

Minamata Convention  
Conference of Parties 4 Statement  
American Dental Association and International Association for Dental Research  
April 2020

The American Dental Association (“ADA”) and the International Association for Dental Research (“IADR”) support the Minamata Convention and, specifically, the current “phase down” approach to dental amalgam. By working together to promote dental disease prevention efforts, the world community can improve public health and thereby decrease the demand for dental amalgam. By working together to promote research into fully effective alternatives to dental amalgam, the world community can assist in efforts to reduce reliance on mercury while still protecting the health of the public. In other words, the current approach to dental amalgam memorialized in the Minamata Convention offers the best chance to protect both the environment and the public. The ADA and IADR oppose the current effort to review or to re-open the negotiations on this topic because such efforts will only divert resources from meaningful action.

For more than 150 years, dental amalgam has served as a safe, durable and affordable material in restoring decayed teeth.<sup>1</sup> Dental amalgam, according to ANSI/ADA Standard No. 1, is an alloy that may include the elements of silver, tin, copper, zinc, indium, mercury and the noble metals (gold, platinum and palladium),<sup>2</sup> though the major components of the alloy are copper, silver, and tin.<sup>4, 8, 11</sup> Amalgamation refers to the mix of the amalgam alloy with liquid mercury (approximately 42 to 50% by weight), resulting in a highly malleable, formable material that subsequently hardens following mixing and compacting into the prepared cavity.<sup>4</sup> The ANSI/ADA standard specifies only the use of capsulated alloy and mercury, which is a prepackaged way of dosing, available in various sizes in order to minimize waste, which is then mixed by an amalgamator (i.e., a mechanical mixer), to minimize mercury vapor leakage.<sup>2</sup>

Amalgam fillings have a higher survivability rate and longevity than the primary alternative material currently available, resin composite restorations.<sup>3-7</sup> While there is no single source for comprehensive data on amalgam use in the United States, evidence demonstrates it is declining.<sup>8-10</sup> (See generally Appendix 1)

The most comprehensive and recent United States data, representing approximately 20 million fillings per year, demonstrates a significant decline in dental amalgam over the past 13 years. (Figure 1)

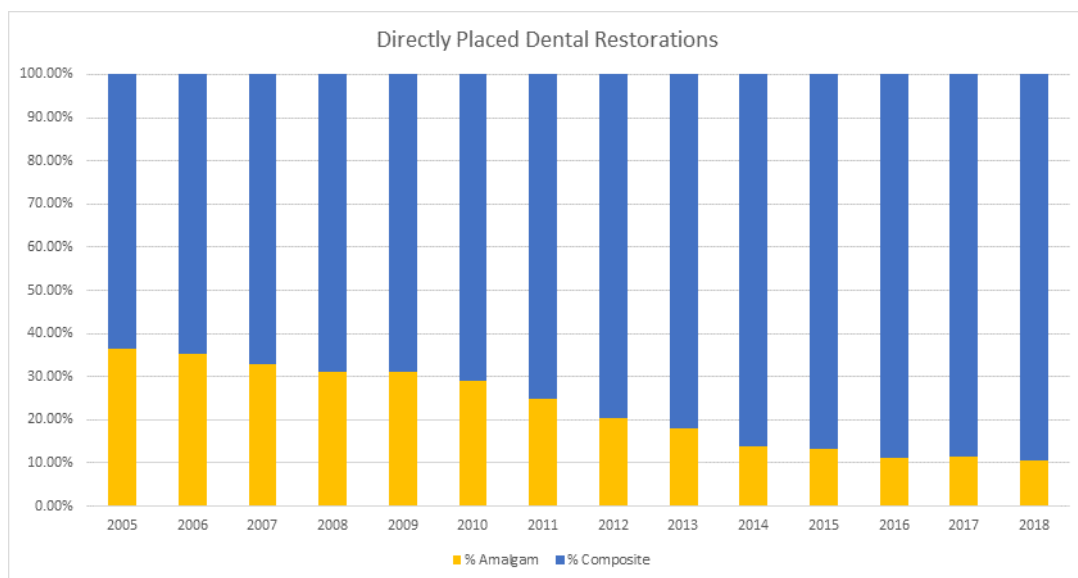


Figure 1: Chart is reprinted, with permission, from the submitted claims database of the Delta Dental Plans Association. This database contains all submitted dental procedures from all of the 39 Delta Dental member companies with employer-based and individual dental plans in all U.S. states and territories. The chart is based upon approximately 300 million total dental restorations placed over 14 years.

