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VIA U.S. MAIL AND EMAIL

June 19, 2016

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Dear Dr. Kirkland and Ms. Denis:

The Methacrylate Producers Association (MPA) is again writing to request that AOEC remove the entry for methyl methacrylate (MMA) from your Exposure Code System, where it is designated as an asthmagen (A) and respiratory sensitizer (Rs).[1] We believe the science does not support these designations.

In conjunction with this, it is important that AOEC and its reviewers differentiate among chemicals that share "acryl" in their names but have distinct chemistries. Specially, Cyanoacrylate resins and polymers are in a separate category from Acrylic/Methacrylic resins (comprising Acrylic acid and its esters and/or Methacrylic acid and its esters) and Acrylic polymers. Monomers and resins should be categorized separately from polymers. It would be useful to also keep in mind that Acrylates and Methacrylates are distinct groups. We believe this will assist clinicians in making accurate assessments and advancing research into the causes of asthma.

[1] http://www.aoecdata.org/ExpCodeLookup.aspx, search on methyl methacrylate.

Classification of MMA

Shaun Clancy forwarded your email of November 13, 2015. We believe the information therein does not support classification of MMA as A or Rs. With respect to the AOEC basis for classifying MMA as A and Rs, you quote from the review of Dr. William Beckett in 2005. He concluded that MMA met Major Criterion 1 for listing as a sensitizing cause of occupational asthma, citing to a study by Lozewicz et al. (1985), and mentioning also a study on polymethylmethacrylate (PMMA) by Basker et al. (1990). You also state that Dr. Kenneth Rosenman reviewed MMA in 2012.

For the reasons detailed in Appendix A, we believe that the Lozewicz study does not support classification of MMA as a sensitizing cause of occupational asthma. A close look at the information therein demonstrates that Major Criterion 1 in fact is not met for either of the two patients in that study who had MMA exposure. And it is inappropriate to use the Basker study on PMMA in evaluating MMA, as the chemical reactions in forming PMMA will have completely altered the chemistry.

Further, the AOEC classifications are inconsistent with other expert reviews of the MMA literature. Indeed, the most recent review of this issue (2012-2015), by the American Conference of Governmental Industrial Hygienists (ACGIH), confirmed other expert evaluations by concluding that MMA does not meet the criteria for a respiratory sensitizer (RSEN) notation.[2] The ACGIH decision is consistent with other academic and regulatory reviews, as detailed in Appendix B to this letter.

Therefore, to enhance the accuracy, credibility and usefulness of the Exposure Code System, AOEC should remove MMA.

Grouping of Chemicals Containing Acyl

As just stated, the chemistry of the polymer PMMA is very different from that of the monomer MMA. This is in general true for acrylate and methacrylate polymers versus their acrylate or methacrylate monomers. There are further differences among cyanoacrylates, acrylates, and methacrylates. We strongly believe that grouping these different and distinct groups of chemistry under the class “Acrylates” or “Acrylics” will not aid clinicians to improve their diagnosis of chemical-induced respiratory disease. Further information on these distinctions is given in Appendix C.

In sum, there is a very strong scientific consensus that the current evidence does not support listing of MMA as an asthmagen/respiratory sensitizer. This is the conclusion of various in-depth, expert reviews conducted from 2000 to 2014.

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[2] ACGIH, 2015 TLVs and BEIs, p. 42; see also letter to Elizabeth Hunt, Executive Director, MPA, from Ryan Peltier, Science and Education Manager, ACGIH (Jan. 30, 2015), attached to Appendix B.

If you should wish, MPA scientists would be willing to meet with you and discuss these data in further detail. Based on the enclosed information, we request that the designations of A and Rs for MMA be removed. Please contact me at (540)-751-2093 or via e-mail at e.hunt@comcast.net to discuss this further.

