LABORATORY EVALUATION

ADA Professional Product Review®
A Publication of the Council on Scientific Affairs

Correction: Tables 2, 4, and 5 in the online version have been revised to reflect that BPA levels fell below the detection limit. Table 6 was revised to reflect data used for calculation of values in subsequent tables.

ADA Laboratory Evaluation: Bisphenol A Released from Resin Based Dental Sealants

This is the third and final article in a series of reports examining the potential release of Bisphenol A (BPA) from resin-based dental materials. Previously, the ADA Professional Product Review presented an overview of Bisphenol A and an evaluation of BPA from resin-based dental composites.[1,2]

Bisphenol A (BPA) raised concern after several studies linked its estrogen-like effects to health problems, prompting many manufacturers of polycarbonate plastic bottles, particularly those used by children, to exclude BPA-derived materials from containers that may hold food.[3] The U.S. Food and Drug Administration called for more research on the chemical, explaining that the agency had "some concerns about the potential effects of BPA on the brain, behavior and prostate glands of fetuses, infants and children."[4] Therefore, it is important to quantify the potential BPA release from resin-based dental sealants.

BPA is not an added ingredient in most dental sealants; however, it can be present as a trace material in resin-based dental sealants containing bisphenol A glycidyl methacrylate (bis-GMA) or other ingredients.[5,6] BPA might also be present due to the degradation of bisphenol A-dimethacrylate (bis-DMA) through the action of salivary esterases. The first report of a dental material with an estrogenic effect involved dental sealants that contained bis-DMA.[7] BPA assembles itself into a long chain that offers low susceptibility to biodegradation, as well as great rigidity and strength.[8] (Read more about the makeup of BPA in "Update: Bisphenol A in Dental Materials," ADA Professional Product Review, Volume 8, Issue 1, March 2013.)

Dental sealants are an important tool in preventing dental caries by providing a barrier on teeth to protect against bacterial decay, particularly when used during a child's formative years.[9-11] Sealants are nonsurgical interventions that are applied to tooth surfaces to fill and seal pits and fissures.[12,13] Resin-based dental sealants are formulated from a mixture of monomers that are commonly based on bis-GMA. Some sealants may contain other monomers, such as bisphenol A dimethacrylate (bis-DMA) and bisphenol A ethoxylate dimethacrylate (bis-EDMA), in order to modify the properties of the resin. Bis-GMA, bis-DMA and bis-EDMA are produced using BPA as a starting ingredient, so residual BPA likely is present in trace amounts in any dental material containing these ingredients.[14-16] In addition, bis-DMA-containing materials are known to release very small quantities of BPA since they are subject to degradation by salivary esterases.[17]

As there are concerns about the potential impact of BPA on health and human development, it is necessary to investigate the amount of unreacted BPA monomer that could be extracted from resin-based dental sealants.

This study will answer the following questions for clinicians:

- What is the maximum amount of BPA that can be extracted in a "worst-case scenario" from various dental sealants?
- How much BPA is eluted from cured (polymerized) sealants over 24 hours in physiologic conditions?
- How much BPA is eluted from cured sealants over 48 hours in physiologic conditions?
- How much BPA is present from unpolymerized sealants that are extracted under physiologic conditions in addition to the BPA that might be present due to the degradation of any bisphenol A-dimethacrylate (bis-DMA) by salivary esterase?
- Do the experimentally observed levels of BPA elution adhere to the acceptable exposure limits specified by the appropriate agencies (U.S. Environmental Protection Agency or EPA; European Food Safety Authority or EFSA)?

Continued on next page

Methods

Dental resin-based sealants were polymerized according to manufacturers' instructions followed by extraction under physiologic conditions (artificial saliva with esterase) at 37°C for 24 hours. Additionally, polymerized sealants were extracted under the same physiologic conditions for a total of 48 hours to show any extended BPA release.

Unpolymerized specimens were dissolved in acetonitrile and used to simulate a "worst-case scenario" and to determine the maximum BPA that could be eluted from the tested dental sealants. Furthermore, another set of unpolymerized sealant specimens were extracted under physiologic conditions for 48 hours to show any extended BPA release. The ADA Laboratory purchased the dental sealants used in this evaluation (Table 1).

