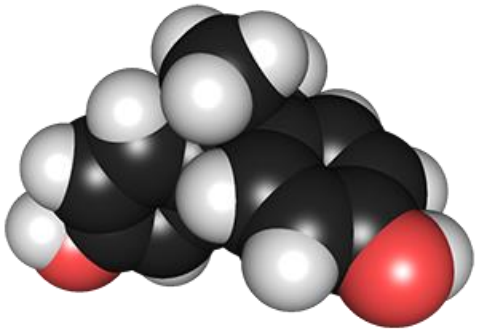
Cavex Quadrant Composite BPA - free

Quadrant Restoratives Quadrant Composites Quadrant Universal LC Articles

Bisphenol-A in dental composites

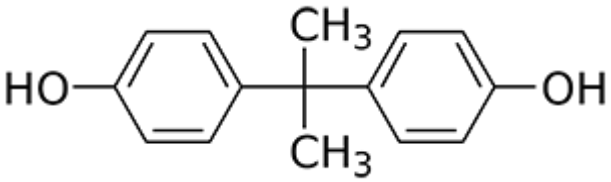
General:

Bisphenol A (BPA), already discovered in 1891, has been used since the 1950's to harden polycarbonate plastics and resins, mainly used for the production of drinking bottles, eyeglass lenses, cell phones and eating utensils. Over the years studies have been conducted to determine possible health effects connected to the exposure of BPA. Opinions vary greatly. Some studies conclude that BPA poses no health risks while others state that BPA causes a number of adverse health effects.



Possible Hazard:

In general, the European's Scientific Committee on Emerging and Newly Identified Health Risks (SCENIHR), the European Chemicals Agency (ECHA), the European Food Safety Authority (EFSA), American Dental Association (ADA) and the US Food and Drug Administration (US-FDA) have concluded that current levels of BPA present no risk to the general population.



Although the scientific evidence at this time does not suggest that the very low levels (4 µg/kg b.w./day) of human exposure to BPA through the diet are unsafe, we have to keep a close eye on matters.

Dental Composites:

BPA derivatives are used as main ingredient for the production of bisphenol A-glycidylmethacrylate (bis-GMA) which is the basic monomer for many dental composites. A recent article showed increased urinary BPA levels within 2 weeks after newly placed composite restorations. Fortunately, these concentrations are no longer detectable 6 month after placement. Another study among 160 composite resins from 31 manufacturers showed that > 85% of the composites in the market are based upon BPA derivatives. The small group using alternative monomers are not necessarily more biocompatible. The safety is not only related to the actual monomer but is more associated with the degree of polymerization. Therefore, additional studies for long-term effects on human health of all the different leaching monomers are still necessary.

Quadrant Composite BPA – free!:

As Cavex takes the risk of BPA very serious, we only use a very high and pure grade bis-GMA in our production, minimizing the amount of bisphenol A. Also additional testing on the leached monomers from composite filling has been performed. Based upon our knowledge and findings of the studies, we can state that our Quadrant composites and bonding are BPA-free and can be used safely.

Haarlem, 28 November 2016

Cavex Holland B.V.

Manager Technical Services

Richard Woortman

Reference:

SCENIHR 02-2015

Final opinion on the safety of the use of bisphenol A in medical devices

PUBLIC HEALTH February 2015

Directorate General for Health and Food Safety

PUBLIC HEALTH

SCENIHR Final Opinion on The safety of the use of bisphenol A in medical devices

Today, the European Commission and its non-food Scientific Committee on Emerging and Newly Identified Health Risks (SCENIHR) have published the final opinion on "**The safety of the use of bisphenol A in medical devices".**

Concern for the safety of vulnerable groups such as infants, pregnant and breast-feeding women when exposed to bisphenol A (BPA) through medical devices have recently been raised. Such medical devices include include implants, catheters, and most dental devices.

This opinion aims to assess whether the use of bisphenol A in these devices could give reasons for safety concerns, to provide indications on limit values for BPA release from medical devices and to identify any patient group, e.g. infants, pregnant and breastfeeding women who would be particularly at risk.

When drafting the final opinion the SCENIHR considered the temporary oral TDI (t-TDI) of 4 µg/kg b.w./day derived by EFSA as a solid base for carrying out the risk assessment for the use of BPA in medical devices. Several exposure scenarios have been evaluated taking into account the material used, information related to BPA leaching, the duration of a single treatment and the frequency of treatments, giving rise to toxicologically relevant acute, short and long term exposure. However, the information available is very limited and in many cases due to the lack of experimental data, only estimations were used.

Concerning exposure via the oral route, it can be concluded that the long term exposure to BPA via dental material is far below the recently derived t-TDI and poses negligible risk for human health associated to BPA exposure.

Some risk for adverse effects may exist, when the BPA is directly available for systemic exposure after non-oral exposure routes, especially for neonates in intensive care units, for infants undergoing prolonged medical procedures and for dialysis patients.

In spite of this, it should be considered also the benefit of medical devices: the survival of neonates, for example, often depends on the availability of the medical devices which causes a relatively high BPA exposure. The possibility to replace BPA in these products should be considered against their efficiency in the treatment, as well as the toxicological profile of the alternative materials, when available.

However, better data on exposure would be beneficial for the refinement of the present risk assessment, to be carried out when new data on exposure via medical devices will be available.

ECHA 12-2015

Committees finalize evaluation of bisphenol A restriction proposal

ECHA's committees finalise evaluation of bisphenol A restriction proposal

ECHA/PR/15/16

ECHA's Committee for Socio-economic Assessment (SEAC) has concluded that the socio-economic benefits of restricting bisphenol A (BPA) in thermal paper are unlikely to be higher than the socio-economic costs. SEAC also noted that there are other considerations in favour of the restriction that should be taken into account by the European Commission in making their decision. The Committee for Risk Assessment (RAC) had previously concluded that the risk for workers handling thermal paper was not adequately controlled.

Helsinki, 7 December 2015 – In May 2014, the French authorities submitted a proposal to restrict BPA because of health risks for pregnant workers and consumers exposed to it in thermal paper - for example when they handle cash register receipts. The population identified as being at risk is unborn children, who are exposed in the uterus.

RAC agreed with the French proposal that BPA may have effects on the mammary glands, as well as on reproduction, metabolism and neuro-behaviour. In addition, and in line with the opinion of the European Food Safety Authority (EFSA), RAC also considered the effects on the immune system.

In September 2015, RAC concluded that the risk for the unborn children of female workers e.g. cashiers handling thermal paper, is not adequately controlled. However, the Committee did not identify a risk to consumers in handing receipts.

In its opinion of 3 December 2015, SEAC considered that the socio-economic benefits were unlikely to be higher than the socio-economic costs of the proposed restriction. However, they also noted that there could be other considerations in favour of the restriction that should be taken into account by the European Commission in making their decision. These included that a relatively small population with low incomes are at risk – cashiers – whereas the costs of the restriction would be spread across all EU consumers in the EU. If the costs of a restriction were translated into increased prices, the amount per working EU-citizen would amount to only about €0.20 – €0.60 per person per year. This was considered affordable by SEAC.

The two committees are required to analyse the restriction from different perspectives and their opinions together provide a scientific basis for the decision-making by the European Commission.

