

Preliminary Screening Information on Possible Classes of Chemicals Used in UV Applications for Future Consideration

Materials for November 3, 2016 Meeting of the Scientific Guidance Panel for
Biomonitoring California¹

The purpose of this document is to provide background information to the Scientific Guidance Panel (SGP) on two possible chemical classes for future consideration as potential designated chemicals under Biomonitoring California: benzophenones and phenolic benzotriazoles. Both of these classes are used in ultraviolet (UV) applications.²

The current document was developed in response to the Panel's request at their November 2010 meeting for the Program to review sunscreen chemicals as a broad category. Evaluating chemical classes provides flexibility to quickly respond to shifts in chemical use; supports the development of broad laboratory panels and non-targeted screening; and uses Program resources efficiently.

For six example chemicals in each class, we summarize preliminary screening information on:

- Chemical identity
- Use and production/import volume
- Some toxicity information
- Selected detections in biological and environmental samples
- Selected information from EPI Suite³

At the November 3 meeting, the Panel will provide input on what next steps, if any, should occur on these two classes. The SGP could request that OEHHA prepare a potential designated chemical document on one or both of these classes; propose further screening or continued tracking of the classes; advise no further action on either class; and/or suggest other classes for possible consideration.

¹ California Environmental Contaminant Biomonitoring Program, codified at Health and Safety Code section 105440 et seq.

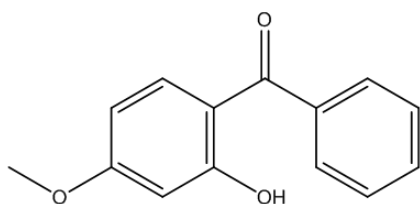
² "UV applications" includes uses as UV stabilizers, UV absorbers, or photoinitiators, for example.

³ Estimation Program Interface Suite™ available at: <https://www.epa.gov/tsca-screening-tools/download-epi-suite-estimation-program-interface-v411>

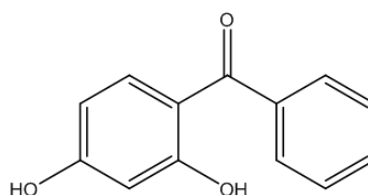
Benzophenones

Benzophenones are used as UV absorbers, UV stabilizers and/or photoinitiators in: sunscreens and other personal care products; plastics, including food contact plastics; paints and other coatings; inks and lacquers for paperboard, including food packaging; fragrances; and pesticide formulations. Structures for six example benzophenones are shown below.

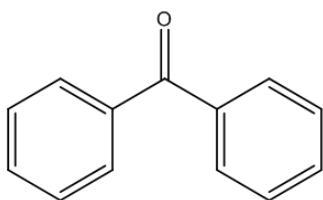
Benzophenone-3 (BP-3) (*already designated*)



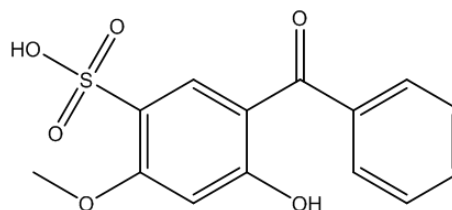
Benzophenone-1 (BP-1)



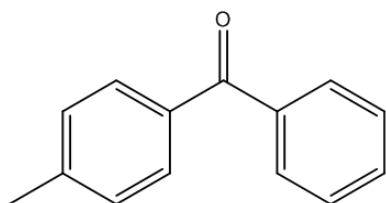
Benzophenone



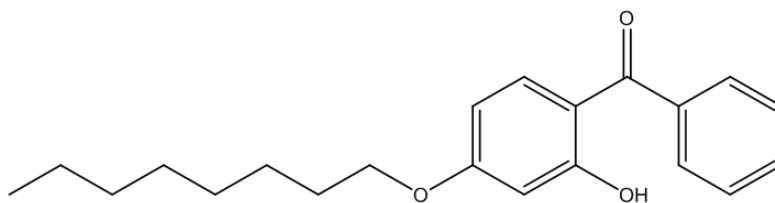
Benzophenone-4 (BP-4)



4-Methylbenzophenone



Benzophenone-12 (BP-12)