Upon the extraction of dental sealants in acetonitrile or artificial saliva, liquid extracts were analyzed using LC-MS/MS by Intertek Pharmaceutical Services (El Dorado Hills, CA). Prior to analysis, extracts were prepared using a liquid-liquid extraction procedure (in artificial saliva lacking porcine esterase or acetonitrile, as appropriate), evaporated to dryness, and reconstituted in a solution of methanol and ammonium acetate. LC-MS/MS was then performed on an AB Sciex API 5000 system. Liquid chromatography was performed on an ACE C18-PFP 100 x 2.1 mm column followed by tandem mass spectrometry in negative ion mode. The detection limit of BPA quantitation was 0.100 ng/mL (0.100 ppb) for samples extracted in artificial saliva and 0.500 ng/mL (0.500 ppb) for those extracted in acetonitrile. Quality control samples and an internal standard (d^{16}-BPA) were used throughout the analyses for accurate quantification of BPA.

Because all pit and fissure sealants tested in this study are classified as class 2 (visible light cured) according to ANSI/ADA Specification No.39-2006, they must be able to achieve a minimum depth of cure of 1.5 mm.[18] Specimen discs of each product representing 3 different lots were prepared in Teflon molds with a 10 mm diameter and 1.0 mm depth for a complete cure following directions for use specified by the manufacturer. An Optilux 501(Kerr) polymerization unit with a light radiant emittance of >600 mW/cm2 was used to cure the sealants.

Immediately after curing, the specimen was weighed, placed in a paraffin-sealed glass vial, and immersed in 2.0 mL of the appropriate solution (acetonitrile or artificial saliva with porcine esterase).[19] Each specimen was extracted at 37°C for the specified times (24 or 48 hours). Specimens were removed from the vials and the extracts stored at 4°C until lab analysis.

For calculation purposes, all BPA values below the analytical detection limit were valued at the detection limit. For instance if one value of three lots was <0.10 ng/mL, then 0.10 ng/mL are used for that lot's value. In these cases, average results of three lots are prefaced by the < symbol. If all samples were below the detection limit, then the result is valued at below the detection limit (BDL).

Table 1. List of Evaluated Products

Sealant	Company
UltraSeal XT hydro	Ultradent 888-230-1420 www.ultradent.com
Clinpro	3M ESPE 800-634-2249 www.3mespe.com
Helioseal F	Ivoclar Vivadent 800-533-6825 www.ivoclarvivadent.us.com
DELTON FS+	Dentsply Caulk 800-877-0020 www.dentsply.com
Embrace WetBond Pit & Fissure Sealant	Pulpdent 800-343-4342 www.pulpdent.com/
Seal-Rite	Pulpdent 800-343-4342 www.pulpdent.com/
FluoroShield	Dentsply Caulk 800-877-0020 www.dentsply.com
Guardian Seal	Kerr 800-537-7123 www.kerrdental.com
BeautiSealant	Shofu Dental Corp 800-827-4638 www.shofu.com
Control Seal	Voco 888-658-2584 www.vocoamerica.com
ClearVue	Denali Corporation 781-826-9190 www.denalicorporation.com/denali__026.htm
Prevent Seal	Itena Clinical (France) 33-14-591-3006 http://itena-clinical.com/index.php?app=3
Tooth Fairy	Septodont Inc. 717-286-0100
ECO-S	Vericom Co. LTD. (S. Korea) 82-31-441-2881 http://vericom.en.ec21.com/Eco-S--2835716_2836127.html

Continued on next page

Table 2. Unpolymerized Sealant in Acetonitrile, 48 hours (n=3)

Sealant	Avg. ng BPA/g sealant	+ s.d.
UltraSeal XT hydro	35.69	2.79
Clinpro	99.57	8.49
Helioseal F	24.00	0.87
DELTON FS+	15.37	1.08
Embrace WetBond Pit & Fissure Sealant	BDL	N/A
Seal-Rite	36.45	13.56
FluoroShield	14.62	1.75
Guardian Seal	20.09	2.54
BeautiSealant	8.62	0.83
Control Seal	13.59	1.29
ClearVue	67.41	9.82
Prevent Seal	35.94	42.46
Tooth Fairy	304.19	26.03
ECO-S	1,502.10	6.47

BDL: Below limit of detection.
N/A: Not applicable.