Next steps

ECHA will send the RAC and SEAC opinions to the European Commission. The Commission needs to decide whether to add BPA to the list of restrictions (Annex XVII of REACH). The REACH Committee - consisting of Member States - assists the Commission in this decision

EFSA 2015

Scientific opinion on bisphenol A

EFSA explains **the Safety of Bisphenol A**

Scientific opinion on bisphenol A (2015)

- What is **bisphenol A** and what has EFSA done?
- What are the **main results** of EFSA's 2015 risk assessment of BPA?
- What **potential** health effects of BPA has EFSA identified?
- What did EFSA find out about **exposure to BPA**?
- What are EFSA's **overall conclusions**?
- **Understanding** EFSA's risk assessment of BPA

What is **bisphenol A** and what has EFSA done?

BPA is a chemical compound used in the manufacture of polycarbonate plastic food contact materials such as re-usable plastic tableware and can coatings (mainly as protective linings. Another widespread application of BPA is in thermal paper commonly used for till/cash register receipts.

EFSA's expert **Panel on Food Contact Materials, Enzymes, Flavourings and Processing Aids (CEF)** decided that the publication of new scientific research on BPA in recent years meant a full re-evaluation of the chemical was necessary.

EFSA's experts estimated the **exposure** to BPA from dietary and non-dietary sources, and assessed the **human health risks** posed by exposure to BPA. The resulting risk assessment was published in January 2015 in the CEF Panel's *"Scientific Opinion on the risks to public health related to the presence of bisphenol A (BPA) in foodstuffs"*.

What are the **main results** of EFSA's 2015 risk assessment of BPA?

- BPA poses **no health risk** to consumers because current exposure to the chemical is too low to cause harm.
- Based on new data and methodologies, EFSA has lowered the estimated safe level, known as the tolerable daily intake (TDI), to 4 micrograms per kilogram of body weight per day. This is **twelve and a half times lower** than the previous level.
- The highest estimates for aggregated exposure to BPA from both dietary and non-dietary sources are **3 to 5 times lower than the TDI**, depending on the age group.
- Dietary exposure is from 4 to 15 times lower than previously estimated by EFSA, depending on the age group.
- Based on animal studies, BPA at high doses (more than 100 times the TDI) is likely to cause adverse effects in the **kidney and liver**. It is also likely to have effects on the **mammary glands** of rodents.
- Uncertainties surrounding potential health effects of BPA on the mammary gland, reproductive, metabolic, neurobehavioural and immune systems have been **quantified and factored** in to the TDI.
- **The TDI is temporary** (t-TDI) pending the outcome of an on-going long-term study in rats involving prenatal as well as postnatal exposure to BPA. This study will help reduce the remaining uncertainties about the potential health effects.

efsa
European Food Safety Authority

EFSA's risk assessment in more detail

What **potential health effects** of BPA has EFSA identified?

- Based on animal studies, BPA at high doses (more than 100 times the TDI) is likely to cause adverse effects in the **kidney and liver**. It is also likely to have effects on the **mammary glands** of rodents. How these effects are caused (the 'mechanism of action') is not clear.
- Possible effects of BPA on the reproductive, nervous, immune, metabolic and cardiovascular systems, as well as in the development of cancer are **not considered likely at present** but they could not be excluded. They add to the overall uncertainty about BPA-related hazards and therefore have been considered in the assessment.
- The kidney effects in mice were the reference point for deriving the safe level, known as the tolerable daily intake (TDI), for BPA in food.
- The TDI **has been lowered** from its previous level of 50 micrograms (µg) per kilogram of body weight per day (or *0.05 milligrams per kilogram of body weight per day*) to 4 µg/kg of bw/day. EFSA is making this change because of new data and a refined risk assessment, and because of uncertainty in the database regarding mammary gland and reproductive, metabolic, neurobehavioural and immune systems.
- The TDI is **temporary** (t-TDI) until the results of ongoing research from the US National Toxicology Program can be incorporated in the evaluation. This research is expected to address many of the remaining uncertainties.
- Based on scientific criteria*, EFSA's experts concluded that the available data do not provide evidence that BPA results in non-monotonic dose-response relationships for the health effects considered.

* The three scientific criteria required as evidence of non-monotonic dose-response (NMDR) relationships:

1) At least two adjacent doses departing from monotonicity or support for the NMDR from a similar study (same species, similar treatments, similar sampling time) on the same effect (this criteria reduces the chance for an incidental finding)
2) A plausible underlying mode of action/overarching concept
3) The reliability of the study and the relevance of the effect for human health should be considered as medium or high (as expressed in Appendix B and C); the reliability of the study results should also include an appropriate statistical treatment of the reported data

How did EFSA's experts calculate the new TDI?

In this opinion, EFSA has used a more refined methodology than before supported by new data. EFSA's experts have quantified uncertainty about some potential effects to be able to factor them in to the risk assessment and the derivation of the t-TDI.

- Experts analysed the toxicological studies already available for the previous evaluations, supplemented with new information and used a method known as **benchmark dosing** to calculate the lowest dose (called the "benchmark dose") at which BPA causes a small adverse effect in the kidneys of mice – in this case a 10% change in the mean relative weight of the organ. EFSA established that this effect would occur at a dose of **8960 µg/kg bw/day**.
- New robust studies that have become available since 2010 allowed EFSA to take better account of the differences in the ways in which various animal species and humans metabolise and eliminate BPA. Using this information, EFSA's experts could convert the dose that causes the adverse effect on the kidneys in mice into an oral equivalent dose for humans of **609 µg/kg bw/day**. This "**human equivalent dose**" is applicable to all exposures to BPA, whether they result from diet or from skin contact, provided that the latter is first converted to a corresponding oral exposure.
- The next step normally involves applying an uncertainty factor of 100 to take into account the differences between species and the differences between individual persons.
- Derivation of the human equivalent dose, based on substance specific-data, meant the differences between species in metabolism and elimination were already considered leaving an uncertainty factor of 25.
- Finally, **an extra factor of six** was included to take into account the uncertainty in the database related to effects on mammary gland and reproductive, neurobehavioural, immune and metabolic systems. The Panel derived this factor of six by performing a detailed uncertainty analysis based on expert judgement.
- Thus, an **overall uncertainty factor of 150** (25 × 6) was applied to the equivalent human dose of 609 µg/kg bw per day to derive the new t-TDI of 4 µg/kg bw/day.

What did EFSA find out about **exposure to BPA**?

- Dietary exposure is from **4 to 15 times lower than previously estimated** by EFSA in 2006, depending on the age group considered. This is due to **better data** and less conservative assumptions for the exposure calculations.
- Dietary exposure to BPA is highest among infants and toddlers. The highest estimates are 4 and a half times below the t-TDI. This is explained by their higher food consumption on a body weight basis.
- Dietary exposure for bottle-fed infants aged 0-6 months is 50-fold below the t-TDI for the highest estimates.
- **Canned food** and, to a lesser extent, non-canned meat and meat products were identified as major contributors to dietary BPA exposure for all age groups.
- Aggregated exposure, which reflects the summated exposure to the toxicologically relevant form of BPA – known as 'unconjugated BPA' – through all routes (diet, dust, cosmetics and thermal paper), is highest for adolescents at over 1 µg/kg bw/day.
- **Uncertainty** in the exposure estimates for non-dietary sources is high because of the lack of supporting data. The uncertainty around dietary exposure is relatively low.

