



Memorandum

Date: August 13, 2001

From: Division of Food Contact Substance Notification Review, Chemistry Group 1

[REDACTED]
A (BPA) [REDACTED]

bisphenol

To: Associate Directorate for Science & Policy
Attention: Mitchell Cheeseman, Ph.D.

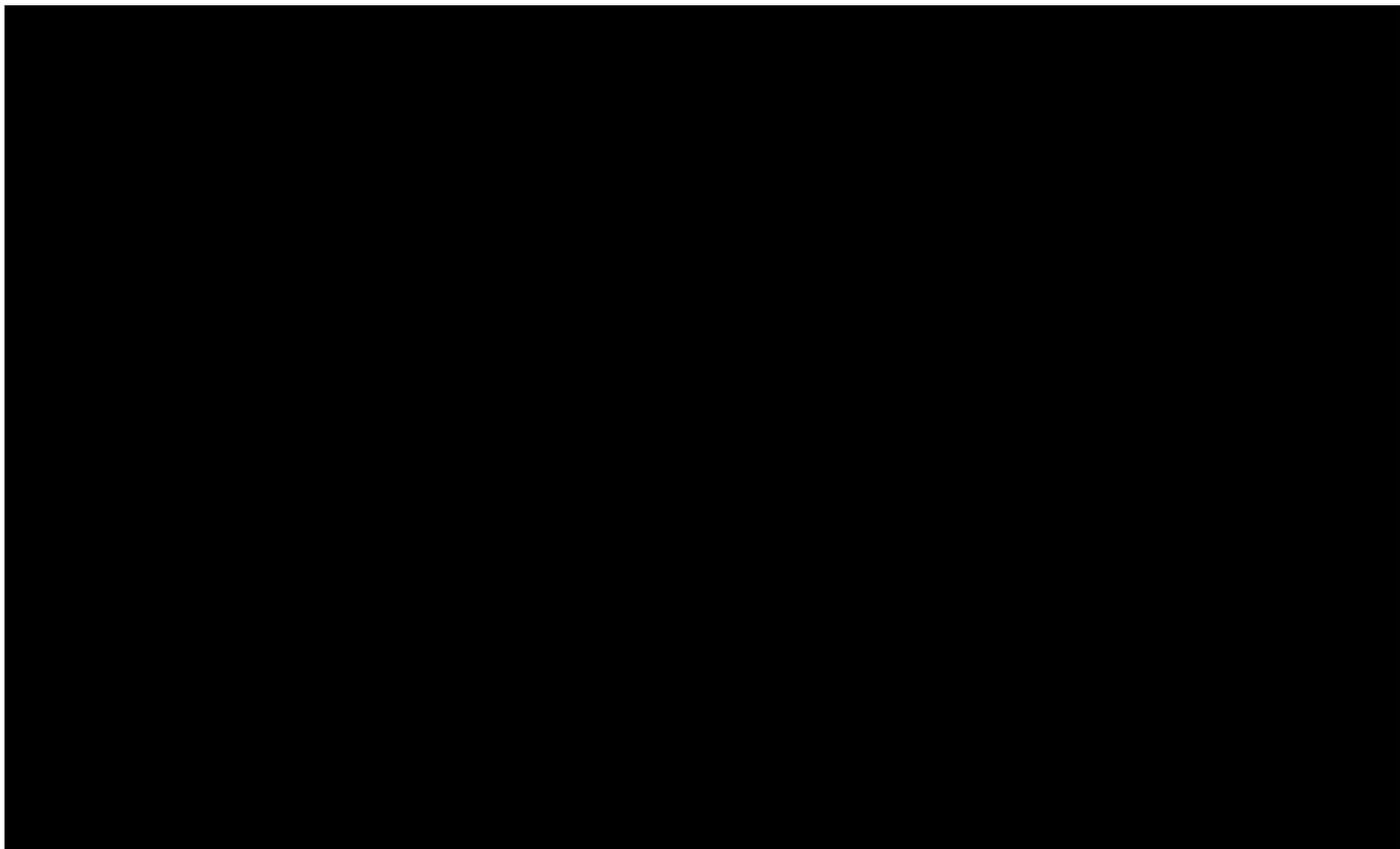
In a facsimile dated 4-3-01, [REDACTED] requested cumulative exposure [REDACTED]s (FCS) [REDACTED] Cumulative exposure to one of the four substances, bisphenol A diglycidyl ether (BADGE), will be addressed in a separate memorandum.