Results

Table 2 shows that BPA could be extracted from all sealant products except Embrace WetBond Pit & Fissure Sealant; the manufacturer does not list a BPA derivative as an ingredient (Table 3). Since the sealants were left unpolymerized and submerged in acetonitrile, all of these values represent the maximum amount of BPA that was extracted from these products, which gives some guidance for potential toxicity. However, under clinical conditions in an aqueous environment, much lower amounts of BPA would be expected. Therefore, products with higher levels of BPA might not necessarily predict higher levels in the oral cavity from polymerized sealant. These values represent a worst-case but not clinically relevant situation, where all possible BPA could be leached from these sealants. None of the products tested contained BPA or bis-DMA as part of their formulation as reported by each manufacturer. As was found in the BPA survey of resin-based composites, BPA normally is present as an unreacted trace material from the manufacture of raw bis-GMA or other BPA derivatives.[2] (Analyses of BPA levels from various sources of raw bis-GMA was discussed in the ADA Professional Product

Table 3. Product Information, as supplied by the manufacturer

Sealant	Country of Manufacture	Contains BPA Derivatives	Resin Composition
UltraSeal XT hydro	US	Yes	bis-GMA[1], UDMA[2], TEGDMA[3]
Clinpro	US	Yes	bis-GMA, TEGDMA
Helioseal F	Lichtenstein	Yes	bis-GMA, UDMA, TEGDMA
DELTON FS+	US	Yes	bis-GMA, bis-GMA based material, hexamethylene diisocyanate, non-aromatic methacrylate
Embrace WetBond Pit & Fissure Sealant	US	No	UDMA, non-aromatic methacrylate
Seal-Rite	US	Yes	Bis-GMA, non-aromatic methacrylate, uncured methacrylate ester monomers
FluroShield	US	Yes	bis-GMA, urethane modified bis-GMA dimethacrylate, dimethacrylate resins, TEGDMA
Guardian Seal	US	Yes	Bis-GMA, non-aromatic methacrylate
BeautiSealant	Japan	No	UDMA, TEGDMA
Control Seal	Germany	Yes	bis-GMA, glycerindimethacrylate
ClearVue	US	No	UDMA, acrylate resins, non-aromatic methacrylate
Prevent Seal	France	No	UDMA, TEGDMA, MAPAE[4] MAETMA[5]
Tooth Fairy	US	No	HDDMA[6]-UDMA resins
ECO-S	S. Korea	Yes	UDMA, TEGDMA, bis-GMA

1. Bisphenol A Diglycidyl Ether Dimethacrylate (Bis-GMA).
2. Urethane Dimethacrylate (UDMA).
3. Triethylene Glycol Dimethacrylate (TEGDMA).
4. Methacrylated phosphoric acid esters (MAPAE).
5. 4-methacryloxyethyltrimellitic acid (MAETMA).
6. 1,6-hexanediol dimethacrylate (HDDMA).

Continued on next page

Review, Volume 9, Issue 3.)[2] Because esterase was not used in this acetonitrile extraction, none of the BPA could be a degradation product of bis-DMA.

Two sealants showed relatively large standard deviations (Seal-Rite, Prevent Seal). This was due to one of the three lots for each product containing BPA values substantially higher than the other two lots. In the case of Seal-Rite, a plausible explanation might be the use of different batches of raw bis-GMA in the manufacture of product lots. However, Prevent Seal does not use bis-GMA or any other BPA derivative in its formulation, so the source of BPA is not clear for this product. ECO-S contained the highest amount of BPA, likely from its bis-GMA component (Table 3).

Table 4 shows that BPA could only be extracted in artificial saliva containing porcine esterase from four products (Guardian Seal, ClearVue, Tooth Fairy and ECO-S). The remaining 10 products showed that any released BPA was at levels below the detection limit of the analytical method. Unpolymerized sealant is present in the oral cavity for only a brief period during application of sealant to the tooth.

Table 4. Unpolymerized Sealant in Artificial Saliva, 48 hrs. (n=3)

Dental Sealant	Avg. ng BPA/g sealant	± s.d.
UltraSeal XT hydro	BDL	N/A
Clinpro	BDL	N/A
Helioseal F	BDL	N/A
DELTON FS+	BDL	N/A
Embrace WetBond Pit & Fissure Sealant	BDL	N/A
Seal-Rite	BDL	N/A
FluroShield	BDL	N/A
Guardian Seal	2.53	0.57
BeautiSealant	BDL	N/A
Control Seal	BDL	N/A
ClearVue	17.51	9.66
Prevent Seal	BDL	N/A
Tooth Fairy	2.88	1.27
ECO-S	7.21	6.57

BDL: Below limit of detection.
N/A: Not applicable.