What is new about this exposure assessment?

This is EFSA's first review of consumer exposure to BPA to cover both dietary and non-dietary sources. It also considers specific groups of the population, e.g. infants, teenagers (10-18 years) and women of child-bearing age (18-45 years).

EFSA's experts have carried out a considerable refinement of the dietary exposure estimates compared to the previous one in 2006 thanks to the availability of more scientific information.

In contrast to previous opinions, based on extensive new data, the relevance of the various exposure routes (diet, dermal, inhalation) can now be better taken into account.

What are EFSA's **overall conclusions**?

The overall conclusion is that BPA poses **no risk to human health** from foodstuffs because current levels of exposure are well below the t-TDI of 4 µg/kg of bw/day. This also applies to pregnant women and to the elderly.

In addition, EFSA's experts concluded that the health concern from the aggregated exposure to BPA from foodstuff, toys, dust, cosmetics and thermal paper is also below the t-TDI of 4 µg/kg bw/day. The uncertainty in the exposure estimate from toys, dust, cosmetics and thermal paper is considerable due to the very limited availability of data.

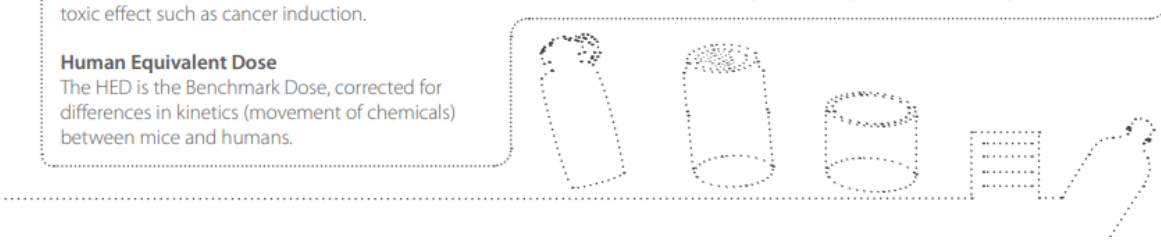
Definitions

What is the Tolerable Daily Intake (TDI)?

The TDI is the estimated quantity of a chemical substance that can be ingested daily over a lifetime without posing a significant risk to health. TDIs are expressed by body weight, usually in milligrams or micrograms (of the substance) per kilogram of body weight, and per day in the case of repeated exposure.

Benchmark Dose
The minimum dose of a substance that produces a clear, low level health risk, usually in the range of a 1-10% change in a specific toxic effect such as cancer induction.

Human Equivalent Dose
The HED is the Benchmark Dose, corrected for differences in kinetics (movement of chemicals) between mice and humans.



Understanding EFSA's risk assessment of BPA

TM-01-15-035-EN-N

EFSA's experts examined both hazards and risks associated with BPA:

1. **Hazard assessment** – uses experimental data from animal and human studies to identify any health effects associated with exposure to BPA.
2. **Risk characterisation** – analyses the extent of the risk posed by the identified hazards to consumers at current levels of exposure to BPA in the population – via oral ingestion, breathing in dust and exposure through the skin.

Are 'hazards' and 'risks' the same?

No, hazards and risks are different. A **hazard** is a possible threat posed to health because of the intrinsic properties of a substance, such as its capacity to damage the kidney or cause cancer. But the **risk** that a substance could cause a harmful effect depends on:

- how much of the substance humans are exposed to
- the length of time of the exposure
- when exposure occurs, i.e. as a fetus, child or adult.

Has EFSA found health hazards associated with exposure to BPA?

Based on animal studies, **BPA at high doses** (more than 100 times the TDI) is likely to cause an adverse effect on the kidney and liver. It is also likely to have effects on the mammary glands of rodents. Effects on fertility and development may be expected at levels of exposure approximately 10,000 times above the t-TDI.

Why has EFSA reduced the Tolerable Daily Intake (TDI)?

Importantly, the reduction of the TDI is not connected to the emergence of new health concerns about BPA. EFSA has reduced the TDI because **the method used to assess the risk from BPA has become more refined** than the one used in evaluations carried out by the Authority between 2006 and 2011.

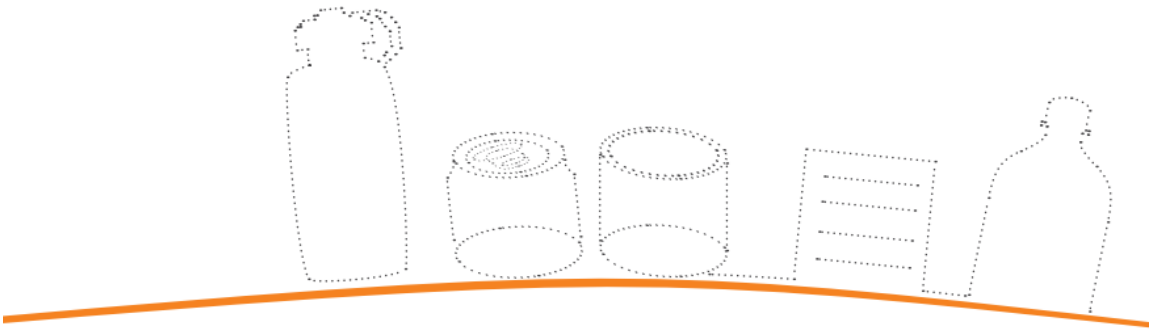
More accurate data is available now so the calculations used in the risk assessment are based on substance-specific information and less on commonly used standard default values. In addition, an extensive analysis based on new techniques shows uncertainty in the database regarding mammary gland and reproductive, metabolic, neurobehavioural and immune systems, which had to be taken into account.

Does this mean that BPA poses a health risk to humans?

EFSA concludes that BPA poses **no health risk** to consumers because current exposure to the chemical is too low to cause harm. EFSA's scientific opinion shows the level of BPA that consumers of all ages are exposed to through the diet is well below the t-TDI of 4 µg/kg of bw/day; the highest estimates for dietary and non-dietary exposure to BPA are 3 to 5 times lower than the t-TDI, depending on the age group. For all population groups, dietary exposure on its own is more than five-fold below the t-TDI. This also applies to pregnant women and to the elderly.

How did EFSA quantify uncertainty and factor this into the risk assessment?

EFSA's experts used new methodologies to take account of the uncertainties regarding potential health effects, exposure estimates and evaluation of risks for humans. By analysing each uncertainty one by one and combining **expert judgement**, the experts were able to quantify these uncertainties and to factor them in to the risk assessment and derivation of the t-TDI.



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EFSA 10-2016

New immune system evidence useful but limited

13 October 2016

Bisphenol A: new immune system evidence useful but limited

New data confirm EFSA's previous conclusion that bisphenol A (BPA) might affect the immune system in animals, but the evidence is too limited to draw any conclusions for human health.

Following a request from the Dutch Ministry of Health, Welfare and Sport, EFSA's experts reviewed two studies by *Ménard et al.* (unpublished at the time of EFSA's last comprehensive evaluation of BPA) and concluded that there were key limitations in the way they were designed and carried out. Furthermore, the data from the studies were too variable to use for setting a new tolerable daily intake (TDI) for BPA.

As stated in 2015, EFSA will review its temporary TDI of 4 micrograms per kilogram of body weight (µg/kg bw/day) after evaluating the scientific evidence on BPA toxicity published since 2012.