This decline has been attributed to aesthetic concerns, as composite resin fillings are deemed more attractive. Although these resin fillings do not yet equal amalgam in durability, cost and ease of placement, these alternative filling materials are improving and this, too, is aiding in the shift from amalgam use. Although amalgam remains a safe, effective, and inexpensive restorative option, general environmental concerns relating to mercury itself led to the adoption of the Minamata convention in 2013, with one of its many goals being the phasing down the use dental amalgam. This phase down is supported by the ADA and IADR.

A true concern for public health focuses efforts on prevention of dental disease and on a safe, effective manner in which to treat the largest amount of non-prevented disease that the available economic resources will allow. Such resources are in short supply on all fronts, from governments, providers and the individual patients. Expenditures toward prevention is cost saving, as no decay means no need for restorations of any kind, including dental amalgam, and should be at the policy forefront.

The worldwide dental community continues to stress the need for preventive measures as more effective and less expensive than surgical intervention in dealing with oral disease. Community water fluoridation, dental sealants, education about basic preventive behaviors and financial incentives encouraging better health practices (e.g. reduced levies on oral hygiene products) will all dramatically improve health because they will collectively work to stop disease before it starts. All of these efforts are in place at some point across the world, although as with all societal changes it will take time to evidence change, as noted most recently at the 2019 Capacity Building Workshop to Accelerate Implementation of the Regional Oral Health Strategy convened by the WHO Regional Office for Africa.<sup>12</sup>

Beyond prevention, the need for repairing diseased teeth still occurs. Dental amalgam fillings are stronger, more durable and less expensive than composite resin fillings. When the convention was negotiated, there was no true and full substitute for dental amalgam with the same features. This has not changed. To promote development of amalgam-equivalent alternatives, resources are better expended on research into acceptable alternatives to amalgam. But time is needed for this work as well. At just two years since the convention came into force (defined as the time of the fiftieth signatory, which was 2017), revisiting the issue of dental amalgam is both premature and counterproductive. The process itself will consume resources better devoted to ongoing prevention and research efforts.

IADR is a non-profit professional association representing over 10,000 members with a mission to advance research and increase knowledge for the improvement of oral health worldwide. In support of this mission, IADR notes that amalgam is the most studied restorative material in use. Further, as one of the Minamata conditions for review of dental amalgam is "The availability to the Parties of mercury-free alternatives that are technically and economically feasible, taking into account the environmental and human health risks and benefits" it is imperative to assess if such alternatives do exist.

The most popular alternative to dental amalgam is composite resin. While offering the advantage of being tooth-colored and thereby more aesthetically pleasing than dental amalgam, composite resin also has significant disadvantages. In addition to the material itself being more expensive, composite resin also requires the provider to maintain a completely dry tooth in a wet environment, uses sophisticated equipment for placement, and adequate refrigeration and electricity to store and cure the material, all or any of which may not be reliable or even accessible in low-resource settings. The most significant disadvantage, however, is that composite resin restorations are less durable than those made from dental amalgam. Composite resin restorations in permanent posterior teeth are twice as likely to fail and carry a higher risk of secondary tooth decay compared to amalgam restorations.<sup>13</sup>

Researchers are addressing deficiencies of alternatives to dental amalgam in a variety of innovative and exciting ways but require continued investments in research to accelerate development of these products, move them from the lab to the market, and to increase their affordability. Related to the phase-down of dental amalgam, while much progress has been made with alternative restorative materials, they are not practical for all clinical situations or in settings that lack a reliable source of electricity or other necessary equipment. Thus, it is important to preserve the availability of dental amalgam as a restorative option until investments in research can deliver an alternative restorative material that addresses these current shortcomings. <sup>14</sup>(See generally Appendix 2)

Dental amalgam is the most affordable treatment option in many cases both in terms of cost of placement and how long it lasts. The 2018 health technology assessment conducted by the Canadian Agency for Drugs and Technologies in Health built on the findings in the Cochrane Review and included an analysis of the comparative safety of dental restorations made of composite resin versus amalgam in children and adults. It concluded that the best available evidence indicates that “amalgam restorations appear to be more clinically efficacious and as safe, while also costing less.”<sup>14</sup> The added cost of alternate treatments, along with need for more frequent replacement, would deter some from getting needed care. In some parts of the world, dental care is provided through national governments and national budgets simply cannot absorb the added costs of alternate treatment materials. Delayed or avoided care due to economic factors is of major concern.