Table 5. Polymerized Sealant Extracted in Artificial Saliva (n=3)

Sealant	24 hrs		48 hrs		Ratio
	Avg. ng BPA/g sealant	± s.d.	Avg. ng BPA/g sealant	± s.d.	48/24 hrs**
UltraSeal XT hydro	1.84	0.27	1.52	0.26	0.82
Clinpro	3.88	0.96	3.85	0.45	0.99
Helioseal F	2.01	0.13	1.97	0.09	0.98
DELTON FS+	<1.50	0.38	<1.90	0.76	1.27
Embrace WetBond Pit & Fissure Sealant	BDL	N/A	<1.58	0.26	BDL24
Seal-Rite	3.92	1.20	4.33	0.65	1.10
FluroShield	<2.49	1.57	<1.72	0.16	0.69
Guardian Seal	4.38	0.21	3.70	1.30	0.85
BeautiSealant	<1.71	0.36	<1.72	0.34	1.01
Control Seal	2.89	0.89	3.42	0.86	1.18
ClearVue	BDL	N/A	<8.60	11.46*	BDL24
Prevent Seal	4.59	1.75	14.63	20.04*	3.19
Tooth Fairy	<2.40	0.23	<2.52	0.66	1.05
ECO-S	9.72	1.18	20.25	14.05*	2.08

* Large s.d. caused by one outlier lot that skewed data towards continued release of BPA.
** Values above 1.00 indicate continued release of BPA past 24 hours of extraction.
BDL: Below limit of detection.
N/A: Not applicable.
BDL24: Ratio not calculated because 24 hour extracts were BDL.

Averages reported as "less than" the numerical value represent those products where one or two lots resulted in measurements below the limit of detection.

Continued on next page

Table 6. Maximum BPA release (ng) per 8 mg sealant

Sealant	Unpolymerized, ACN	Unpolymerized, artificial saliva, 48 hrs	Polymerized, artificial saliva, 24 hrs	Polymerized, artificial saliva, 48 hrs
UltraSeal XT hydro	0.286	<0.001	0.015	0.012
Clinpro	0.797	<0.001	0.031	0.031
Helioseal F	0.192	<0.001	0.016	0.016
DELTON FS+	0.123	<0.001	0.012	<0.015
Embrace WetBond Pit & Fissure Sealant	<0.004	<0.001	<0.011	<0.013
Seal-Rite	0.292	<0.001	<0.031	0.035
Fluroshield	0.117	<0.001	0.020	<0.014
Guardian Seal	0.161	0.020	0.035	0.030
BeautiSealant	0.069	<0.001	0.014	<0.014
Control Seal	0.109	<0.001	0.023	0.027
ClearVue	0.539	0.140	0.016	<0.069
Prevent Seal	0.288	<0.001	0.037	0.117
Tooth Fairy	2.434	0.023	0.019	<0.020
ECO-S	12.017	0.058	0.078	0.162

Extraction of BPA in artificial saliva did not match the relative values found for extraction in acetonitrile. This is not surprising, since unpolymerized sealant is not water soluble.

Table 5 shows that more BPA could be extracted from polymerized sealant than unpolymerized sealant in artificial saliva, excluding ClearVue (Table 4). The ClearVue results may be an aberration due to the value of BPA in one of the three lots tested being substantially higher than the others.

The ratios of 48 hour over 24 hour extractable BPA indicated little to no extended BPA release beyond 24 hours. Only ClearVue, Prevent Seal and ECO-S showed potential for BPA release past 24 hours. However, it is believed that this was caused by a single lot difference out of the three lots for each product. When the aberrant lots were removed, a new average resulted in a ratio close to 1.00, indicating little to no BPA release past 24 hours.

Averages reported as "less than" the numerical value represent those products where one or two lots resulted in measurements below the limit of detection.

To estimate human BPA exposure following sealant placement, it is assumed that 8 mg of sealant is used for each tooth.[20] Table 6 indicates potential BPA release from 8 mg of each sealant product both polymerized and unpolymerized.

The EPA set the chronic oral exposure level to BPA at 50,000 ng/kg body weight/day.[21] The EFSA recently proposed lowering the exposure level to 4,000 ng/kg/body weight/day.[22] The EFSA exposure limit is the tolerable daily intake (TDI), which includes dietary and non-dietary sources for BPA. For this evaluation the more conservative EFSA exposure limit was used to estimate human safe exposure limits for BPA from resin-based dental sealants. The appropriate conversion for exposure limits are included in Tables 7 and 8.

Adult human exposure assumes sealant placement on permanent molars and premolars before eruption of third molars. It is also assumed that normally only one quadrant is sealed during a single office visit. Table 7 shows how many times lower than the EFSA exposure limit each sealant product presents.