Prof Vittorio Silano, Chair of EFSA's expert Panel on Food Contact Materials, Enzymes, Flavourings and Processing Aids (CEF), said: "EFSA's new review will start in 2017 and additional immunological studies such as those by *Ménard et al.* would be useful contributions if the limitations we identified are addressed."

Dr Fleur van Broekhuizen – lead author of a report by the Dutch National Institute for Public Health and the Environment (RIVM) that prompted EFSA's appraisal of the new evidence – said: "RIVM welcomes EFSA's confirmation of our assessment that BPA might affect the immune system. We look forward to the outcome of EFSA's next review of scientific evidence on BPA."

Studies by *Menard et al.* (2014)

The two studies by *Menard et al.* suggested food intolerance and reduced resistance ("impaired immune response") to parasitic infection in rats exposed to 5 µg of BPA per kg bw/day. The doses were administered "perinatally" (i.e. before and just after birth).

EFSA set up a working group of international experts to assess the studies and the authors kindly provided the original data to EFSA for the review.

The CEF Panel concluded that the limitations in the design and conduct of these studies – particularly the use of a single dose for the majority of the tests – prevent meaningful assessment of their relevance for human health. Moreover, for the only effect tested at three BPA doses, when plotted on a graph, the data results are so scattered and variable that they do not allow identification of a reference point for the immunotoxicity of BPA and, therefore, cannot be used to set a TDI.

The main technical limitations of the studies included:

- Only one type of immune response was tested with three BPA doses – evaluating dose-response relationships is not possible below three doses.
- No positive control to account for differences between immune-deficient animals and the tested animals.
- No control for litter effect to account for possible differences between animals from different litters.
- Insufficient study reporting, for example, no information on animal body weight, BPA source, mode of oral administration, number of dams (mothers)/pups.
- Lack of statistical evaluation of the non-monotonic dose response.
- No mention of power analyses – a statistical tool to calculate the minimum effective sample size.

- A statement on the developmental immunotoxicity of bisphenol A (BPA): answer to the question from the Dutch Ministry of Health, Welfare and Sport

What's next?

In December 2014, EFSA reduced the TDI for BPA from 50 to 4 µg/kg bw/day. The TDI was made temporary and EFSA committed to re-evaluate BPA again when a two-year study by the U.S. National Toxicology Program is expected to become available in 2017.

Work is underway at EFSA on a "scientific protocol" to define upfront how to search, review and integrate all the new scientific evidence not included in EFSA's previous assessment. EFSA will consult publicly on this preparatory work in 2017 so stakeholders can have their say before the re-evaluation begins.

ADA 2014

Statement on bisphenol A and dental materials

Bisphenol A

ADA Statement on Bisphenol A and Dental Materials

Bisphenol A (BPA) has been present in many consumer plastic products and food packaging since the 1960s.[1] Some studies have suggested that BPA may have adverse health effects, which has raised concerns about its widespread use.

The food industry uses BPA in the manufacture of hard plastic bottles and the lining that coats metal cans used to hold foods and beverages. Bisphenol A also is found in many other hard plastic products (like toys and plastic tableware). In 2012 in response to a petition from the American Chemistry Council, the FDA removed regulatory authorization for BPA as an additive in baby bottles and spill-proof cups. The FDA stated that this action was not based on safety concerns but rather on the manufacturers' representation that the industry no longer used BPA in those items.[2] BPA is also present in the environment from the release of industrial and household wastes. To a lesser extent, dental materials used to treat and prevent caries can contribute to very low-level BPA exposure for a few hours after placement.[3,4,5]

BPA might be found in dental composites and sealants for two reasons: 1) it's a by-product of other ingredients in dental composites and sealants that have degraded, and; 2) it's a trace material left-over from the manufacture of other ingredients used in dental composites and sealants. ADA research, confirmed by direct communications from dental material manufacturers, indicates that BPA is not used as a formula ingredient in dental materials.

As a product of the degradation of the material in the oral cavity: Composite resins are formulated from a mixture of monomers that are commonly based on bisphenol A diglycidyl ether methacrylate (bis-GMA). Some composite resins may contain other monomers, in addition to bis-GMA, that are added to modify the properties of the resin. An example is bisphenol A dimethacrylate (bis-DMA). Bis-DMA-containing materials can release very small quantities of BPA, because bis-DMA is broken down by salivary enzymes.

As a trace material: BPA is used in the production of other ingredients found in many dental composites and sealants. Bis-DMA and bis-GMA are both produced using BPA as a starting ingredient, so residual BPA, which was not chemically converted into bis-DMA or bis-GMA, is likely present in trace amounts in any dental material containing these ingredients.

The U.S. Department of Health and Human Services (HHS) provides scientific guidance on issues that affect the health of Americans, and the U.S. Food and Drug Administration (FDA) provides advice and recommendations on dental product safety. A 2008 report prepared by the National Toxicology Program (NTP) of the HHS states that, "Dental sealant exposure to bisphenol A occurs primarily with use of dental sealants [containing] bisphenol A dimethacrylate. This exposure is considered an acute and infrequent event with little relevance to estimating general population exposures."[6] The NTP reported that bisphenol A in food and beverages accounts for the majority of daily human exposure.[6] In 2012, the FDA reiterated that "recent studies provide reason for some concern about the potential effects of BPA on the brain, behavior, and prostate gland of fetuses, infants and children." However, the FDA "recognizes substantial uncertainties with respect to the overall interpretation of these studies and their potential implications for human health effects of BPA exposure. These uncertainties relate to issues such as the routes of exposure employed, the lack of consistency among some of the measured endpoints or results between studies, the relevance of some animal models to human health, differences in the metabolism (and detoxification) of and responses to BPA both at different ages and in different species, and limited or absent dose response information for some studies."[1] Based on this conclusion, the FDA continues to provide for the use of BPA in dental materials, medical devices and food packaging.

According to the CDC, dental caries remains the most common chronic disease of children 6 to 19 years of age—4 times more common than asthma among adolescents aged 14 to 17 years.[7] Untreated cavities can cause pain, dysfunction, absence from school, poor appearance and can lead to the spread of infection—problems that greatly affect a child's quality of life. The utility of composite resin materials for both restoring dental health and preventing caries is well established, while any health risks from their use are not. 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.

The ADA is a professional association of dentists committed to the public's oral health. As such, the ADA supports ongoing research on the safety of existing dental materials and in the development of new materials. Based on current research, the Association agrees with the authoritative government agencies that the low-level of BPA exposure that may result from dental sealants and composites poses no known health threat.

