

FDI World Dental Federation Submission

Third Conference of the Parties to the Minamata Convention

Item 9: Review of Annexes A and B of the Convention

FDI World Dental Federation is the official body of over one million dentists worldwide through its 200-member national dental associations and specialized groups.

FDI fully supports the Minamata Convention on Mercury, including its nine provisions on the phase down of use of dental amalgam defined in Annex A, Part II of Article 4.

Article 4.8 of the Convention states that *“no later than five years after the date of entry into force of the Convention, the Conference of the Parties shall review Annex A in accordance with Article 27”*. As the Convention entered into force on August 16, 2017, any review would therefore occur no later than August 16, 2022.

FDI believes any review at this stage of the dental amalgam provisions contained in Annex A would be premature, given that the Convention has not even been in force for two years. It is therefore too early to review the Annex A dental amalgam phase-down measures that ratifying countries are carrying out.

In the event of a review according to Article 4.9(c) the Convention requires the Conference of the Parties to take into account 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”*.

Dental amalgam has been used for over 150 years around the world as a safe¹, durable and cost-effective material to repair tooth decay (dental caries). Although much progress has been made in developing alternative restorative materials, they are still not *“technically and economically feasible”* for many resource-limited settings. FDI agrees with the latest research update on alternative materials from the International Association for Dental Research (see Appendix 1), which found that alternative restorative materials *“... are not practical for all clinical settings or in settings that lack a reliable source of electricity or other necessary equipment ...”* and *“... addressing deficiencies of alternatives to dental amalgam ... require[s] continued investments in research to accelerate development of these products, move them from the lab to the market, and to increase their affordability”*.

FDI therefore urges the Conference of the Parties to maintain the dental amalgam provisions set out in Annex A. The phasing down of dental amalgam before the availability of safe, effective and affordable alternatives,

¹ Systematic evidence reviews from the UK government’s Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment (COT): 1997 COT Statement on the toxicity of dental amalgam); the European Commission’s Scientific Committee on Emerging and Newly Identified Health Risks (SCENIHR): 2015 SCENIHR Opinion on the safety of dental amalgam and alternative dental restoration materials for patients and users; and the US Food and Drug Administration (FDA): 2009 FDA White Paper: FDA Update/Review of Potential Adverse Health Risks Associated with Exposure to Mercury in Dental Amalgam, all concluded that there is no evidence to suggest that exposure to mercury from dental amalgam has an adverse effect on patient health – these reviews included studies on children, pregnant and breastfeeding women.



particularly in resource-limited settings, would negatively impact oral health from both an individual and population perspective.

To help accelerate the phase down of dental amalgam and support countries, FDI calls on WHO to update its 2009 publication *WHO Guidelines on Future Use of Materials for Dental Restoration* with the latest scientific evidence. This document must be updated before any review of the dental amalgam provisions in Annex A take place.

FDI advocates for the continued phase down of use of dental amalgam, but countries and dentists must be given access to safe, effective and affordable alternative restorative materials. This will not become a reality in many countries, particularly in resource-limited settings, without sustainable funding, a greater emphasis on prevention, increased research on amalgam alternatives, and best management practices for amalgam waste.

FDI looks forward to the third Meeting of the Conference of the Parties to the Convention and stands ready to support countries and WHO in the implementation of the phase down of dental amalgam according to the resolution WHA67.11 adopted at the 67th World Health Assembly.



Appendix 1: Update on Dental Amalgam Alternatives from the International Association for Dental Research

Research into Dental Amalgam Alternatives

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.^{1,2} 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.³

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.⁴ 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.⁵

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.⁶

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.⁷ 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.⁸

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.⁹

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.¹⁰ 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.^{11, 12}

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.¹³ 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.¹⁴ 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.^{15, 16}

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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