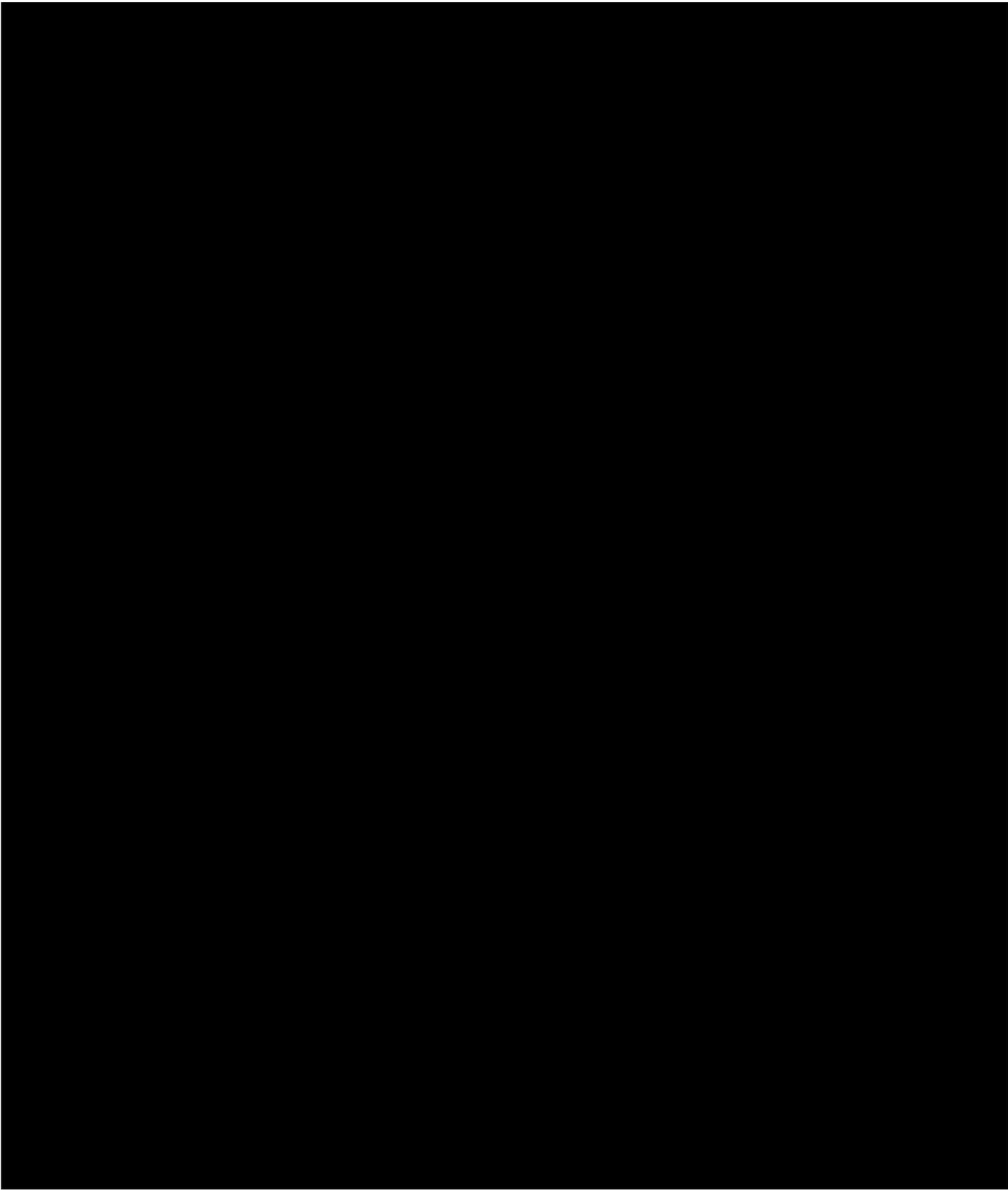
I relied on the following sources for general information:

- a) the file created by Ron Wright (s:\Food Additives\additive.pdf, updated 12-21-00; referred to as the FA file),
- b) the Handbook of Food Packaging Chemicals and Materials (HFPCM, published by Synapse Information Resources), and
- c) the Food Chemical News Guide "Knife and Fork" book (K&F Book)

For those substances that did not have cumulative estimated daily intakes (CEDI) values in the CEDI/ADI database (P:\Edi\EDISrev.mdb), I used SIREN, the FCN tracking spreadsheet (P:\0pa\dpc\tracking.xls) and the collection of recent chemistry memoranda (P:\Crt\Chemistry_Memos) to develop CEDIs.

The three FCSs, regulatory status, cumulative dietary concentrations (CDCs) and CEDIs are discussed below.





2. BISPHENOL A (BPA)

Regulatory Status

FA File

The FA file listing for BPA monomer and its disodium salt are as follows:

BISPHENOL A

Regulations: 21 CFR 175.105 * 21 CFR 175.300

For Use As: FLAVORING

CAS Reg. #: 80-05-7

Synonym(s): 4,4'-ISOPROPYLIDENEDIPHENOL * 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-

Scopenotes: SOURCE--CTFA ICID 6; MI 12, 1338; CCD 11; Combined Chemical
Dictionary CD-ROM.

DISODIUM BISPHENOL A

Regulations: 21 CFR 177.1655 * 21 CFR 177.1580

CAS Reg. #: 2444-90-8

According to the FA file, BPA is also listed as a monomer in several substances, including polymers, as shown in Attachment 2. Inspection of Attachment 2 indicates 1 polymer that is permitted for direct use in food (172.105), while the remaining substances include adhesives (175.105), can coatings (175.300), polyolefin coatings (175.320), polymers (Part 177) and adjuvant substances (Part 178).

The primary polymer listings under Part 177 include polyarylate resins (177.1555), polycarbonate resins (177.1580), polyestercarbonate resins (177.1585), polysulfone resins (177.1655), polyurethane resins for dry food (177.1680), repeat use rubber articles (177.2600) and polyester resins, cross-linked (177.2420). 4,4'-Isopropylidene-epichlorohydrin (BPA-ECH) resins with a minimum molecular weight of 10,000 are also permitted under 177.1440.

HFPCM

The HFPCM listing for BPA monomer is shown in Attachment 3. According to the HFPCM, BPA monomer is only listed in 175.105 and 177.2280.

A search on the keyword "bisphenol A" provided the 6 listings shown in Attachment 4. The regulations cited include 175.105, 177.1440, 177.2280 and 177.2600. For item #3, "epoxy, bisphenol A," inspection of the individual listings under the Araldite and Epon tradenames indicates they all primarily refer to 175.300.

K&F Book

BPA monomer and several BPA-based polymers are cleared under 175.105.

BPA reacted with formaldehyde is cleared as a phenolic resin under 175.105, 175.300, 175.380, 175.390, 176.170 and 177.1210.

BPA is cleared as a monomer in the production of polycarbonate resins under 177.1580.

BPA is cleared as a curing system additive in the production of BPA-epichlorohydrin thermosetting epoxy resins under 177.2280.

BPA-ECH epoxy resins are cleared under 175.105, 175.300, 175.380, 175.390, 176.170, 177.1210 and 177.1650, 177.1400, and 177.2420.

Several BPA-derivatives are permitted for use as polymer adjuvants and processing aids under Part 178.

SIREN and FCN Spreadsheet

A SIREN search on CAS# 80-05-7 produced 8 level 1 hits, 6 of which resulted in amendments to 21 CFR 170-199 (FAP, reg. reg. date):

OB0125, 175.300/176.170, 8-8-63;
1B4262, 177.1655, 6-11-96;
1B4263, 177.2440, 9-20-95;
2B0748, 177.1580, 5-22-63;
4A1318, 172.510, 3-24-65;
5B3898, 177.1585, 2-3-92.