The Convention is an environmentally focused instrument. Nevertheless, certain advocates continue to argue that amalgam use poses a health risk to patients. The evidence does not support this. The evidence did not support it in 2017, or during the negotiations leading up to the final instrument and no new evidence exists to change the clear scientific consensus on amalgam safety. In short, there is no justification to revisit this issue now, so soon after the date on which the convention went into force.

Just two years into the life of the Convention is too soon to assess the effects of the actions to which the signatories are obligated by the Annex A. The Minamata Convention provides for review “no later than five years after entry into force,” or, 2022. (Article 31 defines entry into force as happening “on the ninetieth day after the date of deposit of the fiftieth instrument of ratification, acceptance, approval or accession.”) The terms of any such review support this conclusion. As outlined in Article 4, par. 9C, during any scheduled review, the Conference of Parties shall take into account “[t]he availability to the Parties of mercury-free alternatives that are technically and economically feasible, taking into account the environmental and human health risks and benefits.” While research continues, after only two years into the cycle, no “technically and economically feasible” alternative material has been developed. As noted above, the “human health risks and benefits” also weigh in favor of not prematurely entering into a review. When the appropriate time does come, the ADA, IADR and FDI wish to assure the COP that it remains committed to fully cooperating in a thorough review.

ADA and IADR encourage all nations to devote resources to both prevention and research as the best ways to protect the health of the public, to reduce the need for any restorative work and to reduce the demand for dental amalgam.

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## Appendix 1

Safety of Amalgam  
American Dental Association  
Science Institute  
March 28, 2019

### INTRODUCTION

For more than 150 years, dental amalgam has served as a safe, durable and affordable material in restorative dentistry.<sup>1</sup> Dental amalgam is a mixture of metals: liquid (elemental) mercury and a powdered alloy mostly composed of silver, tin, and copper.

The best scientific evidence suggests that amalgam fillings have a higher survivability rate and longevity than resin composite restorations.<sup>2-6</sup> This document reviews the status of scientific research related to the value and safety of amalgam.

### MATERIAL AND COMPOSITION

To better understand the benefits and safety profile of dental amalgam it is important to understand its composition and specifications. *Amalgam* is any alloy that contains mercury. Mercury appears in elemental, inorganic, and organic forms; the organic form is the primary health concern, as this form is the type commonly found in fish, as methyl mercury (MeHg).<sup>3,7,8</sup> Elemental, or metallic, mercury (Hg<sup>0</sup>) is liquid at room temperature and is the form used in dental amalgam.

Dental amalgam, according to ANSI/ADA Standard No. 1, is an alloy that may include the elements of silver, tin, copper, zinc, indium, mercury and the noble metals (gold, platinum and palladium),<sup>9</sup> though the major components of the alloy are copper, silver, and tin.<sup>3,10,11</sup> Amalgamation refers to the mix of the amalgam alloy with liquid mercury (approximately 42 to 50% by weight), resulting in a highly plastic, formable material that hardens once mixed.<sup>3</sup> The ANSI/ADA standard specifies only the use of capsulated alloy and mercury. Capsulated alloy and mercury comes in various sizes to meet specific clinical needs, minimizes mercury vapor leakage, and amount of waste from any procedure.<sup>9</sup>

ANSI/ADA Standard No. 1 (ISO 1559) covers the specifications for the composition and physical properties requirements for capsulated dental amalgam.<sup>9</sup> The requirements for physical properties of dental amalgam are shown in Table 1, below.

**Table 1. ADA/ANSI Standard No. 1 Physical Properties of Dental Amalgam.<sup>9</sup>**

Creep (%)	Dimensional Change (%)	Compressive Strength (MPa)	
		Min. after 1 hr.	Min. after 24 hrs.
Maximum	Range		
1.0	-0.15 to 0.20	80	300

### BIOCOMPATIBILITY AND TOXICITY

A number of studies have attempted to link dental amalgam to adverse health effects, but literature reviews by national and international public health agencies and organizations continue to concur that amalgam is a safe, affordable restoration material. A 2015 review by the Scientific Committees of the European Commission on the safety of dental amalgam concluded that, while “*reduction in the use of mercury in human activity would be beneficial...no increased risks on adverse systemic effects have been documented in the general population as a whole and it is considered that the current use of dental amalgam does not pose any risk of systemic disease.*”<sup>12</sup> A 2017 systematic review of the potential effect on autoimmunity from various forms of mercury found “*no evidence to implicate a role for Hg<sup>0</sup> [elemental mercury] exposure from dental amalgams in the development or perpetuation of autoimmune disease, apart from some suggestion of individual sensitivity.*”<sup>13</sup>