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ADA 2016

Bisphenol A released from resin based dental sealants

ADA Professional Product Review®

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August 2016

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Bisphenol A Released from Resin Based Dental Sealants

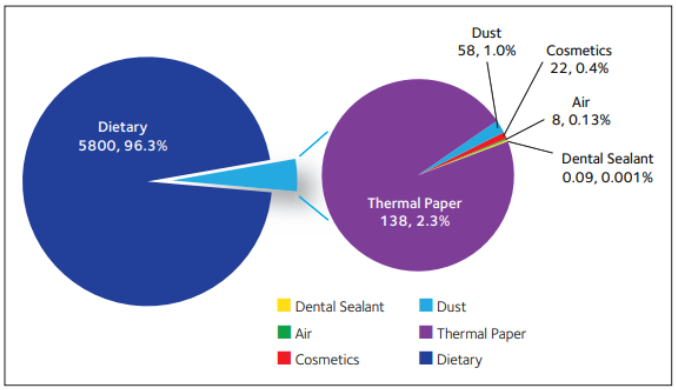
Abstract

Dental sealants are used successfully to prevent occlusal caries. Modern dental sealants penetrate the pits and fissures present on the occlusal surface of molars, allowing dentists to avoid drilling into healthy enamel. Dental sealants also are able to arrest caries progression when placed onto incipient caries, preventing future invasive restorative procedures. Resin-based sealants composed of bisphenol A glycidyl methacrylate (bis-GMA) monomer use bisphenol A (BPA) during the manufacturing process. Bisphenol A has been detected at trace levels on composite resin materials including dental sealants. A variety of adverse effects associated with exposure to BPA have been reported. The US Environmental Protection Agency (EPA) established an exposure level of 50,000 ng/kg body weight/day, which is equivalent to 1,000,000 ng/day for a 6-year-old child, weighing 20 kg.

This report from the Science Institute at the American Dental Association (ADA) demonstrates extremely low BPA release of 0.09 ng associated with the application of four dental sealants. By comparing the overall daily exposure to BPA estimated at 6020 ng/day by the European Food Safety Authority associated with different sources, we found that the contribution from dental sealants is limited to 0.001% when measured after 24 hours. Further analysis reveals that the BPA exposure from dental sealants (0.09 ng) is 100x lower compared to the exposure associated with BPA present in air (8 ng/day). The current results support the data published in 2014 and 2015 issues of the ADA Professional Product Review indicating limited release of BPA from a variety of resin-based dental materials. Our conclusion is that BPA levels in 12 dental sealants evaluated in this report are far below the daily exposure level set by the US EPA. The ADA will continue to monitor dental materials periodically, addressing a variety of concerns relevant to the oral health community.

- BPA has been detected at trace levels on dental sealants
- The US Environmental Protection Agency (EPA) established an exposure level of 50,000 ng/kg body weight/day
- BPA exposure from dental sealants is 0.09 ng and is 100x lower compared to the exposure associated with BPA present in air (8 ng/day)
- BPA levels in dental sealants evaluated in this report are well below the daily exposure level set by the US EPA

Daily BPA Exposure 6-year-old child (source, ng, %)



Daily BPA exposure estimated to a 6-year-old child from a variety of sources based on the European Food Safety Authority (2015). The application of four dental sealants would represent 0.001% of the estimated BPA exposure following the first 24 hours.

ADA American Dental Association®
America's leading advocate for oral health

FDA 2015

Current perspective on BPA in food contact applications

Summary of FDA's Current Perspective on BPA in Food Contact Applications

FDA's current perspective, based on its most recent safety assessment, is that BPA is safe at the current levels occurring in foods. Based on FDA's ongoing safety review of scientific evidence, the available information continues to support the safety of BPA for the currently approved uses in food containers and packaging.

Overview of BPA Usage in Food Contact Applications

BPA is a structural component in polycarbonate beverage bottles. It is also a component in metal can coatings, which protect the food from directly contacting metal surfaces. BPA has been used in food packaging since the 1960s. As is the case when foods are in direct contact with any packaging material, small, measurable amounts of the packaging materials may migrate into food and can be consumed with it. As part of its premarket review of food packaging materials, FDA's food contact regulations and food contact notification program assesses the likely migration from the packaging material to assure that any migration to food occurs at safe levels. Heightened interest in the safe use of BPA in food packaging has resulted in increased public awareness as well as scientific interest. As a result, many exploratory scientific studies have appeared in the public literature. Some of these studies have raised questions about the safety of ingesting the low levels of BPA that can migrate into food from food contact materials. To address these questions the National Toxicology Program, partnering with FDA's National Center for Toxicological Research is carrying out in-depth studies to answer key questions and clarify uncertainties about BPA. On the regulatory front, FDA's regulations authorize FDA to amend its food additive regulations to reflect when certain uses of an additive have been abandoned. FDA can take this action on its own initiative or in response to a food additive petition that demonstrates that a use of a food additive has been permanently and completely abandoned. Recently, FDA granted two petitions requesting that FDA amend its food additive regulations to no longer provide for the use of certain BPA-based materials in baby bottles, sippy cups, and infant formula packaging because these uses have been abandoned. As a result, FDA amended its food additive regulations to no longer provide for these uses of BPA.

Background

BPA is an industrial chemical used to make polycarbonate, a hard, clear plastic, which is used in many consumer products. BPA is also found in epoxy resins, which act as a protective lining on the inside of some metal-based food and beverage cans. Uses of all substances that migrate from packaging into food, including BPA, are subject to premarket approval by FDA as indirect food additives or food contact substances. FDA can make regulatory changes based on new safety or usage information. The original approvals for BPA were issued under FDA's food additive regulations and date from the 1960s. In 2008 FDA released a document titled *Draft Assessment of Bisphenol A for Use in Food Contact Applications*. This draft assessment was reviewed by a Subcommittee of FDA's Science Board, which released its report at the end of October 2008. Also in 2008, the National Toxicology Program Center for the Evaluation of Risks to Human Reproduction, part of the National Institutes of Health, released the *Monograph on the Potential Human Reproductive and Developmental Effects of Bisphenol A*.

By 2009, FDA released reassessments of studies cited in the NTP *Monograph* in addition to other relevant studies that became available after the Monograph's release.The studies were evaluated for their relevance for regulatory hazard and/or risk assessment. In addition to the FDA review process, FDA's Acting Chief Scientist asked five expert scientists from across the federal government to provide independent scientific review of these documents in the fall of 2009. The results of the independent evaluations were released in April 2010, as FDA made the CFSAN report and other relevant information available for public comment. Although the reassessments indicated a need to further evaluate a number of endpoints or biological outcomes, the analyses did not recommend any adjustments to BPA levels reported in food at that time.

Since that time, the FDA has continued to review additional studies as they became available, including those addressing possible low-dose effects.
In the fall of 2014, FDA experts from across the agency, specializing in toxicology, analytical chemistry, endocrinology, epidemiology, and other fields, completed a four-year review of more than 300 scientific studies. The FDA review has not found any information in the evaluated studies to prompt a revision of FDA's safety assessment of BPA in food packaging at this time.
The studies reviewed were published or available from November 1, 2009 to July 23, 2013. The review was documented in four memoranda and their attachments:

- *"Final report for the review of literature and data on BPA" – 6/6/2014*
- *"2014 Updated Review of Literature and Data on Bisphenol A" - 6/6/2014*
- *"2012 Updated Review of Literature and Data on Bisphenol A" - 8/22/2013*
- *"Updated Review of the 'Low-Dose' Literature (Data) on Bisphenol A and Response to Charge Questions Regarding the Risk Assessment on Bisphenol" - 5/24/2011*

J.Am Dent Assoc. 2016.

Changes in Urinary bisphenol A concentrations associated with placement of dental composite restorations in children and adolescents

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Changes in urinary bisphenol A concentrations associated with placement of dental composite restorations in children and adolescents.

Maserejian NN, Trachtenberg FL, Wheaton OB, Calafat AM, Ranganathan G, Kim HY, Hauser R.