Sincerely yours,

Elizabeth K. Hunt,
MPA Executive Director

Appendix A: The AOEC Classifications for MMA Are Not Supported by the Science
Appendix B: Summaries of Reviews of MMA Sensitization Potential
Appendix C: AOEC Should Be a Leader in Adopting More Precise Nomenclature

cc: Anna Allen, MD, MPH
President, AOEC Board of Directors
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APPENDIX A
The AOEC Classifications for MMA Are Not Supported by the Science

As you know, MPA wrote to AOEC in 2004 requesting that Methyl Methacrylate (MMA, CAS Number: 80-62-6) be removed from classification as an asthmagen and respiratory sensitizer. After a review of the existing information by Professor William S. Beckett M.D., M.P.H., in 2005, AOEC decided to retain the listing for MMA. In 2012, Dr. Kenneth Rosenman undertook a review of acrylic acid, which mentioned MMA. AOEC appears to have interpreted this as a confirmation of its listing for MMA.

In 2011, an article was published in the peer reviewed journal, *Critical Reviews in Toxicology*, by Professor Jonathan Borak, Clinical Professor of Epidemiology & Public Health and Clinical Professor of Medicine at Yale University.[1] Professor Borak and co-workers conducted a systematic review according to the requirements of the American College of Chest Physicians for an evidence-based approach to medicine. The review encompassed all available information including *in silico*, *in chemico*, *in vitro*, and *in vivo* toxicology literature, and also epidemiologic and occupational medicine reports related to the respiratory effects of MMA. Dr. Borak and his co-authors concluded that, on a weight of evidence, both experimental and observational, MMA is not a respiratory sensitizer. Rather, it likely acts as respiratory irritant that, like other common irritants, can trigger asthma in predisposed asthmatics.

Dr. Borak's review is consistent with other international and American agency reviews, including the ACGIH conclusion last year (see Appendix B). We therefore aver there are sufficient grounds for AOEC to look critically again at the basis for regarding MMA as an Asthmagen and Respiratory Sensitizer. Review of that information indicates that there is not in fact sufficient evidence to maintain the A and Rs designations for MMA.

The data in Lozeciwz et al. (1985) does not meet the AOEC criteria for listing as an asthmagen

In the Final Report of Year 3 of Project, February 2005, Professor Beckett concluded "Methyl methacrylate meets AOEC Major Criterion 1. (Lozewicz S, Davison A, Hopkirk A, Burge P, Boldy D, Riordan J, McGivern D, Platts B, Davies D, Newman Taylor, A. Occupational asthma due to methyl methacrylate and cyanoacrylates. Thorax 1985;40:836-839)." On this basis he stated "Methyl methacrylate meets AOEC criteria for a sensitizing cause of occupational asthma …" A closer look reveals that the Lozewicz study does not support this conclusion.

Lozewicz et al., 1985 reported seven cases of occupational asthma, of which two – Patients 6 and 7 – had been exposed to MMA-containing materials. Analysis of the information given in

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[1] Borak J, Fields C, Andrews LS, Pemberton MA (2011). Methyl methacrylate and respiratory sensitization: a critical review. Crit Rev Toxicol. 41(3):230-68, http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3072694/.

Lozeciwz et al. for these two patients against Major Criterion 1 reveals that that the criterion is not met.[2]

Patient 6 was a 40-year-old male dental assistant who had worked for several years on dental prosthetic trays before he experienced work-related symptoms of chest tightness, dyspnea, and cough that persisted for several hours after mixing "pMMA powder with MMA liquid." He gave no history of wheeze or breathing difficulty other than the work-related episodes. Spirometry and nonspecific inhalation challenge (NSIC) were not reported and PEFR away from work was normal although during the week rest between SIC he showed a "morning dip" of 17% in PEFR that resolved by midday. SIC was positive (24% fall in PEFR which resolved within 2 hours) after simulated workplace exposure mixing "PMMA powder with MMA liquid" monomer for 20 minutes. Repeat testing 1 week later resulted in a similar response. Placebo testing was not performed.