A recent health technology assessment (HTA) report published by the Canadian regulatory authorities focuses on evaluating the effectiveness and safety of dental amalgam to help decision-makers determine if the dental material should continue to be used in Canada. The report looked into the efficacy of direct dental restorations using amalgam versus composite resins in permanent posterior teeth, as well as, compared the safety of the two dental materials in children and adults. This comprehensive systematic review concluded that both materials are clinically efficacious and safe, while highlighting the low cost of dental amalgam. The authors also stated that the decision of which material should be used needs to be made jointly with the patients to weigh in the desired outcomes of the treatment and cost. Meanwhile, the research community should work on developing cost effective, effective and safe materials that can be used by all patients.<sup>14</sup>

#### Defining Exposure Levels:

Although the World Health Organization has estimated that 2 µg/kg body weight per day as the tolerable intake of total mercury per day,<sup>15</sup> the U.S. EPA uses a more stringent estimate of 0.1 µg/kg/day.<sup>16</sup> The EPA estimate translates to approximately 5.8 µg/day for a 130-pound person. In terms of levels of inhaled mercury vapor, U.S. EPA and the Agency for Toxic Substances and Disease Registry have established 0.2 µg/m<sup>3</sup> as the minimal risk level (MRL) <sup>17-19</sup>

#### Sources of Mercury Exposure:

Mercury appears in elemental, inorganic, and organic forms; the organic form is the primary health concern, as this form is the type commonly found in fish, as methylmercury (MeHg).<sup>3, 7, 8</sup> Elemental, or metallic, mercury (Hg<sup>0</sup>) is liquid at room temperature and is the form used in dental amalgam. Up to 0.2 µg/m<sup>3</sup> of mercury has been measured in the general air,<sup>17</sup> and the consumption of fish exposes the average person to about 3.5 µg/day (MeHg),<sup>3, 17</sup> while total contribution of food to mercury exposure per day may be as high as 20.0 µg.<sup>3</sup>

Amalgam fillings release mercury vapor equivalent about 0.2 to 0.4 µg/day for each amalgam-filled tooth surface.<sup>20, 21</sup> These values are below the EPA established reference dose of 0.1 µg/kg of body weight/day.

#### Dental Amalgam as a Source of Mercury Exposure

Overall, the data demonstrate that over time, mercury exposure in the US, has been on the decline and that exposure levels in the general population have been below levels of regulatory concern. A 2015 study <sup>22</sup> looked at occupational exposure of mercury among a convenience sample of dentists and found their levels to be similar to that of the US general population. A 2016 study used the two NHANES datasets that included complete dental health exams and found an association between number of dental restorations and levels of inorganic mercury and total mercury <sup>23</sup> though all were well below the EPA reference dose equivalent of 5.8 µg/L.<sup>16, 23</sup> Elemental mercury is poorly absorbed by the digestive system, and though trace levels of mercury vapor may be released by amalgam fillings, particularly during chewing. Studies consistently show that mercury leakage from fillings is within safe limits established by the EPA and other public health organizations. <sup>15, 16</sup>

#### Potential Adverse Effects

##### Allergies:

Minor topical allergic reaction to amalgam is the primary adverse event reported. Allergic reactions related to dental amalgam are experienced in less than 1% of the treated population, and usually consist of contact dermatitis, oral lichenoid lesions, gingivitis, and stomatitis; removal of the amalgam normally relieves these symptoms.<sup>3, 24, 25</sup> Amalgam is associated with burning mouth syndrome less frequently than for other dental materials <sup>25, 26</sup> Allergy to mercury is as common as allergies to any metal, although in vitro tests have demonstrated higher cytotoxicity levels in copper and zinc than mercury.<sup>11</sup>

##### Effects on the renal and central nervous systems:

Scientific studies do not support the association between amalgams and effects on the renal and central nervous systems even though both are particularly vulnerable to mercury toxicity.<sup>3, 27, 28</sup>

## ADDRESSING SAFETY THROUGH REGULATIONS AND POLICY

In 2009, with the support of the ADA, the FDA reclassified dental mercury from Class I to Class II, along with amalgam alloy. The 2009 reclassification included a literature review to determine the risks from mercury in dental amalgam and potential mitigation procedures. The review concluded that "there is insufficient evidence to support an association between exposure to mercury from dental amalgams and adverse health effects in humans, including sensitive subpopulations."<sup>8</sup>

In the United States, dentists use precapsulated amalgam formulations which reduce waste, mercury vapor leakage, and provides a more consistent mercury/alloy ratio.<sup>3, 9</sup> This is both consistent with ADA policy and EPA regulations.

