 70 deg.C for 2 hours, using a volume-to-surface ratio of 2 milliliters per square inch.

(d) 4,4'-Isopropylidenediphenol, CAS Reg. No. 80-750-7, migration into food contacting articles made with 4,4'-Isopropylidenediphenol-epichlorohydrin resins must be lower than the specific migration limit of 0.5 nanograms of the substance per kilogram of food. If the specific migration

limit is below the limit of quantification (based on 95% confidence that the false negative rate is less than 5%) using the most sensitive method, the concentration must be below the limit of quantification.

(e)~~(d)~~ The provisions of this section are not applicable to 4,4'-isopropylidene-diphenol-epichlorohydrin resins listed in other sections of subchapter B of this chapter.

MODIFY EXISTING Sec. 177.1580 Polycarbonate resins.

Polycarbonate resins may be safely used as articles or components of articles intended for use in producing, manufacturing, packing, processing, preparing, treating, packaging, transporting, or holding food, in accordance with the following prescribed conditions:

(a) Polycarbonate resins are polyesters produced by:

(1) The condensation of 4,4'-iso-propylidenediphenol and carbonyl chloride to which may have been added certain optional adjuvant substances required in the production of the resins; or by

(2) The reaction of molten 4,4'-iso-propylidenediphenol with molten diphenyl carbonate in the presence of the disodium salt of 4,4'-isopropylidenediphenol.

(3) The condensation of 4,4'-isopropylidenediphenol, carbonyl chloride, and 0.5 percent weight maximum of *a* 2,*a* 6-bis (6-hydroxy-*m*- tolyl) mesitol to which may have been added certain optional adjuvant substances required in the production of branched polycarbonate resins.

(b) The optional adjuvant substances required in the production of resins produced by the methods described in paragraph (a)(1) and (3) of this section may include substances generally recognized as safe in food, substances used in accordance with a prior sanction or approval, and the following:

List of substances	Limitations
p-tert-Butylphenol	
Chloroform	
p-Cumylphenol (CAS Reg. No. 599-64-4)	For use only as a chain terminator at a level not to exceed 5 percent by weight of the resin.
Ethylene dichloride	
Heptane	
Methylene chloride	
Monochlorobenzene	Not to exceed 500 p.p.m. as residual solvent in finished resin.

Pentaerythritol tetrastearate (CAS Reg. No. 115-83-3)	For use only as a mold release agent, at a level not to exceed 0.5 percent by weight of the finished resin.
Phenol (CAS Reg. No. 108-95-2)	
Pyridine	
Toluene: (CAS Reg. No. 108-88-3)	Not to exceed 800 parts per million as residual solvent in finished resin.
Triethylamine	

(c) Polycarbonate resins shall conform to the specification prescribed in paragraph (c)(1) of this section and shall meet the extractives limitations prescribed in paragraph (c)(2) of this section.

(1) *Specification.* Polycarbonate resins can be identified by their characteristic infrared spectrum.

(2) *Extractives limitations.* The polycarbonate resins to be tested shall be ground or cut into small particles that will pass through a U.S. standard sieve No. 6 and that will be held on a U.S. standard sieve No. 10.

(i) Polycarbonate resins, when extracted with distilled water at reflux temperature for 6 hours, shall yield total extractives not to exceed 0.15 percent by weight of the resins.

(ii) Polycarbonate resins, when extracted with 50 percent (by volume) ethyl alcohol in distilled water at reflux temperature for 6 hours, shall yield total extractives not to exceed 0.15 percent by weight of the resins.

(iii) Polycarbonate resins, when extracted with *n*- heptane at reflux temperature for 6 hours, shall yield total extractives not to exceed 0.15 percent by weight of the resins.

(d) Polycarbonate resins may be used in accordance with this section except in infant feeding bottles (baby bottles) and spill-proof cups, including their closures and lids, designed to help train babies and toddlers to drink from cups (sippy cups).

(e) 4,4'-Isopropylidenediphenol, CAS Reg. No. 80-50-7, migration into food contacting articles made with polycarbonate resins must be lower than the specific migration limit of 0.5 nanograms of the substance per kilogram of food. If the specific migration limit is below the limit of quantification (based on 95% confidence that the false negative rate is less than 5%) using the most sensitive method, the concentration must be below the limit of quantification.

MODIFY EXISTING Sec. 177.1585 Polyestercarbonate resins.