The clinically relevant condition of cured sealant extracted in artificial saliva for 24 hours at 37°C, ranged from almost 900,000 times lower for ECO-S than the BPA exposure limit to greater than 6 million times lower for Embrace WetBond Pit & Fissure Sealant after sealing one quadrant in an adult (Table 7). Furthermore, all of the sealants demonstrated BPA exposure well below established exposure limits, even if two quadrants were sealed in one adult office visit.

For estimating BPA exposure in children, it is assumed that sealants are applied to all eight primary molars and premolars during one office visit. Table 8 shows how many times lower than the EFSA exposure limit each sealant product presents. Although the amount of sealant placed on one primary tooth likely is somewhat less than on a permanent tooth, the conservative amount of 8 mg of sealant is assumed to be applied to each primary tooth for the purpose of estimating BPA exposure in children.

Continued on next page

Table 7. Number of times lower than the adult daily oral intake limit of BPA from sealants* *(Continued on next page.)*

Sealant**	1 Tooth Sealed				4 Teeth Sealed (one quad w/o 3rd molar)			
	Unpolymerized in ACN	Unpolymerized in artificial saliva	Polymerized in artificial saliva, 24 hrs	Polymerized in artificial saliva, 48 hrs	Unpolymerized in ACN	Unpolymerized in artificial saliva	Polymerized in artificial saliva, 24 hrs	Polymerized in artificial saliva, 48 hrs
UltraSeal XT hydro	980,694	>350,000,000	19,004,597	.>23,084,217	245,174	>87,500,000	4,751,149	>5,771,054
Clinpro	351,511	>350,000,000	9,027,234	9,089,104	87,878	>87,500,000	2,256,808	2,272,276
Helioseal F	1,458,399	>350,000,000	17,382,033	17,721,654	364,600	>87,500,000	4,345,508	4,430,414
DELTON FS+	2,277,279	>350,000,000	23,363,043	>18,458,447	569,320	>87,500,000	5,840,761	>4,614,611
Embrace WetBond Pit & Fissure Sealant	>70,000,000	>350,000,000	>24,452,547	>22,110,454	>17,500,000	>87,500,000	>6,113,136	>5,527,613
Seal-Rite	960,317	>350,000,000	>8,919,744	8,086,100	240,079	>87,500,000	>2,229,936	2,021,525
FluroShield	2,393,724	>350,000,000	14,077,674	20,372,487	598,431	>87,500,000	3,519,418	>5,093,121
Guardian Seal	1,742,562	13,829,132	7,989,869	9,449,121	435,640	3,457,283	1,997,467	2,362,280
BeautiSealant	4,058,548	>350,000,000	20,498,963	20,365,551	1,014,637	>87,500,000	5,124,741	>5,091,387
Control Seal	2,574,876	>350,000,000	12,128,816	10,244,383	643,719	>87,500,000	3,032,204	2,561,096
ClearVue	519,236	1,998,349	17,232,159	4,069,256	129,809	499,587	4,308,040	>1,017,314
Prevent Seal	973,802	>350,000,000	7,621,943	2,391,645	243,451	>87,500,000	1,905,486	597,911
Tooth Fairy	115,059	12,135,884	14,587,787	13,905,460	28,765	3,033,971	3,646,947	>3,476,364
ECO-S	23,301	4,855,918	3,599,745	1,728,238	5,825	1,213,979	899,936	432,060

* Limit of 2.8 x 10^5 ng BPA/70 kg is proposed by European Food Safety Authority (EFSA) 2015; EPA values would be 12.5 x these EFSA values. For example, if 8 mg sealant was placed on one tooth and 0.01 ng BPA was released after 24 hours then the BPA exposure level would be 280,000/0.01 or 28,000,000 times lower than the EFSA limit.
** 8 mg sealant/tooth.

Similar to the toxicity profiles found in adults, the more clinically relevant condition of cured sealant extracted in artificial saliva for 24 hours at 37°C, ranged from over 64,000 times lower for ECO-S than the BPA exposure limit to over 436,000 times lower for Embrace WetBond Pit & Fissure Sealant after sealing all 8 primary molars and premolars during one office visit. None of the sealants exceeded exposure limits for children.

Discussion/Conclusions

All dental sealant products tested, except Embrace Wet Bond Pit & Fissure Sealant, showed extractable levels of BPA when dissolved in acetonitrile, representing worst-case levels of potential BPA exposure (Table 2). Formulations provided by manufacturers did not always predict potential BPA content, since some did not list any BPA derivatives in their products (BeautiSealant, ClearVue, Prevent Seal and Tooth Fairy) (Table 3), yet BPA could be detected in their products.