First espoused in the ADA Best Management Practices, passage of the 2017 EPA amalgam separator rule now requires installation of International Organization for Standardization (ISO) compliant amalgam separators in dental offices in which amalgam is among the restoration materials used. These separators capture in excess of 95% of all mercury discharged in the office waste water stream.

## CONCLUSIONS

Clinical Value: Dental amalgam is a, durable and affordable material in restorative dentistry which has been safely used for more than 150 years.<sup>1</sup> Current evidence supports the conclusion that amalgam restorations are most likely to last longer than resin composite fillings<sup>2-6</sup>; though issues of esthetic and environmental factors are increasingly of concern to healthcare professionals and authorities.<sup>10, 29, 30</sup>

Safety: Because there is a consistent failure linking dental amalgam to adverse health effects, systematic literature reviews published by national and international public health agencies and organizations conclude that amalgam is a safe, effective and affordable restoration material.

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Appendix 2  
Update on Research into Dental Amalgam Alternatives  
International Association for Dental Research  
May 21, 2019

### **Challenges with current restorative materials**

The most popular alternative to dental amalgam is **composite resin**. While offering the advantage of being tooth-colored and thereby more aesthetically pleasing than dental amalgam, composite resin also has significant disadvantages. In addition to the material itself being more expensive, composite resin also requires maintaining a completely dry tooth in a wet environment, sophisticated equipment for placement, and refrigeration and electricity to store and cure the material, which may not be reliable or even accessible in some settings. The most significant disadvantage, however, is that composite resin restorations are less durable than those made from dental amalgam. Composite resin restorations in permanent posterior teeth are twice as likely to fail and carry a higher risk of **secondary tooth decay** compared to amalgam restorations.<sup>1, 2</sup> Secondary decay occurs after the restoration is placed. Decay at the tooth and composite bonding layer is the most common reason that restorations fail.

One major focus of research on alternative restorative materials is extending the life of the restoration. In 2013, the United States National Institutes of Health/National Institute of Dental and Craniofacial Research (NIDCR) funded six, five-year projects for a total over \$13 million through its “Design and Development of Novel Dental Composite Restorative Systems” Cooperative Agreement Program. The goal of this program was to double the durability of current composites by creating new composite restorative systems based on entirely new chemistries.

The following update on research on alternative restorative materials highlights key themes and strategies for addressing their shortfalls as well as the challenges that must be addressed with examples from ongoing projects. Several candidate materials developed by the six NIDCR-funded cooperative projects have demonstrated significant promise in meeting research milestones and are starting to transition out of academic research laboratories to industry laboratories via technology transfer agreements. Overall, it is reasonable to speculate that it takes approximately 10 years to translate this new research to human use and market entry.

These examples are provided without endorsement of one over another. This summary was compiled with input from researchers funded by the aforementioned cooperative agreement program; Dr. Rainer Guggenberger’s presentation, “Amalgam Replacement: The Manufacturer’s Perspective,” at the 97th IADR General Session & Exhibition in San Francisco, CA in 2017; and IADR members Drs. Gottfried Schmalz and Paulo Cesar for perspectives from European and Brazilian dental material scientists, respectively.

**The take-home message of this summary is that while this is an active and exciting area of research where significant progress has been made, in the short-term, alternatives to dental amalgam are still less than optimal based on clinical, economic or practical reasons. Therefore, it is important to ensure the access of dental amalgam as a restorative option until investments in research can deliver an alternative restorative material that addresses current shortcomings.**

### **Increased longevity**

Composite resins are made of a **resin plus filler** that reduces shrinkage of the restoration and can lend other desirable physical properties. A commonly used resin in composite restorations is called Bis-GMA (Bisphenol A-Glycidyl Methacrylate). One reason composites have a short lifetime is because the chemical bonds holding the Bis-GMA resin together, called esters, can be broken by water and enzymes in the oral cavity.