Possible Classes of Chemicals Used in UV Applications

Chemical identity	US production/import volume (lbs)	EPI Suite information ⁴	Some toxicity information	Selected detections
Benzophenone-3 (BP-3)⁵ CASRN: 131-57-7 Synonyms: (2-hydroxy-4-methoxyphenyl)-phenylmethanone; oxybenzone <i>Metabolites include:</i> <i>BP-1, BP-2, BP-8</i>	1986: >500K - 1M 1990: >1M - 10M 1994: >1M - 10M 1998: >1M - 10M 2002: 10K - 500K 2006: No data 2012: 100K - 500K	MW: 228.25 Log K_{ow} : 3.79 (exp) Water sol: 68.56 mg/L BCF: 38.24 L/kg Half-lives (hours) Air 1.28 Water 900 Soil 1,800 Sediment 8,100	<ul style="list-style-type: none"> • Indications of estrogenic, anti-estrogenic, and anti-androgenic activity • Cytotoxic in human neuroblastoma cells at environmentally relevant doses • ToxCast⁶: endocrine activity; immune- and inflammation-related effects 	<ul style="list-style-type: none"> • Urine • Serum • Breast milk • Adipose tissue • Aquatic organisms (fish, mussels, clams) • Dust
Benzophenone CASRN: 119-61-9 Synonym: diphenylmethanone <i>Metabolites include:</i> <i>4-hydroxy-benzophenone</i>	1986: >1M - 10M 1990: >1M - 10M 1994: >1M - 10M 1998: >1M - 10M 2002: >1M - 10M 2006: 1 - <10M 2012: 3,867,158	MW: 182.22 Log K_{ow} : 3.18 (exp) Water sol: 103.3 mg/L BCF: 15.14 L/kg Half-lives (hours) Air 72.2 Water 360 Soil 720 Sediment 3,240	<ul style="list-style-type: none"> • Carcinogenicity (listed under Proposition 65) • Indications of estrogenic and anti-androgenic activity • ToxCast: endocrine activity; developmental toxicity in zebrafish 	<ul style="list-style-type: none"> • Urine • Dust
4-Methylbenzophenone CASRN: 134-84-9 Synonym: (4-methylphenyl)phenylmethanone	1986: No data 1990: No data 1994: 10 - 500K 1998: 10 - 500K 2002: 10 - 500K 2006: No data 2012: Withheld	MW: 196.25 Log K_{ow} : 3.69 (est) Water sol: 32 mg/L BCF: 33.07 L/kg Half-lives (hours) Air 39.2 Water 900 Soil 1,800 Sediment 8,100	<ul style="list-style-type: none"> • Cytotoxic in human neuroblastoma cells at environmentally relevant doses • ToxCast: endocrine activity; immune- and inflammation-related effects 	<ul style="list-style-type: none"> • None located

⁴ MW = molecular weight; Log K_{ow} = log octanol-water partition coefficient; exp = experimental, est = estimated; water sol = water solubility at 25°C; BCF = bioconcentration factor in L/kg wet-wt (abbreviated L/kg).

⁵ BP-3 is already on the list of designated chemicals and is included here for comparison purposes.

⁶ Selected activity from US EPA's high-throughput chemical Toxicity Forecaster (ToxCastTM) program, available at: <https://actor.epa.gov/dashboard/>.

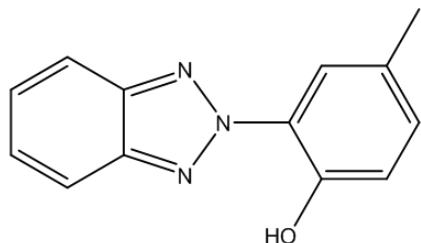
Possible Classes of Chemicals Used in UV Applications

Chemical identity	US production/ import volume (lbs)	EPI Suite information ⁴	Some toxicity information	Selected detections
Benzophenone-1 (BP-1) CASRN: 131-56-6 Synonyms: (2,4-dihydroxyphenyl)- phenylmethanone; 2,4- dihydroxybenzophenone <i>BP-1 is commercially used and is also a metabolite of BP-3.</i>	1986: >1M - 10M 1990: >1M - 10M 1994: >1M - 10M 1998: 10K - 500K 2002: 10K - 500K 2006: <500K 2012: 31,680	MW: 214.22 Log K _{ow} : 2.96 (est) Water sol: 413.4 mg/L BCF: 10.9 L/kg Half-lives (hours) Air 1.28 Water 360 Soil 720 Sediment 3,240	<ul style="list-style-type: none"> • Indications of estrogenic and anti-androgenic activity • ToxCast: endocrine activity; effects on cellular metabolism 	<ul style="list-style-type: none"> • Urine • Dust
Benzophenone-4 (BP-4) CASRN: 4065-45-6 Synonyms: 5-benzoyl-4-hydroxy-2- methoxybenzenesulfonic acid; sulisobenzone	1986: No data 1990: 10K - 500K 1994: 10K - 500K 1998: 10K - 500K 2002: 10K - 500K 2006: No data 2012: Withheld	MW: 308.31 Log K _{ow} : 0.37 (est) Water sol: 20,290 mg/L BCF: 3.162 L/kg Half-lives (hours) Air 3.44 Water 900 Soil 1,800 Sediment 8,100	<ul style="list-style-type: none"> • Indications of estrogenic, anti-estrogenic, and anti-androgenic activity • ToxCast: endocrine activity 	<ul style="list-style-type: none"> • Urine • Placental tissue
Benzophenone-12 (BP-12) CASRN: 1843-05-6 Synonyms: (2-hydroxy-4-octoxyphenyl)- phenylmethanone; octabenzene	1986: >1M - 10M 1990: >1M - 10M 1994: >1M - 10M 1998: >1M - 10M 2002: >1M - 10M 2006: 1M - <10M 2012: 1,979,838	MW: 326.44 Log K _{ow} : 6.96 (est) Water sol: 0.03693 mg/L BCF: 200.2 L/kg Half-lives (hours) Air 1.18 Water 360 Soil 720 Sediment 3,240	<ul style="list-style-type: none"> • ToxCast: decreased cell viability; effects on cellular metabolism; immune- and inflammation-related effects 	<ul style="list-style-type: none"> • None located