Abstract

BACKGROUND:

Bisphenol A-glycidyl methacrylate (bis-GMA)-based dental composite restorations may release bisphenol A (BPA). The authors assessed changes in urinary BPA concentrations over a 6-month follow-up period in children and adolescents who received bis-GMA-based restorations.

METHODS:

The authors collected data from 91 study participants aged 3 to 17 years who needed composite restorations. Participants provided urine samples and information on BPA-related exposures before and at approximately 1 day, 14 days, and 6 months after treatment. The authors used multivariable linear regression models to test associations between the number of surface restorations placed and the changes in urinary BPA concentrations.

RESULTS:

Participants had a mean (standard deviation [SD]) of 1.4 (1.0) for surfaces restored with composite at the first treatment visit and 2.3 (1.6) for surfaces restored during the entire study period. Mean (SD) change in urinary BPA concentrations between pretreatment and day 1 was 1.71 (9.94) nanograms per milliliter overall and 0.87 (5.98) after excluding 1 participant who had 8 surfaces restored at the visit. Overall, the authors observed an association between a greater number of composite surface restorations placed and higher urinary BPAconcentrations in the 1-day sample (posterior-occlusal exponentiated coefficients [e(β)] = 1.47; 95% confidence interval [CI], 1.18-1.83; $P < .001$), but the association was attenuated after the authors restricted the sample to the 88 participants who had up to 4 restorations (e(β) = 1.19; 95% CI, 0.86-1.64), and they did not observe any association using 14-day (e(β) = 0.94; 95% CI, 0.75-1.18) or 6-month (e(β) = 0.88; 95% CI, 0.74-1.04) samples.

CONCLUSIONS:

Placement of bis-GMA-based restorations in children and adolescents may produce transient increases in urinary BPAconcentrations that are no longer detectable in urine samples taken approximately 14 days or 6 months after treatment. After placement of a few restorations, increases in urinary BPA concentrations may not be detectable, owing to a high level of variation in background BPAexposure.

PRACTICAL IMPLICATIONS:

These results suggest that leaching of BPA from newly placed composite restorations ceases to be detectable in urine within 2 weeks after restoration placement. The potential human health impact of such short-term exposure remains uncertain.

The Open Dentistry Journal 2016.

Bisphenol A Release: Survey of the Composition of Dental Composite Resins

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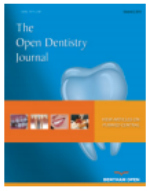

CASE REPORT

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Received: April 6, 2016 Revised: June 15, 2016 Accepted: July 27, 2016

Abstract:

Background:

Bisphenol A (BPA) is an endocrine disruptor with potential toxicity. Composite resins may not contain pure BPA, but its derivatives are widely used. Several studies found doses of BPA or its derivatives in saliva or urine of patients after composite resin placement.

Objective:

The aims of this study were to establish an exhaustive list of composite resins marketed in Europe and their composition, and to assess the extent of BPA derivatives used.

Methods:

A research on manufacturers' websites was performed to reference all composite resins marketed in Europe, then their composition was determined from both material safety data sheets and a standardized questionnaire sent to manufacturers. Manufacturers had to indicate whether their product contained the monomers listed, add other monomers if necessary, or indicate "not disclosed".

Results:

160 composite resins were identified from 31 manufacturers and 23 manufacturers (74.2%) responded to the survey. From the survey and websites, the composition of 130 composite resins (81.2%) was: 112 (86.2%) based on BPA derivatives, 97 (74.7%) on bis-GMA, 17 (13.1%) without monomer derived from BPA (UDMA, sometimes with TEGDMA) and 6 (4.6%) with UDMA (only); 1 (0.8%) did not contain a BPA derivative or UDMA or TEGDMA. Pure BPA was never reported.

Conclusion:

This work has established a list of 18 composite resins that contain no BPA derivative. Manufacturers should be required to report the exact composition of their products as it often remains unclear or incomplete.

Keywords: Biocompatibility, Bisphenol A, Composite resin, Monomer.

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INTRODUCTION

Bisphenol A (BPA) is an organic compound used in the industrial production of polycarbonates and epoxy resins [1]. However, BPA is an endocrine disruptor, with potential toxicity *in vitro* [2] and *in vivo* [3]. Among other effects, it can cause changes in the structure of the unborn child's mammary glands - promoting further tumor development - and has effects on the brain and behavior, the female reproductive system, and metabolism and obesity [4]. Infants, young children and pregnant or lactating women are the most sensitive [5]. Thus, the manufacturing of baby bottles containing BPA has been banned by the European Union since 2011. From January 1, 2015, France has banned BPA in all food packaging. In its latest comprehensive re-evaluation of BPA exposure and toxicity, the European Food Safety Authorities has concluded no risks at actual exposure levels [6]. However, a lower Tolerable Daily Intake (TDI) has been set at 4µg/kg bw/day (ie 12.5 times less than the last TDI). Besides, its possible "low-dose effect" [7 - 9], defined as "any biological changes occurring in the range of typical human exposures, or biological changes that occur at doses below those used in traditional toxicology studies" was suspected.

Pure BPA is not a component of dental composite resins. However, derivatives of BPA - from pure BPA - are widely used: bisphenol A diglycidyl methacrylate (bis-GMA) especially, but also bisphenol A dimethacrylate (bis-DMA), polycarbonate-modified bis-GMA (PC bis-GMA), ethoxylated bisphenol A glycol dimethacrylate (bis-EMA) and 2,2-bis[(4-methacryloxy polyethoxy)phenyl]propane (bis-MPEPP).

Several studies have investigated the levels of BPA and its derivatives in the saliva or urine after polymerization of a restoration made of a composite resin containing at least one of these monomers. The results vary: some studies *in vitro* [10] and *in vivo* [11] have detected some levels (in very low doses) and others do not detect any [12]. This BPA elution would result from impurities in the synthesis of resins or their degradation [13]. These variations can be explained by the different susceptibility of BPA derivatives to hydrolysis by salivary esterases. Bis-GMA does not undergo this reaction, because its chemical structure with stable ether bonds prevents hydrolysis. However, bis-DMA hydrolyzes at its ester bonds, releasing an amount of BPA that is not negligible. These differences could also be related to the detection technique [14]. Furthermore, a recent study showed absorption of BPA by the sublingual area in dogs, allowing its direct entry into the bloodstream, by passing the digestive system and liver and multiplying its bioavailability by a factor of 80 [15].

Yet, the exact composition of the composite resins on the market and the potential composite resins without BPA derivatives are not known. No study has sought to identify all monomers contained in the marketed composite resins.

The objectives of this study were first, to provide an exhaustive list of the composite resins sold in Europe and detail their composition and second, to estimate the number of composite resins using BPA or BPA derivatives (bis-GMA, bis-DMA, bis-EMA, bis-MPEPP, PC bis-GMA) in their manufacturing.

MATERIALS AND METHODOLOGY

To reference all composite resins sold in Europe, a search was conducted of the manufacturers' websites. Next, the composition of the composite resins was searched on the materials' safety data sheet (MSDS) and using a standardized questionnaire sent to manufacturers. This questionnaire listed 13 monomers found in the MSDS and in the various studies of these materials; the manufacturer had to indicate, for each product, if the material contained these monomers or not, or else write "not disclosed" (ND). The manufacturer could also add monomers to the proposed list (Table **1**). Manufacturers were contacted by email and/or telephone and the details were transmitted by email; they had 4 months to answer and an extra 2 months after a reminder email. When the manufacturer had not answered or the information was not available (MSDS, internet), the result was noted as "ND". All results were recorded and analyzed by using Microsoft Excel 2008, v12.3.6.