A search of the FCN tracking spreadsheet produced no FCNs relating to BPA. In this instance, the results of both the SIREN and FCN tracking searches will be of questionable utility in developing a CEDI for BPA. However, as

discussed below, we recently addressed the CEDI for BPA and may only need to revise the CEDI based on notifications effective within the last year or so.

Exposure

The CEDI/ADI database did not contain a CEDI value for BPA.

The most recent CEDI for BPA is contained in a chemistry memorandum dated 5-2-00 on FAP 9Z4681 (K. Paquette to J. Smith). In that memorandum we concluded (p. 8) that exposure estimates presented in a previous 3-13-96 memorandum (A. Bailey to G. Diachenko) remained valid. In the 3-16-96 memorandum, we concluded that (p. 11):

"Adult cumulative exposure to BPA from its use in can enamels and PC-based polymers is expected to be no greater than 3.7 ppb, corresponding to an EDI of less than 11 µg/p/d (based on an adult daily food intake of 3 kg). Infant cumulative exposure to BPA from its use in PC infant bottles and can enamels for infant formula is expected to be no greater than 8.3 ppb (6.6 ppb + 1.7 ppb), corresponding to an EDI of less than 7 µg/p/d (based on an infant daily liquid intake of 820 g)".

FAPs 1B4262 and 1B4262

Recently, FAPs 1B4262 and 1B4263 amended 177.1655 and 177.2420, respectively. In a chemistry memorandum dated 7-6-94 on 1B4262 (R. McDaniel to R. White), the DC for BPA was concluded to be 0.14 ppb under 177.1655. In a chemistry memorandum dated 7-28-94 on 1B4263 (R. McDaniel to R. White), the DC for BPA was concluded to be 0.22 ppb under 177.2440. However, both of these regulations are for BPA-based polymers primarily³ intended for repeat-use applications. In our 3-13-96 memorandum we concluded that (p. 9):

"PC-based polymers are intended for repeated-use by the adult consumer. Given the large quantity of food processed over the service lifetime of the typical PC-based food-contact article, dietary exposure to BPA would be insignificant in comparison to BPA exposure for can enamels."

Although our original analysis in 1996 did not explicitly consider exposure to BPA from polysulfone (177.1655) and polyethersulfone (177.2420) resins, based on the above rationale we now conclude that the current CDCs for BPA remain valid, i.e. adults, 3.7 ppb; infants, 8.3 ppb.