Setting this information against the elements of Major Criterion 1:

i) *Specific inhalation challenge indicates occupational asthma (i.e. immediate or delayed fall in FEV1 after exposure) in at least one patient with asthma who appears to have developed the asthma as a result of exposure to the implicated substance.*
FEV1 was not measured; therefore, there is insufficient information to determine whether this element was met. Although a reduction in PEFR was observed, this could equally be explained as being due to irritation of responsive airways.

ii) *Peer reviewed study should indicate a response to sub-irritant levels (emphasis added) of sensitizing substances*
There was no reporting of the exposure levels used during the SIC nor that they were sub-irritant; therefore, there is insufficient information to determine that this criterion element was met. MMA vapour is classified as irritating to the respiratory system, so that a 20 minute exposure to vapor in a confined space (as was done in the study) would likely have caused irritation of the respiratory tract.

iii) *Ideally, a positive challenge will be controlled by negative challenges in asthmatic patients who are not believed to be sensitized to the particular substance, but this design is not characteristic of many specific exposure challenges*
No negative challenge was made; therefore, it cannot be determined whether this element of the criterion was met. PEFR measurements during the week rest showed a "morning dip" of 17% that resolved by midday indicating the presence of hyperresponsive airways.

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[2] Revised Protocol: Criteria for Designating Substances as Occupational Asthmagens on the AOEC List of Exposure Codes, Revised September 2008, http://www.aoec.org/content/Asthmagen_Protocol_10-25-08.pdf.

In summary, there is insufficient information to conclude that any element of Major Criterion 1 was met. From the data, it is clear that the patient had a form of hyperreactive airways that had developed over time. From the observation of "morning dips" in PEFR of 17% it is apparent that other factors in the home were contributing to his respiratory condition. It is not clear whether workplace exposure to PMMA dust and MMA vapor had aggravated this condition, but causation cannot be unequivocally assumed. There was no evidence of specificity in the PEFR response. Indeed, the "morning dips" would suggest that it was non-specific. This coupled with the fact that MMA vapors are irritating to the respiratory system points to no meeting of the criterion on the basis of Patient 6.

Patient 7 was a 52-year-old male railway cable joiner who described headache, sweating, and lassitude when working with an "acrylic cold curing resin system containing MMA." He had smoked "for many years" and reported episodes of cough and wheeze that were "not clearly work related." The duration of exposure before onset of symptoms was not specified. Spirometry was not reported. PEFR "indicated asthma," there was "no fall in FEV1" following histamine inhalation challenge, and SIC was negative "using the resin." SPT was negative for common inhalant allergens.

Setting Patient 7's information against the elements of Major Criterion 1:

i) *Specific inhalation challenge indicates occupational asthma (i.e. immediate or delayed fall in FEV1 after exposure) in at least one patient with asthma who appears to have developed the asthma as a result of exposure to the implicated substance.*
The patient was a long-term smoker with reduced PEFR performance indicative of obstructed airways. Since his reported episodes of cough and wheeze were "not clearly work related," they fail to suggest that asthma (if present) was a result of exposure to the implicated substance. This is further supported by the observation that SIC was **negative** using the resin.

ii) *The peer-reviewed study should indicate a response to sub-irritant levels of sensitizing substances.*
The SIC was negative so no causal link between the resin and the symptoms was established at any level.

iii) *Ideally, a positive challenge will be controlled by negative challenges in asthmatic patients who are not believed to be sensitized to the particular substance, but this design is not characteristic of many specific exposure challenges*
There was no evidence of sensitization or indeed of asthma other than the reduced PEFR performance, which may be explained by the fact that he was a long-term smoker.

In summary, it was clear that Patient 7 had obstructed airways that had developed from many years of smoking. The episodes of cough and wheeze, while not clearly work-related, were being

triggered by some other factors that had not been established; since the SIC with the resin was negative, it can be concluded that any "other factor" was not MMA.

Thus, neither of the two patients in the Lozewicz study provides a sufficient basis to conclude that MMA meets Major Criterion 1 for listing as an asthmagen. Note that Lozewicz et al. (1985) was included in all international and national reviews on MMA and asthma, particularly the review by Dr. Borak in 2011 and the more recent review by ACGIH, all of which concluded that MMA is not a respiratory sensitizer.