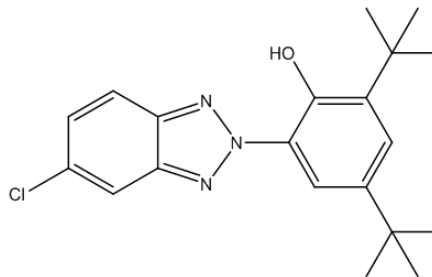
Phenolic Benzotriazoles

Phenolic benzotriazoles are used as UV absorbers and/or stabilizers in: plastics, including for food contact materials and electronics; paints and other coatings; cosmetics; fragrances; textiles, including clothing; and pesticide formulations. Structures for six example phenolic benzotriazoles are shown below.

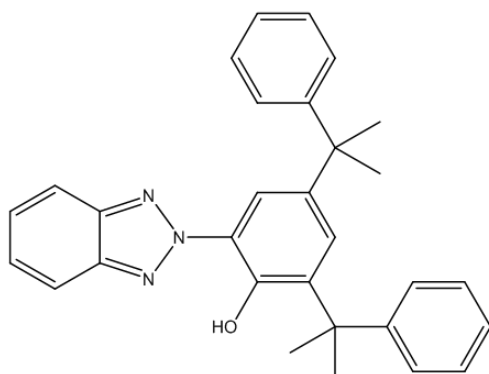
UV P



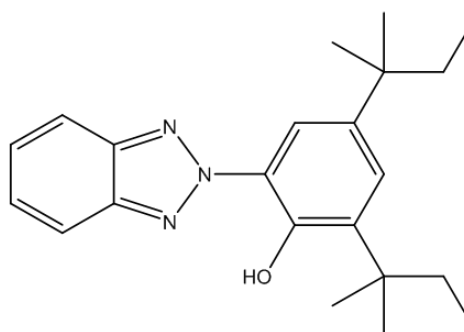
UV 327



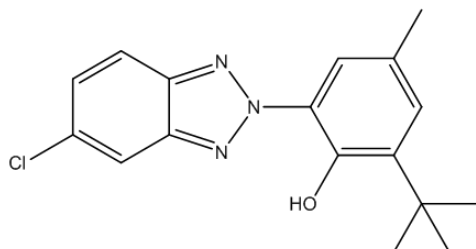
UV 234



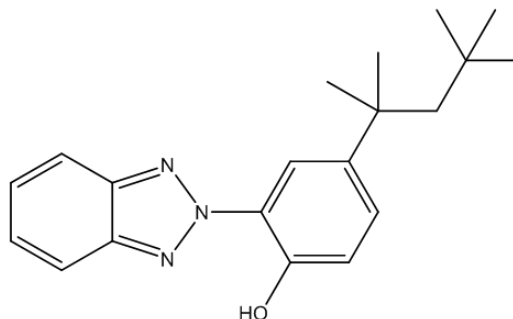
UV 328



UV 326



UV 329



Possible Classes of Chemicals Used in UV Applications

Chemical identity	US production/ import volume (lbs)	EPI Suite information	Some toxicity information	Selected detections
UV P CASRN: 2440-22-4 Synonyms: 2-(benzotriazol-2-yl)-4-methylphenol; drometrizole	1986: >1M - 10M 1990: >1M - 10M 1994: >1M - 10M 1998: >1M - 10M 2002: >500K - 1M 2006: 500K - <1M 2012: 605,074	MW: 225.25 Log K _{ow} : 4.31 (exp) Water sol: 25.59 mg/L BCF: 324.1 L/kg Half-lives (hours) Air 8.43 Water 900 Soil 1,800 Sediment 8,100	<ul style="list-style-type: none"> • NTP studies underway⁷ • Indications of anti-androgenic activity • Indications of aryl hydrocarbon receptor (AhR) pathway activation • ToxCast: endocrine activity; AhR pathway activation 	<ul style="list-style-type: none"> • Breast milk • Fish
UV 234 CASRN: 70321-86-7 Synonym: 2-(benzotriazol-2-yl)-4,6-bis(2-phenylpropan-2-yl)phenol	1986: >1M - 10M 1990: >1M - 10M 1994: >1M - 10M 1998: >1M - 10M 2002: >1M - 10M 2006: 1M - <10M 2012: 1M - 10M	MW: 447.58 Log K _{ow} : 7.67 (est) Water sol: 0.001648 mg/L BCF: 3,741 L/kg Half-lives (hours) Air 11.8 Water 1,440 Soil 2,880 Sediment 13,000	<ul style="list-style-type: none"> • NTP studies underway • ToxCast: effects on xenobiotic metabolism 	<ul style="list-style-type: none"> • Fish • Dust
UV 326 CASRN: 3896-11-5 Synonyms: 2-tert-butyl-6-(5-chlorobenzotriazol-2-yl)-4-methylphenol; bumetrizole	1986: 10K - 500K 1990: 10K - 500K 1994: >500K - 1M 1998: >500K - 1M 2002: >500K - 1M 2006: 500K - <1M 2012: 394,026	MW: 315.81 Log K _{ow} : 5.55 (est) Water sol: 0.6838 mg/L BCF: 1,283 L/kg Half-lives (hours) Air 17.2 Water 1,440 Soil 2,880 Sediment 13,000	<ul style="list-style-type: none"> • NTP studies underway • Indications of AhR pathway activation • ToxCast: effects on xenobiotic metabolism; increased cell proliferation 	<ul style="list-style-type: none"> • Breast milk • Aquatic organisms (fish, mussels, and other) • Dust