Table 1. List of the surveyed monomers (found in materials' safety data sheet and various studies of these resin composites and proposed to manufacturers) that resin composites can contain.

Monomer (abbreviation)	Monomer (detailed chemical name)
Bisphenol A	2,2-bis(4-hydroxyphényl)propane
Bis-GMA	2,2-bis[4-(3-methacryloxy-2-hydroxypropoxy)phenyl]propane
PC Bis-GMA	Polycarbonate-modified bis-GMA
Bis-DMA	2,2-bis-(4-(méthacryloxy) phenyl) propane
Bis-EMA or EBPADMA	Ethoxylated bisphenol-A glycol dimethacrylate

(Table 1) contd.....

Monomer (abbreviation)	Monomer (detailed chemical name)
Bis-MPEPP or BPEDMA	Bisphenol A polyethoxy dimethacrylate or 2,2-bis(4-methacryloxy poly-ethoxyphenyl)propane
UDMA	Urethane dimethacrylate or 1,6-di(methacryloyloxyethylcarbamoyl)-3,3,5-trimethylhexan
TEGDMA	Triethylene glycol dimethacrylate
HEMA	Hydroxyethyl methacrylate
HEDMA	Hexane diol dimethacrylate or 2-hydroxyethyl dimethacrylate
TMPTMA	Trimethylolpropane trimethacrylate
4-MET	4-methacryloxyethyl trimellitic acid
IBMA	Isobutyl methacrylate

RESULTS

A total of 160 composite resins were identified from 31 companies (Table **2**); 23 companies (74.2%) responded to the survey, with complete responses for 119/135 composite resins they marketed (88%). For the 8 manufacturers who did not respond (25.8%), the search of the internet and especially the MSDS provided responses for 11 of the 25 composite resins marketed (44%).

Table 2. List of the 160 composite resins marketed in Europe by 31 manufacturers and type of response (R) from the manufacturer (1: response; 2: partial response; 0: no response).

Fabricant	R	Composite Resins
3M ESPE	1	Filtek Bulk Fill Fluide, Filtek P60, Filtek Silorane, Filtek Supreme XTE, Filtek Supreme XTE fluide, Filtek Z250, Filtek Z500, Z100 MP
Alpha Dent	0	Alpha II AP, Alpha Flow, Alpha-Dent Light Cure, Alpha-Dent Self Cure
Apol	1	Ivoa, Ivoa flow, Xtrem nano, Sharkcomp, Sharkflow
Bisco	1	Aelite Aesthetic Enamel, Aelite All Purpose Body, Aelite LS Posterior, Aelite LS Packable, Aelite Flo, Aelite Flo LV
Cavex	1	Quadrant Anterior Shine, Quadrant Universal LC, Quadrant Flow
Centrix	1	C-R Hybrid, VersaFlo, VersaLite
Coltene Whaledent	1	Miris 2, Synergy D6, Synergy D6 Flow, Synergy Nano formula Duo Shades
Cosmedent	0	Renamel Flowable Microhybrid, Renamel Flowable Microfill, Renamel Microfill (+ superBrite), Renamel Posterior, Renamel Microhybrid (+ SuperBrite), Renamel Nano
DenMat	2	Virtuoso Flowable, Virtuoso Universal, Nuance, Nuance Flow
Dentoria	0	Flexfil
Dentsply	2	Ceram.X Duo, Ceram.X Mono +, Esthet.X HD, Esthet.X Flow, Quixfil TM, Spectrum TPH3, SDR, Surefill
Elsodent	1	Cirus, Must Flow
GC	1	EverX posterior, G-Aenial Anterior, G-Aenial posterior, G-Aenial Flow, G-Aenial Universal Flo, Kalore, Gradia Direct (X), Gradia Direct Flo, Gradia Direct LoFlo
Henry Schein	0	Natural Elegance, 20/20, Natural Elegance Flowable
Heraeus Kulzer	1	Charisma, Charisma Classic, Durafill VS, Charisma Flow, Solitaire 2, Venus, Venus Diamond, Venus Pearl, Venus Diamond flow, Venus Bulk Fill, Venus Flow
Itena	1	Reflectys, Reflectys Flow, Perfect Feel Flow
Ivoclar Vivadent	1	IPS Empress Direct, IPS Empress Direct Flow, Tetric, Tetric Ceram HB, Tetric EvoCeram, Tetric EvoCeram Bulk Fill, Tetric EvoFlow
Jeneric Pentron	1	Alert, Artiste, Flow-It ALC, Fusio Self-adhesive, Simile
Kent Dental	0	Kentfil Anterior, Kentflow, Kentfil Posterior, Microhybrid + Kent, Nanohybrid Kent Dental
Kerr Hawe	2	Herculite XRV Ultra, Herculite XRV, Point 4, Premise, Premise Flowable, Revolution 2, SonicFill, Vertise Flow (autoadhésif)
Kuraray	1	Clearfil AP-X, Clearfil Majesty ES-2, Clearfil Majesty Esthetic, Clearfil Majesty Flow, Clearfil Majesty ES Flow, Clearfil Majesty Posterior, Clearfil Photo Bright, Clearfil Photo Posterior, Clearfil Posterior 3, Clearfil F II
Micerium	1	Enamel Plus HFO, Enamel Plus HFO Flow, Enamel Plus HRi, Enamel Plus HRi Flow
Pulpdent	0	Flows-Rite
R&S	0	Nanofil, Suprafil
Saremco	1	Saremco microhybrid composite, els (extra low shrinkage)
Shofu	0	Beautifil II, Beautifil Flow, Beautifil Flow Plus
Southern Dental Industries (SDI)	2	Glacier, Ice, Rok, Wave (3 viscosities)
Sun Medical	1	Fantasista, Metafil CX, Metafil Flo
Tokuyama	1	Estelite Sigma Quick, Estelite Posterior, Estelite Asteria, Estelite Color, Estelite Flow Quick, Estelite Flow Quick High Flow, Palfique Estelite LV

(Table 2) contd.....

Fabricant	R	Composite Resins
Ultradent	1	Amelogen Plus, Permaflo, Permaflo DC
Voco	2	Admira, Admira Flow, Alfacomp LC, Amaris, Amaris Flow, Arabesk Flow, Arabesk, Arabesk Top, Grandio, Grandio Flow, Grandio SO, Grandio SO Flow, Grandio SO Heavy Flow, X-tra Base, X-tra fil

In total, 12 monomers were found in these 130 (119+11) composite resins; pure BPA was never reported. Table **3** reports their frequency of use.

Table 3. List of the 12 monomers contained in the surveyed composite resins (CR) and their frequency of use (among the 130 CR whose composition was established).

Monomers	Number of CR (%)
Bis-GMA	97 (74,6)
TEGDMA	79 (60, 8)
UDMA	68 (52,3)
Bis-EMA ou EBPADMA	28 (21,5)
Bis-MPEPP ou BPEDMA	10 (7,7)
HEDMA	4 (3,1)
PC Bis-GMA	3 (2,3)
TPPTMA	3 (2,3)
HEMA	2 (1,5)
Bis-DMA	1 (0,8)
4-MET	1 (0,8)
IBMA	1 (0,8)

Table 4. List of the composite resins that contain no bis-GMA, no BPA-derivative (with UDMA), or neither BPA-derivative nor UDMA.