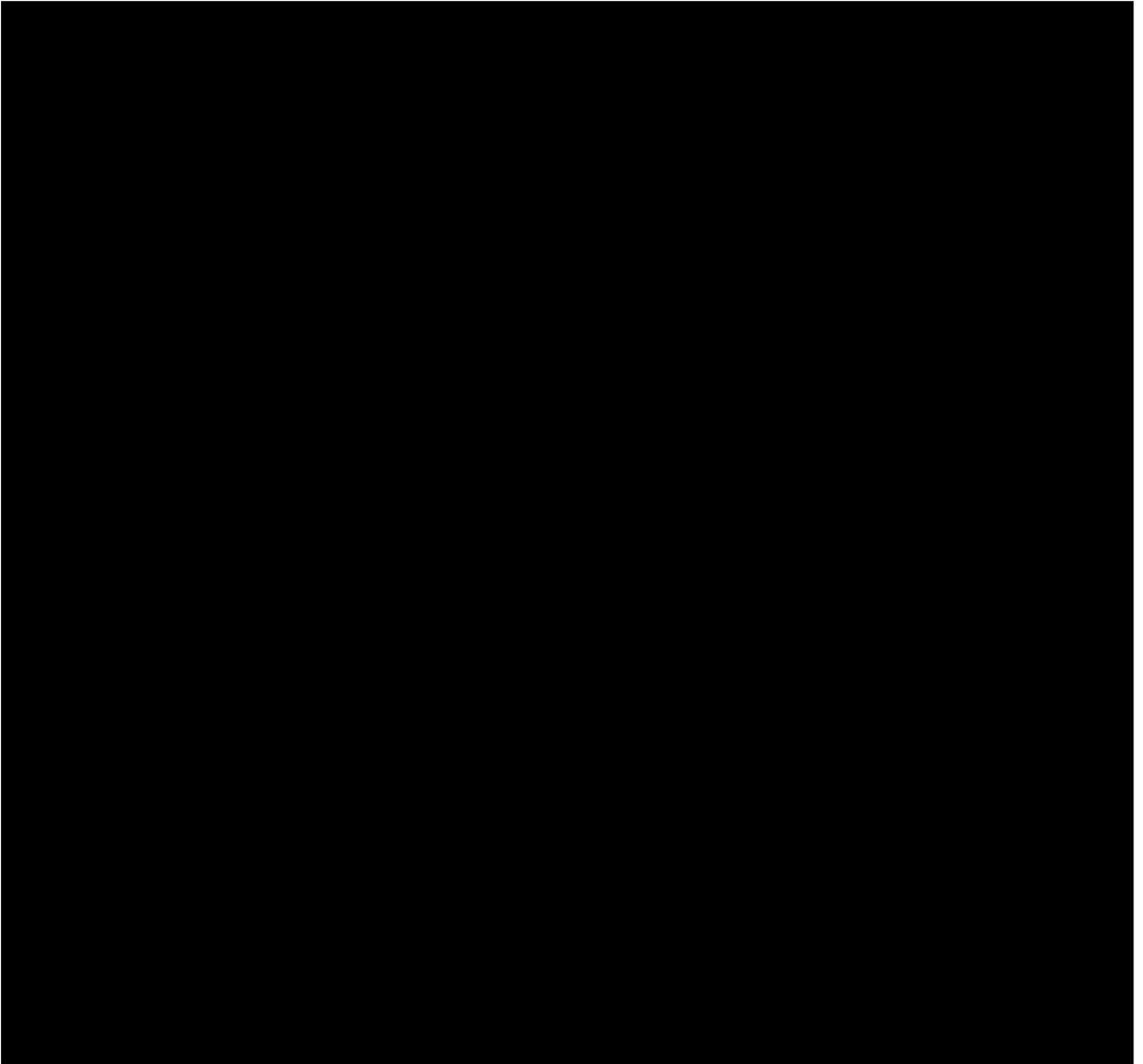




Allan B. Bailey



Attachment 1



Attachment 2
BPA Regulations

Part 172

ANOXOMER

Regulations: 21 CFR 172.105(FAP 0A3517)

For Use As: ANTIOXIDANT * PRESERVATIVE

CAS Reg. #: 60837-57-2

Synonym(s): POLY(BISPHENOL A-CO-TERT-BUTYLHYDROQUINONE-CO-4-TERT-BUTYLPHENOL-CO-DIVINYLBENZENE-CO-4-METHOXYPHENOL-CO-4-METHYLPHENOL)

Part 175

BISPHENOL A BIS(2-HYDROXYPROPYL) ETHER

Regulations: 21 CFR 175.105

CAS Reg. #: 116-37-0

POLY(BISPHENOL A-CO-FORMALDEHYDE)

Regulations: 21 CFR 175.105 * 21 CFR 175.300

CAS Reg. #: 25085-75-0

POLY(BISPHENOL A-CO-FORMALDEHYDE-CO-PENTAERYTHRITOL-CO-ROSIN, MALEATED)

Regulations: 21 CFR 175.105

CAS Reg. #: 68152-61-4

POLY(FORMALDEHYDE-CO-XYLENE) CONDENSED WITH BISPHENOL A-EPICHLOROHYDRIN

Regulations: 21 CFR 178.3297 * 21 CFR 175.380(FAP 4B1248, FAP 9B2322)

For Use As: POLYMER

Part 177

BISPHENOL A-EPICHLOROHYDRIN COMPOUND

Regulations: 21 CFR 177.2420(FAP 5B1753) * 21 CFR 175.320(FAP 6B1983)

For Use As: POLYMER

CAS Reg. #: 20232-24-0

BISPHENOL A, POLYBUTYLATED

Regulations: 21 CFR 175.105(FAP 1B0233) * 21 CFR 177.2600

POLY(BISPHENOL A-CO-CARBONIC ACID)