One strategy to solve this problem is to change the resin used in the composite from one held together by ester bonds to one held together by a different chemical bond called ether. Ethers are more stable and

durable against degradation caused by water and enzymes than their ester-based counterparts. For example, an ether-based resin called TEG-DVBE (triethylene glycol divinylbenzyl ether) has demonstrated no unfavorable interactions with water, which avoids degradation of the material and increases durability.<sup>3</sup>

Another research group developed a resin system called OASys (Oxirane-Acrylate IPN System). OASys is a mixture of an ester-based resin called acrylate and another molecule called oxirane. Even though acrylate is an ester-based molecule, it has a different chemistry than Bis-GMA resin. This gives the acrylate a **high degree of polymerization**, meaning that almost every monomer, or unit, of acrylate is linked to another monomer of acrylate, and there are few free monomers of acrylate left in the mixture. This high degree of polymerization means that the resin degrades more slowly. OASys also has half the wear rate – reduction of the material due to abrasive forces – than resin used in conventional composites.<sup>4</sup> Future directions of this resin system include mixing oxirane with modified acrylates that should reduce the affinity of the resin for water, giving it even more protection from water degradation and increasing its mechanical strength to resist fracture that may occur during chewing.

Yet another research group approached this problem by changing the composite filler instead of the resin. Rather than filling the resin with glass or ceramics, as is typically done, this research group filled the resin with a molecule called thiourethane. The resulting thiourethane-based composite is twice as fracture resistant as the standard material.<sup>5</sup>

### **Reduced shrinkage from polymerization**

As alluded to above, after the resin is placed in the tooth, the individual monomers of the resin have to be linked together through a process called polymerization, or **curing**. The curing step can cause the restoration to shrink and pull away from the tooth causing stress and even fragmentation of the tooth or gaps at the restoration/tooth margin.

OASys has two polymerization phases – a fast phase and a slow phase. Acrylate and oxirane polymerize independently, i.e., acrylate monomers only bond with other acrylate monomers and oxirane monomers only bond with other oxirane monomers. The acrylate polymerizes quickly, which will allow the restoration to harden quickly in the clinic while the oxirane polymerizes slowly. The slow polymerization phase of the oxirane reduces stress on the tooth from shrinkage.

OASys as well as the TEG-DVBE-based and thiourethane-based composite have all demonstrated reduced shrinkage stress up to 50% of the conventional composite resin.

### **Improved adhesive technology**

Composite restorations must be bonded to the tooth with an **adhesive** that creates a strong bond between the composite and the tooth. Enzymes can cause degradation of the bonding layer between the adhesive and underlying tooth structure and are often the cause of failure for composite restorations. Using the appropriate adhesive is critical to ensuring the durability of the restoration-tooth bonding layer. Choosing the correct adhesive, therefore, adds complexity and lengthens the time needed to place these dental restorations. Adhesive technology has improved and has been simplified to a single bottle of adhesive that can be used with various tooth preparation techniques. Some new materials even incorporate the adhesive into the composite, eliminating the need for a separate adhesive step.

Preparation of the tooth for restoration results in a **smear layer** of debris that physically prevents bonding of the dentin – the tooth layer just beneath the outer enamel layer – to the adhesive. Currently, three techniques are used to overcome this challenge: **etch-and-rinse**, **self-etch** and **universal** or **multi-mode adhesive systems**. Using the etch-and-rinse technique, the smear layer is removed with acid that is rinsed away before adding a primer and adhesive. This technique is sensitive to over or under-drying, which can compromise the bonding of the adhesive and the durability of the restoration. Additionally, the acid used in the etch-and-rinse technique can be very harsh and lead to post-operative tooth sensitivity. The self-etching technique is a simplified process that can be reduced to one or two steps and requires less time. It is also less sensitive to moisture conditions and can use milder acids that should reduce post-operative pain. However, the adhesive layer is more permeable to water in this technique, which can

ultimately weaken the bond between the tooth and the restoration leading to decreased durability and life of the restoration. Universal or multi-mode adhesives systems can be used either with the etch-and-rinse or self-etch techniques and can be used on either dentin or enamel.<sup>6</sup>

With respect to adhesive technology on the aforementioned restorative materials, the development of a thiourethane-based composite required the development of a new adhesive. The resulting adhesive again replaced vulnerable ester bonds with material containing a bond less vulnerable to degradation called an amide bond. Laboratory tests showed that the amide bond-containing material maintained its bond strength after six months, whereas the ester-based adhesive did not.<sup>7</sup> OASys and TEG-DVBE-based composite are able to be used with adhesives currently used in dental practice.