None of the sealants' packaging list bis-DMA as an ingredient. Bis-DMA is a BPA derivative and was identified as the source of BPA through degradation by salivary esterases from a dental sealant in one of the earliest studies associating estrogenicity with dental sealants.[7,17] Therefore, bis-DMA no longer is a concern for BPA exposure from dental sealants.

Unpolymerized sealant extracted in artificial saliva with esterase showed lower overall release of BPA than polymerized sealant in artificial saliva (Tables 4 and 5). Reasons for this may include high hydrophobic properties of uncured sealant and the formation of an oxygen inhibited layer on the surface of cured sealant making extraction of BPA easier than unpolymerized sealant.

The ratios of 48 hour over 24 hour extractable BPA indicated little to no extended BPA release beyond 24 hours (Table 5). Only ClearVue, Prevent Seal and ECO-S showed potential for BPA release past 24 hours. However, it is believed that this was caused by a single lot difference out of the three lots tested for each product. Thus BPA exposure following sealant placement must be considered as an acute rather than a chronic exposure.

Continued on next page

Table 7. Number of times lower than the adult daily oral intake limit of BPA from sealants* *(Continued from previous page.)*

Sealant**	8 Teeth Sealed (two quads w/o 3rd molar)			
	Unpolymerized in ACN	Unpolymerized in artificial saliva	Polymerized in artificial saliva, 24 hrs	Polymerized in artificial saliva, 48 hrs
UltraSeal XT hydro	122,587	>43,750,000	2,375,575	>2,885,527
Clinpro	43,939	>43,750,000	1,128,404	1,136,138
Helioseal F	182,300	>43,750,000	2,172,754	2,215,207
DELTON FS+	284,660	>43,750,000	2,920,380	>2,307,305
Embrace WetBond Pit & Fissure Sealant	>8,750,000	>43,750,000	>3,056,568	>2,763,806
Seal-Rite	120,040	>43,750,000	>1,114,968	1,010,763
FluroShield	299,216	>43,750,000	1,759,709	>2,546,560
Guardian Seal	217,820	1,728,641	998,734	1,181,140
BeautiSealant	507,319	>43,750,000	2,562,370	>2,545,693
Control Seal	321,859	>43,750,000	1,516,102	1,280,548
ClearVue	64,904	249,794	2,154,020	>508,657
Prevent Seal	121,725	>43,750,000	952,743	298,956
Tooth Fairy	14,382	1,516,985	1,823,473	>1,738,182
ECO-S	2,913	606,990	449,968	216,030

* Limit of 2.8 x 10^5 ng BPA/70 kg is proposed by European Food Safety Authority (EFSA) 2015; EPA values would be 12.5 x these EFSA values. For example, if 8 mg sealant was placed on one tooth and 0.01 ng BPA was released after 24 hours then the BPA exposure level would be 280,000/0.01 or 28,000,000 times lower than the EFSA limit.
** 8 mg sealant/tooth.

Do the observed BPA levels in these sealants comply with current exposure limits? The EPA chronic oral exposure level to BPA is 50,000 ng/kg body weight/day[21] or 3.5 x 10^6 ng/70 kg/day for an adult and 0.5 x 10^6 ng/10 kg for a child. This limit is based on toxicity studies in rats and includes a 1,000-fold lower uncertainty factor for human oral toxicity. The EFSA proposed lowering the oral BPA exposure level to about one twelfth of the EPA exposure level, which is 2.8 x 10^5 ng/70 kg/day for an adult and 0.4 x 10^5 ng/10 kg for a child.[22] This evaluation uses the more conservative EFSA exposure limit to estimate human safe exposure limits for BPA from resin-based dental sealants.

All of the sealant products evaluated were below BPA daily oral exposure limits set by the EPA and the more conservative EFSA proposed limits, although the BPA safety margins overall were lower for children than for adults (Tables 7 and 8). Under simulated clinical conditions (artificial saliva with esterase extraction) for both polymerized (24 hours) and unpolymerized sealant (48 hours), BPA levels ranged from over 6 million to more than 35,000 times lower than the proposed EFSA limit for children. Similarly, for adults the exposure range was over 87 million to over 499,000 times lower following treatment of one quadrant. EPA limits would be 12.5 times these proposed EFSA ranges.

Safety margins were lower for composites than sealants.[2] This is likely due to the higher mass of one composite restoration per office visit (250 mg) compared to sealants, where a maximum mass of 64 mg is used over eight teeth per office visit. This results in a lower potential for BPA release from sealants compared to composites.