Polyestercarbonate resins may be safely used as articles or components of articles intended for use in producing, manufacturing, packing, processing, preparing, treating, packaging, or holding food, in accordance with the following prescribed conditions:

(a) Polyestercarbonate resins (CAS Reg. No. 71519-80-7) are produced by the condensation of 4,4'-isopropylidenediphenol, carbonyl chloride, terephthaloyl chloride, and isophthaloyl chloride such that the finished resins are composed of 45 to 85 molepercent ester, of which up to 55 mole-percent is the terephthaloyl isomer. The resins are manufactured using a phthaloyl chloride/carbonyl chloride mole ratio of 0.81 to 5.7/1 and isophthaloyl chloride/terephthaloyl chloride mole ratio of 0.81/1 or greater. The resins are also properly identified by CAS Reg. No. 114096-64-9 when produced with the use of greater than 2 but not greater than 5 weight percent *p* -cumylphenol (CAS Reg. No. 599-64-4), as an optional adjuvant substance in accordance with paragraph (b)(2) of this section.

(b) *Optional adjuvants.* The optional adjuvant substances required in the production of resins identified in paragraph (a) of this section may include:

(1) Substances used in accordance with § 174.5 of this chapter.

(2) Substances identified in § 177.1580(b).

(3) Substances regulated in § 178.2010(b) of this chapter for use in polycarbonate resins complying with § 177.1580:
Provided, That the substances are used in accordance with any limitation on concentration, conditions of use, and food types specified in § 178.2010(b) of this chapter.

(c) Polyestercarbonate resins shall conform to the specifications prescribed in paragraph (c)(1) of this section and shall meet the extractive limitations prescribed in paragraph (c)(2) of this section.

(1) *Specifications.* Polyestercarbonate resins identified in paragraph (a) of this section can be identified by their characteristic infrared spectrum. The resins shall comply with either or both of the following specifications:

(i) The solution intrinsic viscosity of the polyestercarbonate resins shall be a minimum of 0.44 deciliter per gram, as determined by a method entitled "Intrinsic Viscosity (IV) of Lexan (R) Polyestercarbonate Resin by a Single Point Method Using Dichloromethane as the Solvent," developed by the General Electric Co., September 20, 1985, which is incorporated by reference in accordance with 5 U.S.C. 552(a) and 1 CFR part 51. Copies are available from the Office of Food Additive Safety, Center for Food Safety and Applied Nutrition (HFS-215), Food and Drug Administration, 5001 Campus Dr., College Park, MD 20740, or may be examined at the Food and Drug Administration's Main Library, 10903 New

Hampshire Ave., Bldg. 2, Third Floor, Silver Spring, MD 20993, 301-796-2039, or at the National Archives and Records Administration (NARA). For information on the availability of this material at NARA, call 202-741-6030, or go to: *http://www.archives.gov/federal_register/code_of_federal_regulations/ibr_locations.html.*

(ii) A minimum weight-average molecular weight of 27,000, as determined by gel permeation chromatography using polystyrene standards.

(2) *Extractives limitations.* The polyestercarbonate resins to be tested shall be ground or cut into small particles that will pass through a U.S. standard sieve No. 6 and that will be held on U.S. standard sieve No. 10.

(i) Polyestercarbonate resins, when extracted with distilled water at reflux temperature for 6 hours, shall yield total nonvolatile extractives not to exceed 0.005 percent by weight of the resins.

(ii) Polyestercarbonate resins, when extracted with 50 percent (by volume) ethyl alcohol in distilled water at reflux temperature for 6 hours, shall yield total nonvolatile extractives not to exceed 0.005 percent by weight of the resins.

(iii) Polyestercarbonate resins, when extracted with *n* -heptane at reflux temperature for 6 hours, shall yield total nonvolatile extractives not to exceed 0.002 percent by weight of the resins.

(3) *Residual methylene chloride levels in polyestercarbonate resins.* Polyestercarbonate resin articles in the finished form shall not contain residual methylene chloride in excess of 5 parts per million as determined by a method titled "Analytical Method for Determination of Residual Methylene Chloride in Polyestercarbonate Resin," developed by the General Electric Co., July 23, 1991, which is incorporated by reference in accordance with 5 U.S.C. 552(a) and 1 CFR part 51. Copies are available from the Center for Food Safety and Applied Nutrition (HFS-200), Food and Drug Administration, 5001 Campus Dr., College Park, MD 20740, or may be examined at the National Archives and Records Administration (NARA). For information on the availability of this material at NARA, call 202-741-6030, or go to: *http://www.archives.gov/federal_register/code_of_federal_regulations/ibr_locations.html*.

(d) 4,4'-Isopropylidenediphenol, CAS Reg. No. 80-50-7, migration into food contacting articles made with polyestercarbonate resins must be lower than the specific migration limit of 0.5 nanograms of the substance per kilogram of food. If the specific migration limit is below the limit of quantification (based on 95% confidence that the false negative rate is less than 5%) using the most sensitive method, the concentration must be below the limit of quantification.

MODIFY EXISTING Sec. 177.2280 4,4'-Isopropylidenediphenolepichlorohydrin thermosetting epoxy resins.