Regulations: 21 CFR 177.1580(FAP 2B0748) * 21 CFR 178.1005
For Use As: POLYMER
CAS Reg. #: 25037-45-0

POLY(BISPHENOL A-CO-DIPHENYL ISOPHTHALATE-CO-DIPHENYL
TEREPHTHALATE)

Regulations: 21 CFR 177.1555(FAP 6B3965)
For Use As: POLYMER
CAS Reg. #: 51706-10-6

POLY(BISPHENOL A-CO-EPICHLOROHYDRIN)

Regulations: 21 CFR 175.105(FAP 1B0233, FAP 2B0650) * 21 CFR
177.1440 * 21 CFR 175.300(FAP 1B0474, FAP 4B1415, FAP 0B0125,
FAP 1B0182)
For Use As: POLYMER
CAS Reg. #: 25068-38-6

POLY(BISPHENOL A-CO-ISOPHTHALOYL CHLORIDE-CO-PHOSGENE-CO-
TEREPHTHALOYL CHLORIDE)

Regulations: 21 CFR 177.1585(FAP 5B3898, FAP 5B4470)
For Use As: POLYMER
CAS Reg. #: 71519-80-7

POLY(BISPHENOL A-CO-ISOPHTHALOYL CHLORIDE-CO-PHOSGENE-CO-
TEREPHTHALOYL CHLORIDE), BIS(4-CUMYLPHENYL) ESTER

Regulations: 21 CFR 177.1585(FAP 5B4470)
For Use As: POLYMER
CAS Reg. #: 114096-64-9

POLY(BISPHENOL A-CO-4,4'-DICHLORODIPHENYL SULFONE)

Regulations: 21 CFR 177.1655
CAS Reg. #: 25154-01-2
Scopenotes: SOURCE--21 CFR 177.1655a1. CAS RN--CAS uses 25135-
51-7 for the SRU, 25154-01-2 for the monomer nomenclature; the
CFR uses 25154-01-2.

POLY(BISPHENOL A-CO-4,4'-DICHLORODIPHENYLSULFONE-CO-4,4'-
SULFONYLBISPHENOL)

Regulations: 21 CFR 177.2440(FAP 1B4263) * 21 CFR 177.1655(FAP
1B4262)
For Use As: POLYMER
CAS Reg. #: 88285-91-0

POLYETHERSULFONE RESIN

Regulations: 21 CFR 177.2440

POLYSULFONE RESIN

Regulations: 21 CFR 177.1655
For Use As: POLYMER

PPG BISPHEENOL A ETHER
Regulations: 21 CFR 177.2420 * 21 CFR 175.105
For Use As: POLYMER
CAS Reg. #: 37353-75-6

PPG-2-7.5 BISPHEENOL A ETHER
Regulations: 177.2420

PPG-3-4 BISPHEENOL A ETHER
Regulations: 21 CFR 177.1680(FAP 0B2478)
For Use As: POLYMER

Part 178

BISPHEENOL A DIHYDROGEN PHOSPHITE
Regulations: 21 CFR 178.2010(FAP 9B2391)
For Use As: POLYMER * STABILIZER

POLY(BISPHEENOL A-CO-FORMALDEHYDE-CO-PENTAERYTHRITOL-CO-WOOD
ROSIN, MALEATED)
Regulations: 21 CFR 178.3870(FAP 1B0269)
For Use As: DEFOAMER * SIZE PROMOTER

Bisphenol A

CAS **80-05-7**; EINECS/ELINCS **201-245-8**

Synonyms: **BPA; DIAN; DPP; Bis (4-hydroxyphenyl) dimethylmethane; Bis (4-hydroxyphenyl) propane; 2,2'-Bis (4,4'-hydroxyphenyl) propane; 2,2-Bis (p-hydroxyphenyl) propane; 4,4'-Bisphenol A; p,p'-Dihydroxydiphenyldimethylmethane; 4,4'-Dihydroxydiphenylpropane; 2,2-(4,4-Dihydroxydiphenyl) propane; p,p'-Dihydroxydiphenylpropane; β-Di-p-hydroxyphenylpropane; Dimethyl bis (p-hydroxyphenyl) methane; Dimethylmethylene-p,p'-diphenol; Diphenylolpropane; 2,2-Di (4-phenylol) propane; 4,4'-Isopropylidenebisphenol; p,p'-Isopropylidenebisphenol; 4,4'-Isopropylidenediphenol; p,p'-Isopropylidenediphenol; 4,4'-(1-Methylethylidene) bisphenol; Phenol, 4,4'-(1-methylethylidene) bis-; Phenol, 4,4'-isopropylidenedi-**