### **Glass ionomer cement and resin-modified glass ionomers**

**Glass ionomer cement** is another alternative to dental amalgam. Glass ionomers are self-adhering, self-curing and release fluoride and calcium ions to remineralize the enamel but are lacking in strength and wear resistance, especially for larger areas of tooth decay. The strength of glass ionomers can be improved by adding a resin. For example, a newer glass ionomer product reinforced with resin called Cention® N (manufactured by Ivoclar Vivadent) has shown improvements in strength and can be used in primary teeth and to treat certain types of decay.

Glass ionomer, however, can be appropriate for some situations. A technique called **atraumatic restorative treatment**, or **ART**, has been implemented in various settings, especially developing countries. ART uses highly viscous glass ionomers and does not require electricity or running water. It requires a minimally invasive procedure and is acceptable for children but not adults. ART began in the 1990s with a focus on developing countries and is now used in many countries at various stages of economic development. However, a systematic review comparing ART using high-viscosity glass ionomer cement with conventional treatment – including treatment with dental amalgam and composite resin – showed a higher risk of failure with the former in the primary teeth of children.<sup>8</sup>

### **Added antimicrobial activity**

The most common reason for failure of composite resin restorations is secondary tooth decay. One way to reduce secondary decay is to supplement materials with antimicrobial agents such as silver nanoparticles. In one study, composite resin synthesized with different amounts of silver nanoparticles inhibited the growth of tooth decay-causing bacteria *S. mutans* between 50-98% of composite resin synthesized without silver nanoparticles.<sup>9</sup>

Investigators are exploring the potential of a new antimicrobial agent that may selectively inhibit the growth of acid-producing bacteria, not just *S. mutans*, at low pH. Subsequently, the antimicrobial agent has been demonstrated to maintain the pH of the oral cavity above 5.5, below which tooth demineralization may take place.<sup>10</sup> If added to composite resin restoratives, it may be possible to prevent or reduce the risk of secondary caries.

Another strategy is to create materials with inherent antimicrobial activity. Laboratory tests have shown that the OASys material itself has antimicrobial properties and that supplementing OASys with silver nanoparticles had a negligible effect on antimicrobial activity.

### **Self-healing technology**

Micro-cracks occur in the composite restoration that are difficult to detect and impossible for the dentist to repair. Self-healing composites include microcapsules within the filler containing healing materials. Micro-cracks in the restoration break open the microcapsule, releasing the healing materials which form glass ionomer cement, filling the micro-crack and extending the life of the restorations.<sup>11, 12</sup>

### **Safety and Regulation**

These novel composites are still in the early development phases. Testing on safety has been limited with more studies planned, and regulatory requirements vary by country. The United States Food and Drug Administration (FDA) requires manufacturers to gain approval before marketing novel composite resins and to show that the novel composite resin is at least as safe and effective as those currently on the

market. Manufacturers need to assess and mitigate risks for mechanical failure, adverse effects on tissue and improper use of the composite resin.<sup>13</sup> In the European Union, market access of new dental materials will be subject to the Regulation on Medical Devices (MDR), which will come into force in 2020. A number of prerequisites have to be met that show conformity with the basic requirements of the law.<sup>14</sup> As another example, the Brazilian Health Regulatory Agency, or ANVISA, requires documentation and testing of any new product before approval even if the product is already approved in the U.S. and Europe. This is a relatively long process that usually takes more than 2 years.

So far, studies of OASys in cells and animal models have not shown any adverse health effects. Thiourethane-based composites increase polymerization of the resin, so there is less leakage than from conventional composites, and they perform similarly to conventional composites in safety tests on cells. TEG-DVBE-based composite is still undergoing safety tests. Although the components of self-healing composites have already been separately introduced into the clinic, clinical testing is still needed for these composites.

### **Ease of use**

The restoration process with composites can be simplified by using **bulk-fill** and **flowable composites**. Bulk-fill composites can be placed in a single large increment or just a few smaller increments which simplifies and speeds up placement as opposed to traditional composites, which are placed in several thin layers. However, one problem with bulk-fill composites is that it is difficult to cure the material in bulk, and bulk-curing can cause shrinkage and deformation of the restoration. Flowable composites are less viscous than earlier composites and easier to use.

OASys, thiourethane-based, and TEG-DVBE-based composites can be placed and cured in bulk. OASys is not yet flowable, but that is a future goal for this material. Thiourethane-based composite itself is also not flowable but could be made flowable by the eventual manufacturer.