The Basker et al. study does not support listing of MMA as an asthmagen

Dr. Beckett's 2005 report stated, "A case report also documents an asthmatic response to a non-occupational chronic mucous membrane exposure to a cured poly(methyl methacrylate) denture base resin (Basker R, Hunter A, Highet A. A severe asthmatic reaction to poly(methyl methacrylate) denture base resin. British Dental Journal 1990; 169:250-251)."

It is inappropriate to use this report in a review of MMA, a monomer. The study was of cured poly(methylmethacrylate) (PMMA). In curing, the MMA acyl group is completely incorporated into the polymer backbone, rendering it non-reactive (i.e., chemically and biologically inert).

The 2012 Review by Dr. Roseman does not appear to include a review of MMA, and therefore does not support continued listing of MMA as an asthmagen and respiratory sensitizer

Towards the end of 2012 you commissioned a review of Medical Literature for agents already listed or nominated to be listed on the AOEC Exposure Code List of Designated Asthmagens, by Professor Kenneth D. Rosenman, MD, FACE, FACPM of the Department of Medicine, Michigan State University. In your November 13, 2015 email to Shaun Clancy (and others), you state, "In an effort to be thorough, Dr. Rosenman included an updated review of methyl methacrylate in his report. The result of his review was that methyl methacrylate was retained as a sensitizer and acrylic acid was returned to sensitizer status." However, our review of Dr. Rosenman's report shows no evidence that he actually had reviewed the MMA literature.

Dr. Rosenman's report provides summaries of his review of 25 substances and provides a listing recommendation for each. There is no summary or recommendation for MMA. In each of the summaries for acrylic acid, PMMA, and TMPTA/2-hydroxypropyl acrylate, the report states:

> Various acrylate compounds have previously been reviewed: polymethylmethacrylate, acrylic acid and methylmethacrylate in 2005 and ethyl methacrylate; ethyoxlated TMPTA (CAS# 028961-43-5) in 2004 and cyanoacrylate in 2002. Only methylmethacrylate and cyanoacrylate met the AOEC criteria as an asthmagen.[3]

[3] Rosenman K (2012). Review of Medical Literature for Agents Already Listed or Nominated to be listed on the AOEC Exposure Code List of Designated Asthmagens, pages 4, 17 and 22.

There is no other mention of MMA, except for a sentence under acrylic acid: "Esters and salts of acrylic acid are known as acrylates (i.e. methylmethacrylate)."[4]

Thus, the report indicates only that Dr. Rosenman took note of the prior review of MMA and its outcome, not that he undertook a re-review of MMA. Nor did he provide any explicit recommendation that MMA continue to be listed. Thus, it appears AOEC has conducted no actual review of MMA since 2005, and therefore has not considered the reviews of Dr. Borak and ACGIH (see Appendix B).

We note that Dr. Rosenman's reviews of acrylic acid and PMMA cannot be used to make a determination about MMA on the basis of it also being an acrylate. As discussed in Appendix C, the various groups of acrylates have differing chemistries, and so must each be evaluated on their own database.

Conclusion

As shown above, the Lozewicz et al. (1985) study does not demonstrate that MMA meets Major Criterion 1 for listing as an asthmagen. Nor does the Basker et al. (1990) study of PMMA provide a basis for evaluating MMA monomer. And the 2012 review of Dr. Rosenman does not appear to have included an updated review of MMA. In particular, there is no evidence that Dr. Roseman reviewed the Borak et al. (2011) review, which included review of the Lozewicz study and concluded MMA is not a respiratory sensitizer, and he of course could not have reviewed ACGIH's 2015 determination to not designate MMA as a respiratory sensitizer.

Thus, the science does not support designation of MMA as an asthmagen or respiratory sensitizer.

[4] *Id*. at 4.