Empirical: **C₁₅H₁₆O₂**

Formula: **(CH₃)₂C(C₆H₄OH)₂**

Properties: Wh. to lt. brn. cryst. or flakes; phenolic odor; sol. in oxygenated solvs., alcohol, aq. alkaline sol'ns., acetic acid, benzene, ketones; sl. sol. in CCl₄; insol. in water; m.w. 228.31; dens. 1.195 (25/25 C); vapor pressure 0.2 mm Hg (170 C); m.p. 153 C; b.p. 220 C (4 mm); flash pt. 79.4 C

Toxicology: OSHA **PEL:CL 0.5 ppm; LD50 (oral, rat) 3250 mg/kg, (IP, mouse) 150 mg/kg, (skin, rabbit) 3000 mg/kg; LC50 (inh., rat) 200 ppm; poison by IP route; mod. toxicity by ing., inh., and skin contact; skin and eye irritant; experimental teratogen, reproductive effects; TSCA listed**

Precaution: **Combustible; incompat. with strong oxidizers, strong bases, acid chlorides, acid anhydrides**

Hazardous Decomp. Prods.: **Heated to decomp., emits acrid and irritating fumes**

Storage: Store under ambient conditions, away from oxidizing materials

Uses: Phenolic resin comonomer; intermediate in mfg. of polymers, epoxy, polycarbonate, phenoxy, polysulfone, polyetherimide, polyarylate, and polyester resins, **flame retardants, rubber chemicals, fungicides, antioxidants, dyes; hard resin for finished prods. incl. laminates, powd. coatings, bondable coatings, molding powds.; in food-pkg. adhesives; curing system additive for bisphenol A-epichlorohydrin epoxies for food contact**

Regulatory: FDA 21CFR §175.105, 177.2280

Attachment 4

1. Bisphenol A/epichlorohydrin resin

CAS 26402-79-9

Synonyms: 4,4'-Isopropylidenediphenol/epichlorohydrin resin; Poly (bisphenol A-co-epichlorohydrin)

Properties: Lt. yel. translucent pellets; dens. 1.180

Toxicology: **Toxic; harmful by inh., ing., skin contact; skin/eye irritant;** may cause heritable **genetic damage; cancer suspect agent; mutagen; target organs: nerves, liver, kidneys, bladder, brain**

Precaution: **Incompat. with strong oxidizing agents**

Hazardous Decomp. Prods.: **CO, CO₂**

Storage: Keep tightly closed in cool, dry, well-ventilated place

Uses: **Food pkg.**

Regulatory: FDA 21CFR §177.1440

2. Epoxy, bisphenol A/epichlorohydrin

CAS 25068-38-6

Synonyms: **Bisphenol A, (chloromethyl) oxirane polymer; Bisphenol A, epichlorohydrin polymer; (Chloromethyl) oxirane, 4,4'-(1-methylethylidene) bisphenol copolymer; Epoxy resin; Epoxy resin ERL-2795; 4,4'-Isopropylidenediphenol-epichlorohydrin epoxy resin; 4,4'-Isopropylidenediphenol, polymer with 1-chloro-2,3-epoxypropane; Phenol, 4,4'-isopropylidenedi-, dimer with 1-chloro-2,3-epoxypropane; Phenol, 4,4'-isopropylidenedi-, polymer with 1-chloro-2,3-epoxypropane; Phenol, 4,4'-(1-methylethylidene) bis-, polymer with (chloromethyl) oxirane**