The ADA Council on Scientific Affairs provided the following statement on BPA:

"The ADA fully supports continued research into the safety of BPA; but, based on current evidence, the ADA does not believe there is a basis for health concerns relative to BPA exposure from any dental material."[23]

The evaluations of resin-based dental composites and sealants for potential BPA release clearly showed that the amounts of BPA that could be ingested within a 24-hour period do not exceed established human exposure limits. Therefore, this evidence provides support that resin-based dental materials do not present a health hazard.

Why might a sealant marketed as "BPA free" test positive for BPA? There could be several explanations. For example, the statement may be based on an analytical BPA detection limit, such as parts per million (ppm), whereas BPA could be detected when evaluated at the parts per billion (ppb) level. An industry standard defining the term "BPA-free" could help clarify such claims. As another example, a product may not contain BPA, but may contain a BPA derivative, such as bis-GMA. Accurately listing relevant product ingredients in material data sheets could help dentists know more precisely what they are using. Nevertheless, these observations are not clinically relevant because the amount of BPA was below accepted exposure limits and presents no health hazard.

Considerations for applying dental sealants. BPA may be released into the mouth after the application of pit and fissure dental sealants predominantly through the formation of an oxygen-inhibited layer of partially cured sealant. Azarpazhooh and Main recommend that dental providers reduce the potential for BPA exposure from dental sealants by treating

Continued on next page

Table 8. Number of times lower than the child daily oral intake limit of BPA from sealants*

Sealant**	Unpolymerized in ACN, 48 hrs	Unpolymerized in artificial saliva, 48 hrs	Polymerized in artificial saliva, 24 hrs	Polymerized in artificial saliva, 48 hrs
UltraSeal XT hydro	17,512	>6,250,000	339,368	412,218
Clinpro	6,277	>6,250,000	161,201	162,305
Helioseal F	26,043	>6,250,000	310,393	316,458
DELTON FS+	40,666	>6,250,000	417,197	>329,615
Embrace WetBond Pit & Fissure Sealant	>1,250,000	>6,250,000	>436,652	>394,829
Seal-Rite	17,149	>6,250,000	>159,281	144,395
FluroShield	42,745	>6,250,000	251,387	>363,794
Guardian Seal	31,117	246,949	142,676	168,734
BeautiSealant	72,474	>6,250,000	366,053	>363,670
Control Seal	45,980	>6,250,000	216,586	182,935
ClearVue	9,272	35,685	307,717	>72,665
Prevent Seal	17,389	>6,250,000	136,106	42,708
Tooth Fairy	2,055	216,712	260,496	>248,311
ECO-S	416	86,713	64,281	30,861

* Limit of 0.4 x 10^5 ng BPA/10 kg is proposed by European Food Safety Authority (EFSA) 2015; EPA values would be 12.5 x these EFSA values. For example, if 64 mg sealant was placed over 8 teeth and a total of 0.08 ng BPA was released after 24 hours, the BPA exposure level would be 40,000/0.08 or 500,000 times lower than the EFSA limit.
** 8 teeth sealed, 8 mg sealant/tooth.

the polymerized surface layer using one of the following procedures[24]:

- Use a mild abrasive, or pumice on a cotton or a prophylaxis cup
- Gargle with water for older children and adults
- Wash the surface of the sealant for 30 seconds with an air-water syringe with suction to remove fluids and debris from a child's mouth.

Also, assure that the sealant is fully cured by adhering to manufacturers' instructions and making sure that the curing light is functioning properly. Detailed information on the effective use of curing lights is available in past issues of the ADA Professional Product Review.[25-26]

These steps can help reduce or remove the oxygen-inhibited layer of under-cured resin and can help limit both the amount and duration of potential oral BPA exposure.

Mr. Stephen E. Gruninger is assistant director, Research and Laboratories, ADA Science Institute. Dr. Amer Tiba is a research associate, Research and Laboratories, ADA Science Institute. Mr. Rashad Vinh is a research assistant, Research and Laboratories, ADA Science Institute.