4,4'-Isopropylidenediphenol-epichlorohydrin thermosetting epoxy resins may be safely used as articles or components of articles intended for repeated use in producing, manufacturing, packing, processing, preparing, treating, packaging, transporting, or holding food, in accordance with the following prescribed conditions:

(a) The basic thermosetting epoxy resin is made by reacting 4,4'-isopropylidenediphenol with epichlorohydrin.

(b) The resin may contain one or more of the following optional substances provided the quantity used does not exceed that reasonably required to accomplish the intended effect:

Allyl glycidyl ether	As curing system additive.
Di- and tri-glycidyl ester mixture resulting from the reaction of epichlorohydrin with mixed dimers and trimers of unsaturated C18 monobasic fatty acids derived from animal and vegetable fats and oils	As modifier at levels not to exceed equal parts by weight of the 4,4'-isopropylidenediphenol-epichlorohydrin basic resin and limited to use in contact with alcoholic beverages containing not more than 8 percent of alcohol.
1,2-Epoxy-3-phenoxypropane	As curing system additive.
Glyoxal	Do.
4,4'-Isopropylidenediphenol	Do.
4,4'-Methylenedianiline	Do.
m-Phenylenediamine	Do.
Tetrahydrophthalic anhydride	Do.

(c) In accordance with good manufacturing practice, finished articles containing the resins shall be thoroughly cleansed prior to their first use in contact with food.

(d) 4,4'-Isopropylidenediphenol, CAS Reg. No. 80-50-7, migration into food contacting articles made with 4,4'-Isopropylidenediphenolepichlorohydrin thermosetting epoxy resins must be lower than the specific migration limit of 0.5 nanograms of the substance per kilogram of food. If the specific migration limit is below the limit of quantification (based on 95% confidence that the false negative rate is less than 5%) using the most sensitive method, the concentration must be below the limit of quantification.

(e)~~(d)~~ The provisions of this section are not applicable to 4,4'-isopropylidenedi-phenol-epichlorohydrin resins listed in other sections of parts 174, 175, 176, 177, 178 and 179 of this chapter.

MODIFY EXISTING Sec. 177.2440 Polyethersulfone resins as follows:

Polyethersulfone resins identified in paragraph (a) of this section may be safely used as articles or components of articles intended for repeated use in contact with food in accordance with the following prescribed conditions:

(a) For the purpose of this section, polyethersulfone resins are:

(1) Poly(oxy-*p* -phenylenesulfonyl-*p* -phenylene) resins (CAS Reg. No. 25667-42-9), which have a minimum number average molecular weight of 16,000.

(2) ~~1,1'-sulfonylbis[4-chlorobenzene] polymer with 4,4'-(1-methylethylidene)bis[phenol] (maximum 8 percent) and 4,4'-sulfonylbis[phenol] (minimum 92 percent) (CAS Reg. No. 88285-91-0), which have a minimum number average molecular weight of 26,000.~~

~~(3)~~ In paragraphs (a)(1) ~~and (a)(2)~~ of this section, the minimum number average molecular weight is determined by reduced viscosity in dimethyl formamide in accordance with ASTM method D2857-70 (Reapproved 1977), "Standard Test Method for Dilute Solution Viscosity of Polymers," which is incorporated by reference. Copies may be obtained from the American Society for Testing Materials, 100 Barr Harbor Dr., West Conshohocken, Philadelphia, PA 19428-2959, or may be examined at the Office of Food Additive Safety (HFS-200), Center for Food Safety and Applied Nutrition, Food and Drug Administration, 5001 Campus Dr., College Park, MD 20740, 240-402-1200 or at the National Archives and Records Administration (NARA). For information on the availability of this material at NARA, call 202-741-6030, or go to: *http://www.archives.gov/federal_register/code_of_federal_regulations/ibr_locations.html* .

(b) The basic resins identified in paragraphs (a)(1) ~~and (a)(2)~~ of this section may contain optional adjuvant substances described in § 174.5(d) of this chapter and the following:

List of substances	Limitations
Diphenylsulfone	Not to exceed 0.2 percent as residual solvent in the finished basic resin described in paragraph (a)(1) of this section.
Dimethyl sulfoxide	Not to exceed 0.01 percent as residual solvent in the finished basic resin described in paragraph (a)(1) of this section.
N-methyl-2-pyrrolidone	Not to exceed 0.01 percent as residual solvent in the finished basic resin described in paragraph (a)(2) of this section.

(c) The finished food-contact article, when extracted at reflux temperatures for 2 hours with the following four solvents, yields net chloroform-soluble extractives in each extracting solvent not to exceed 0.02 milligram per square inch of food-contact surface: distilled water, 50 percent (by volume) ethyl alcohol in distilled water, 3 percent acetic acid in distilled water, and *n* -heptane.

(Note: In testing the finished food-contact article, use a separate test sample for each required extracting solvent.)

(d) In accordance with good manufacturing practice, finished food-contact articles containing the polyethersulfone resins shall be thoroughly cleansed before their first use in contact with food.