Classification: Polymer

Definition: A type of epoxy resin made from bisphenol A and epichlorohydrin

Empirical: **(C₁₈H₂₁ClO₃)_n**

Formula: **(C₁₅H₁₆O₂ • C₃H₅ClO)_n**

Properties: M.w. (320.82)_n

Toxicology: **LD50 (oral, rat) 1100 mg/kg, (skin, rabbit) > 20 ml/kg; mod. toxic by ing. and skin contact**

Hazardous Decomp. Prods.: **Heated to decomp., emits acrid smoke and fumes**

Uses: **Thermosetting resin for coatings, elec., civil engineering, matrix, adhesive applics.; in food-contact articles for repeated use**

Regulatory: FDA 21CFR §177.2280

Manuf./Distrib.: ...**Sigma**

Trade names: [REDACTED]

See also: ...**Epoxy resin**

3. Epoxy, bisphenol A

Synonyms: **Bisphenol A epoxy resin; Epoxy bisphenol A resin**

Toxicology: **TSCA listed**

Uses: **Heat stabilizer for PVC; exc. halogen capture for flame retardant resins; vehicle or binder in surf. coatings; food-contact coatings; laminating, potting, encapsulation, casting, tooling, coatings, and flooring applics.**

Manuf./Distrib.: **...Archway Sales; ...Ashland; ...Baychem; ...Cardolite; ...Ciba Spec. Chems./Addit.**

...GCA; ...Lenape Ind.; ...Lomas Int'l.; ...Reichhold; ...Samson

...Shell; ...United Min. & Chem.

Trade names:

[REDACTED]

4. Bisphenol A, polybutylated

CAS 68784-69-0

Synonyms: **4,4'-Isopropylidenediphenol, polybutylated; Polybutylated bisphenol A; Polybutylated 4,4'-isopropylidenediphenol**

Uses: **Preservative in food-pkg. adhesives; antioxidant for rubber, latex, automotive and appliance prods.; antioxidant in food-contact rubber articles for repeated use**

Regulatory: **FDA 21CFR §175.105, 177.2600**

5. [REDACTED] [...Shell]

Chem. Descrip.: **...Epoxy resin (diglycidyl ether of bisphenol A)**

Uses: For applics. requiring low visc. without visc. reducing modifiers or reactive diluents, e.g., **laminating binders**, castings, encapsulations, functional and decorative flooring, filament winding, patching compds., high-build **coatings**; fiber-reinforced composites and **pipe, tooling and molding compds.**, construction/elec./aerospace **adhesives**, grouting

compds.; **food pkg. adhesives, coatings, paper, closures with sealing gaskets for food containers**

Regulatory: FDA 21CFR §175.105, 175.300, 175.320, 176.170, 176.180, 177.1210, 177.2280

Properties: Gardner 2 max. liq.; dens. 9.7 lb/gal; visc. 8500 cps; flash pt. (COC) 243 C; EEW 178-186

6. Epoxy resin

CAS **25928-94-3**

Synonyms: **Condensation prods., epoxy; Epoxides, polymers, epoxy resins; Epoxy compds.; Ethers, cyclic, epoxides, polymers; Plastics, epoxy; Polyethers, epoxy resins**

Classification: Polymer

Definition: A thermosetting resin based on the reactivity of the epoxide group

Toxicology: **LD50 (oral, rat) 2200 mg/kg; strong skin irritant in uncured state; poison by inhalation; mod. toxic by ingestion; little or no toxicity in cured state**

Hazardous Decomp. Prods.: **Heated to decomp., emits toxic fumes of Cl⁻**

Uses: **Plasticizer for surface coatings; adhesive for composites, metals, glass, ceramics; casting metal-forming tools and dies; encapsulation of elec. parts; cements and mortars; rigid foams; stabilizer, modifier for other resins;** biomaterial for pharmaceutical topicals, slow-release, and microencapsulation prods.; **diluent;** in **food-contact coatings;** in **food-contact polysulfide polymer/polyepoxy resins**

Regulatory: FDA 21CFR §175.300, 177.1390, 177.1650

Trade names:

See also: ...**Epoxy, bisphenol A/epichlorohydrin**