References

1. Gruninger SE, Tiba A and Koziol N. Update: Bisphenol A in Dental Materials. ADA Professional Product Review 2013;8.1: 2-5.
2. The ADA Professional Product Review. Determination of Bisphenol A Released from Resin-Based Dental Composite Restoratives. ADA Professional Product Review 2014;9(3):2-8.
3. NTP-CERHR Monograph on the Potential human reproductive and development effects of bisphenol A. National Toxicology Program, U.S. Department of Health and Human Services. National Institutes of Health. NIH Publication No. 08-5994.2008.
4. Bisphenol A (BPA). U.S. Food and Drug Administration. FDA Public Health Focus.
5. Fleisch AF, Sheffield PE, Chinn C, Edelstein BL, Landrigan PJ. Bisphenol A and related compounds in dental materials. Pediatrics 2010;126:760.
6. Van Landuyt KL, Nawrot T, Geebelen B, De Munck J, Snauwaert J, Yoshihara K, et al. How much do resin-based dental materials release? A meta-analytical approach. Dental Materials 2011;27:723–47.
7. Olea N, Pulgar R, Pérez P, Olea-Serrano F, Rivas A, Novillo-Fertrell A, Pedraza V, Soto AM, Sonnenschein C. Estrogenicity of resin-based composites and sealants used in dentistry. Environmental Health Perspectives 1996;104(3): 298-305.
8. Artham T, Doble M. Biodegradation of aliphatic and aromatic polycarbonates. Macromolecular Bioscience 2008;8:14–24.
9. Ahovuo-Saloranta A, Hiiri A, Nordblad A, Makela M, Worthington HV. Pit and fissure sealants for preventing dental decay in the permanent teeth of children and adolescents. Cochrane Database Systematic Reviews 2008;4:CD001830.

Continued on next page

10. Truman BI, Gooch BF, Sulemana I, et al. Reviews of evidence on interventions to prevent dental caries, oral and pharyngeal cancers, and sports-related craniofacial injuries. Am J Prev Med 2002;23:21–54.
11. Momoi Y, Hayashi M, Fujitani M, et al. Clinical guidelines for treating caries in adults following a minimal intervention policy – evidence and consensus based report. J Dent 2012;40:95–105.
12. Beauchamp J, Caufield PW, Crall JJ, et al. American Dental Association Council on Scientific Affairs. Evidence-based clinical recommendations for the use of pit and fissure sealants: a report of the American Dental Association Council on Scientific Affairs. JADA 2008;139:257–68.
13. Griffin SO, Oong E, Kohn W, Vidakovic B, Gooch BF. CDC dental sealant systematic review work group et al. The effectiveness of sealants in managing caries lesions. J DenT Res 2008;87:169–74.
14. Bowen RL, inventor. Method of preparing a monomer having phenoxy and methacrylate groups linked by hydroxyl glycerol groups. U.S. patent 3179623. April 1965.
15. Bowen RL. Use of epoxy resins in restorative materials. J Dent Res 1956;35:360-9.
16. Bowen RL. Properties of silica-reinforced polymer for dental restorations. JADA 1963;66:57-64.
17. Atkinson JC, Diamond F, Eichmiller F, Selwitz R, Jones G. Stability of bisphenol A, triethylene-glycol dimethacrylate, and bisphenol A dimethacrylate in whole saliva. Dent Mater 2002;18(2):128-35.
18. ANSI/ADA Specification No.39/ISO 6874: 2006 (reaffirmed 2011). Pit and fissure sealants.
19. ANSI/ADA Specification No. 41 2010. Recommended standard practices for biological evaluation of dental materials. Section 8.4.3.
20. Fung EK, Ewoldsen NO, St. Germain HA, et al. Pharmacokinetics of bisphenol A released from a dental sealant. JADA 2000;131(1):51-8.
21. U.S. Environmental Protection Agency. 1993. Integrated risk information: Bisphenol A (CASRN 80-05-7). EPA Bisphenol A Accessed March 3, 2015.
22. EFSA Panel on Food Contact Materials, Enzymes, Flavourings and Processing Aids (CEF), 2015. Scientific Opinion on the risks to public health related to the presence of bisphenol A (BPA) in foodstuffs: Executive summary. EFSA Journal 2015;13(1):3978, 22 pp. doi:10.2903/j.efsa.2015.3978. http://www.efsa.europa.eu/en/efsajournal/doc/3978.pdf Accessed March 3, 2015.
23. Council on Scientific Affairs. April 2013. Bisphenol A: ADA Statement on Bisphenol A and Dental Materials. http://www.ada.org/en/member-center/oral-health-topics/bisphenol-a Accessed March 3, 2015.
24. Azarpazhooh A, Main PA. Is There a Risk of Harm or Toxicity in the Placement of Pit and Fissure Sealant Materials? A systematic Review. J Can Dent Assoc. 2008;74(2):179-183.
25. The ADA Professional Product Review. Product Forum highlights how to improve curing light effectiveness. ADA Professional Product Review 2014;9(4):26-9. Accessed March 3, 2015.
26. The ADA Professional Product Review. Effective use of curing lights: A guide for the dental practitioner. ADA Professional Product Review 2013;8(2).

ISSN 1930-8736