To encourage dentists to use these novel composites once they reach market, researchers are trying to develop systems that do not have a steep learning curve. Thiourethane-based and TEG-DVBE-based composite do not require dentists to learn new techniques or purchase new equipment. Similarly, with OASys, the dentist can use the adhesive system that they prefer to use whereas previous composites based on this resin required a proprietary bonding agent.

### **Other current advances**

Another advance with composite resins has been the advent of **universal composites**, which can be used in restorations in teeth in front or back of the mouth.

There have also been advances with **indirect restorations**. Dental amalgam, composite resins and glass ionomers are **direct restorations** – that is, the restorative material is placed and formed directly in the tooth. Indirect restorations are made and formed outside of the tooth then placed into the tooth.

**CAD/CAM**, which stands for **computer-aided design** and **computer-aided manufacturing**, can enable accurate design and production of indirect restorations and may become more widely used as the technology becomes simpler, cheaper and more accessible. Finally, 3D printing holds possibilities for the future of indirect restorations, but high-performing dental materials need to be optimized for 3D printing fabrication techniques.

### **Future direction of restorative materials research**

Generally, future research of restorative materials will focus on multifunctional materials that have remineralizing and antimicrobial activities; can reinforce the underlying dentin structure for more durable bonding; and improve strength, flexibility and the life of the restoration while ensuring safety. For example, a group from Brazil is testing a new composite containing a calcium salt that has shown the ability to remineralize artificial enamel caries in a laboratory setting.<sup>15, 16</sup>

Fiscal year (FY) 2018 marked the final year of NIDCR's five-year award. Following interactions with FDA and industry experts organized by NIDCR in 2017, grantees made significant progress to optimize the nanoscale properties of their candidate dental composites by implementing strategic feedback on product

development and regulatory requirements. The newly-developed dental materials have shown unique features such as self-healing and anti-microbial properties. Additionally, investigators have demonstrated improvements in mechanical performance, biocompatibility, ease of clinical handling, and durability of candidate dental resins combined with nanoparticle-based materials. In this way, grantees were enabled to accelerate product development activities in 2018 and several groups reported pursuing commercialization strategies via partnerships with industry, product licensing, or via startup ventures. Several patents have been issued to date stemming from this program and future efforts will build on current success towards the clinical translation of novel dental materials with superior longevity and durability. NIDCR's support towards development of new nanomaterials-based dental composites will continue at least until FY2021.

### **Lingering challenges**

The development of new dental materials will require sufficient and sustained investment in research. However, securing funding for research on new dental materials can be a challenge when competing with other research priorities and because of the belief that this area is the purview of industry. In Europe, several manufacturers have intensive and innovative research programs that involve university research groups, but they are primarily focused on testing new materials that have already been developed and are less interested in the basic research required to create new materials.

To the IADR's knowledge, only one oral health project was funded within the European Union's 75 billion Euro joint research program called Horizon 2020, but this project was not focused on materials science. There will be a continuation of this program called Horizon Europe with a planned investment of 100 billion Euros starting in 2020 and lasting until 2027. However, there are still a number of uncertainties regarding this program, for example, due to the unresolved questions of the Brexit. IADR members of the Continental European Division and Pan European Region are trying to get a dedicated call within this new program for research related to the Minamata Convention on Mercury and the consequences on the health system.

Once these or other restorative materials are available, practicing dentists will have to be convinced to use a new material, and dental curriculums will have to teach restorations with new materials. Researchers are also working to create and simplify procedures to aid in this transition.

Another challenge is establishing performance standards to ensure quality and high clinical performance. NIDCR has partnered with the U.S. National Institute of Standards and Technology to develop appropriate standards for novel restorative materials.

In at least the short-term, cost will continue to be a barrier. These new technologies will be expensive and may not be suitable in all settings, especially as dentistry becomes increasingly digital. Digitization will make restorations more precise and easier to place, but these technologies will not be available in places that lack a reliable source of electricity at a minimum or access to more sophisticated tools, computers and accompanying software.

### **Conclusion**

Researchers are addressing deficiencies of alternatives to dental amalgam in a variety of innovative and exciting ways but require continued investments in research to accelerate development of these products, move them from the lab to the market, and to increase their affordability. Related to the phase-down of dental amalgam, while much progress has been made with alternative restorative materials, they are not practical for all clinical situations or in settings that lack a reliable source of electricity or other necessary equipment. Thus, it is important to preserve the availability of dental amalgam as a restorative option until investments in research can deliver an alternative restorative material that addresses these current shortcomings.

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