Composite resins	Manufacturers			
Aelite Flo	Bisco	Without bis-GMA		
Aelite Flo LV	Bisco			
Alert*	Jeneric Pentron			
Quixfil TM	Dentsply			
SDR	Dentsply			
Venus Bulk Fill	Heraeus Kulzer			
Venus Diamond flow	Heraeus Kulzer			
Estelite Flow Quick	Tokuyama			
G-Aenial Anterior	GC			
G-Aenial Flow	GC			
G-Aenial posterior	GC			
G-Aenial Universal Flo	GC			
Kalore	GC			
Aelite LS Packable	Bisco		Without bis-GMA or BPA-derivative: resin composite with UDMA * with also TEGDMA	
Clearfil Majesty ES Flow*	Kuraray			
Clearfil Majesty Flow*	Kuraray			
Fantasista*	Sun Medical			
Fusio*	Jeneric Pentron			
Gradia Direct (X)	GC			
Gradia Direct Flo*	GC			
Gradia Direct LoFlo*	GC			
Metafil CX*	Sun Medical			
Perfect Feel	Itena			
Perfect Feel Flow*	Itena			
Renamel Microfill (+ superBrite)	Cosmedent			
Tetric*	Ivoclar Vivadent			
Venus Diamond	Heraeus Kulzer			
Venus Pearl	Heraeus Kulzer			
Wave (3 viscosités)	Southern Dental			
Xtrem nano	Apol			
Filtek Silorane	3M			Without BPA-derivative or UDMA

Among the 130 composite resins: 112 (86.2%) contained BPA derivatives, 97 (74.7%) bis-GMA and 43 (33.1%) bis-GMA and urethane dimethacrylate (UDMA); 17 (13.1%) contained no monomer derived from BPA (UDMA, sometimes with TEGDMA) and 6 (4,6%) with UDMA (only); 1 (0.8%) did not contain a BPA derivative or UDMA or TEGDMA (Table **4**). 18 (13.8%) composite resins without any BPA derivative were identified. Among the 33 composite resins (25.4%) that did not contain bis-GMA, 24 (18.5%) did not contain bis-EMA and 18 (13.8%) did not contain bis-MPEPP. A single composite resin contained bis-DMA.

DISCUSSION

The adverse estrogenic effects of BPA are well established, which explains the new regulations banning this molecule, especially in food containers [4]. The elution of BPA sometimes detected after the making of a composite resin restoration remains far below toxic levels and at a certain time after placement, unpolymerized monomers would be completely absorbed into saliva, posing little risk of chronic low-dose BPA exposure, so some authors still encourage the use of molecules made from BPA [14, 16].

However, two factors seem to follow the recommendations against BPA content in composite resins. The first is related to the 2008 results of Bellinger *et al*. [17], who demonstrated that in children 6 to 10 years' old, the presence of composite resins was associated with a psychosocial behavior that was worse than with amalgams. These results were confirmed and clarified by Maserejian *et al*. in 2012 [18], who indicated that the psychosocial behavior was worse for children with bis-GMA than UDMA composite resin restorations. Fortunately, the last studies of this team are more reassuring concerning sealants and fluid composite resin [19] and concerning the renal function of the children [20] or their immunity markers [21]. Recently, Maserejian *et al*. [22] in 2016 showed that placement of bis-GMA-based restorations in children and adolescents may temporarily increase BPA concentration in urine, but no longer detectable 14 days or 6 months after treatment. Second, BPA may have greater effects at low than high doses. Wozniack *et al*. [23] registered effects at doses of 1 pmol. The American National Toxicology Program [24] states that these low-dose effects can occur from 0.23 mg/L. This theory remains controversial [25]. However, the European Food Safety Authority decided last year recently to divide by 10 the maximum daily dose allowed (or 5 mg/kg/day).

Moreover, exposure to BPA during gestation could induce increased spontaneous abortion, abnormal gestation time, reduced birth weight, increased male genital abnormalities, childhood obesity, but also altered behavior, disrupted neurodevelopment in children and increased asthma risk [26]. Because of these potential adverse developmental effects after prenatal exposure to BPA, it would be cautious to limit exposure to unpolymerized dental resin materials during pregnancy. Thus, it could be relevant to select composite resins that do not contain these derivatives for at-risk populations, such pregnant women [27] and as children [28].

Moreover, patients may ask about the possible bis-GMA content of composite resins. Whatever the opinion of the practitioner, he or she must know the composition of the composite resins used. In this study, 160 composite resins currently marketed by 31 manufacturers in Europe were identified. The composition of 130 (marketed by 23 manufacturers) was established: 112 (86.2%) contain BPA derivatives. Although we had a good response rate (74.2%), we could not obtain the composition of all the products because of strategic reasons, lack of reliable representatives or trade secrets.

In total, 25.8% of the manufacturers did not agree to communicate the composition of their composite resins. They are not required to indicate the exact composition of the materials, which should be required as for drugs. MSDS forms indicate the product's composition only partially, often mentioning only the family of the molecules.

However, we should be cautioned against choosing one of the 18 composite resins without BPA derivatives: the latter contain other monomers that are not necessarily more biocompatible. Indeed, BPA is not the only potentially toxic monomer in composite resins; others may be toxic [29]. In particular, the structure of TEGDMA and HEMA can be degraded by salivary esterases and result in liposoluble metabolites that could accumulate in fatty tissues [30]. Even UDMA, deemed less risky, may present some cytotoxicity beyond a certain concentration [31]. Whatever the composite resin, a certain rate of unpolymerized monomers is released, which is associated with their characteristics, the degree of polymerization and the release medium [32].

Indirect and CAD-CAM composite restorations maximize the conversion rate and thus minimize the release. Certain procedures reduce exposure to free monomers due to direct composite restorations: rubber dam use, prolonged curing (up to double the recommended time) or a second curing step after covering the restoration with glycerin. In addition, these free monomers are mostly present on the surface of the material, where the exposure to oxygen inhibits

polymerization. Hence, Rueggeberg *et al*. [33] and Komurcuoglu *et al*. [34] showed that brushing the restoration's surface with pumice allowed for removal of the inhibition layer and eliminated more than 90% of the residual monomers. Applying a dry or wet cotton roll and, to a lesser extent, water/air spray also enables their withdrawal up to 70%. Sasaki *et al*. [35] showed that gargling with warm water for 30 sec after placement of the composite resin may reduce salivary levels of BPA.

Finally, using alternative materials without resin would be ideal; some high-viscosity glass ionomers or inorganic biomaterials, carbomers (albeit with lower mechanical and aesthetic properties) or ceramic (for extended restorations) may be considered.

CONCLUSION

This study has established a list of 18 BPA derivative-free products that can be used on a daily basis by the general practitioner. The respective long-term effects on human health of the different monomers remain unclear and deserve to be the subject of cohort studies.

Manufacturers should be required to report the exact composition of their products, as is required in the pharmaceutical industry, so that practitioners are able to communicate it to patients and to meet the traceability requirements.

CONFLICT OF INTEREST

The authors confirm that this article content has no conflict of interest.

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