⁷ NTP (National Toxicology Program) is currently studying phenolic benzotriazoles. Tests include short-term toxicity, toxicokinetics, and genetic toxicology. More information is available at: <http://ntp.niehs.nih.gov/testing/noms/search/summary/nm-n21204.html>.

Possible Classes of Chemicals Used in UV Applications

Chemical identity	US production/ import volume (lbs)	EPI Suite information	Some toxicity information	Selected detections
UV 327 CASRN: 3864-99-1 Synonym: 2,4-ditert-butyl-6-(5-chlorobenzotriazol-2-yl)phenol	1986: 10K - 500K 1990: 10K - 500K 1994: 10K - 500K 1998: 10K - 500K 2002: 10K - 500K 2006: <500K 2012: Withheld	MW: 357.89 Log K _{ow} : 6.91 (est) Water sol: 0.02628 mg/L BCF: 10,160 L/kg Half-lives (hours) Air 19.5 Water 1,440 Soil 2,880 Sediment 13,000	<ul style="list-style-type: none"> • NTP studies underway • Included on ECHA Candidate List of substances of very high concern based on vP/vB⁸ • ToxCast: not tested 	<ul style="list-style-type: none"> • Breast milk • Porpoise blubber • Aquatic organisms (fish, mussels, and other) • Dust
UV 328 CASRN: 25973-55-1 Synonym: 2-(benzotriazol-2-yl)-4,6-bis(2-methylbutan-2-yl)phenol	1986: >1M - 10M 1990: >1M - 10M 1994: >1M - 10M 1998: >1M - 10M 2002: >1M - 10M 2006: 1M - <10M 2012: 2,246,476	MW: 351.50 Log K _{ow} : 7.25 (est) Water sol: 0.01479 mg/L BCF: 6,006 L/kg Half-lives (hours) Air 16.3 Water 1,440 Soil 2,880 Sediment 13,000	<ul style="list-style-type: none"> • NTP studies underway • Included on ECHA Candidate List of substances of very high concern based on PBT⁹ and vP/vB • ToxCast: no clear indications of activity 	<ul style="list-style-type: none"> • Breast milk • Dolphin plasma and porpoise blubber • Aquatic organisms (fish, mussels and other) • Dust
UV 329 CASRN: 3147-75-9 Synonyms: 2-(benzotriazol-2-yl)-4-(2,4,4-trimethylpentan-2-yl)phenol; octrizole	1986: >500K - 1M 1990: >1M - 10M 1994: 10K - 500K 1998: >1M - 10M 2002: >1M - 10M 2006: 1M - <10M 2012: 500K - 1M	MW: 323.44 Log K _{ow} : 6.21 (est) Water sol: 0.1678 mg/L BCF: 5,843 L/kg Half-lives (hours) Air 8.03 Water 1,440 Soil 2,880 Sediment 13,000	<ul style="list-style-type: none"> • NTP studies underway • ToxCast: increased cell cycle arrest; endocrine activity; immune- and inflammation-related effects 	<ul style="list-style-type: none"> • Breast milk • Fish

⁸ vP/vB = very persistent and very bioaccumulative⁹ PBT = persistent, bioaccumulative, and toxic

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Benzophenones

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