APPENDIX B
Summaries of Reviews of MMA Sensitization Potential

- In 2012, ACGIH announced it was reviewing substances designated as sensitizers (SEN), including MMA, for update to respiratory sensitizer (RSEN) and/or dermal sensitizer (DSEN).[1] Initially ACGIH proposed to give MMA both a DSEN and a RSEN notation, but after further review made a new proposal for a DSEN notation only.[2] The final vote of the ACGIH Board was to adopt the DSEN (and not RSEN).[3]

- Borak et al. (2011) is an exhaustive review of the literature on exposure to MMA and PMMA and respiratory effects, including asthma.[4] The main author of this publication is a Clinical Professor of Epidemiology & Public Health and Clinical Professor of Medicine at Yale University who is certified in Internal Medicine, Occupational Medicine, and Toxicology. The authors found sufficient scientific grounds to conclude that MMA is not causally related to the development of asthma. Rather, the effects reported in the literature are more consistent with primary irritation—in some cases possibly provoking pre-existing asthmatic conditions.

- In January 2001, the OECD (Organization for Economic Co-operation and Development) completed its Screening Inventory Dataset (SIDS) Initial Assessment Report (SIAR) for MMA, concluding that "There is no convincing evidence that methyl methacrylate is a respiratory sensitizer in humans."[5] The review panel consisted of medical, toxicological and regulatory experts from the governmental agencies of the member OECD countries (Australia, Austria, Belgium, Canada, Czech republic, Denmark, Finland, France, Germany, Greece, Hungary, Ireland, Italy, Japan, Korea, Norway, Poland, Portugal, Slovak Republic, Spain, Sweden, Switzerland, The Netherlands, UK, USA) as well as from the European Commission, UNEP, and WHO.

- In April 2001, the European Union finalized its Risk Assessment for MMA.[6] This six-year risk assessment reviewed published and unpublished (company confidential) studies/reports on MMA, and in Section 4.1.2.5 concluded that "no convincing evidence

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1 ACGIH, 2012 TLVs and BEIs, p. 67.

2 See attached letter to Ian Kimber, Professor of Toxicology and Associate Dean, Manchester University, from Ryan Peltier, Science and Education Manager, ACGIH (Jan. 31, 2014).

3 ACGIH, 2015 TLVs and BEIs, p. 42; see also attached letter to Elizabeth Hunt, Executive Director, MPA, from Ryan Peltier, Science and Education Manager, ACGIH (Jan. 30, 2015).

4 Borak J, Fields C, Andrews LS, Pemberton MA (2011). Methyl methacrylate and respiratory sensitization: a critical review. Crit Rev Toxicol. 41(3):230-68, http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3072694/.

5 OECD SIDS, Methyl Methacrylate, CAS No.: 80-62-5, UNEP Publications, Geneva, Switzerland, http://www.inchem.org/documents/sids/sids/Foreword.pdf.

6 European Chemicals Bureau (2002), methyl methacrylate, CAS No: 80-62-6, EINECS No: 201-297-1, European Union Risk Assessment Report PL-1 22, EUR 19832 EN, http://www.echa.europa.eu/documents/10162/7c9a0eb6-9b7f-4fd6-846b-d480e8e0003d.

was found that MMA acts as a respiratory sensitiser in humans". The review panel consisted of the leading medical and toxicological experts of the Competent Authorities in the European Union as well as the World Health Organisation. The report was also reviewed and approved by an independent panel of International Peer Scientists/Professors/clinicians comprising the Scientific Committee for Toxicity, Ecotoxicity and the Environment (CSTEE). The review specifically addressed asthma and concludes: "The literature reports isolated cases of asthma in the context of MMA exposure. Substance-specific broncho-constriction or delayed asthmatic responses respectively were confirmed only in very few cases. Asthmatic reactions seem to be restricted to exposure levels which primarily result in respiratory tract irritation."

- In 2002, Health Canada (HC) actually reversed its 1996 decision to classify MMA as a respiratory sensitizer (which required all products containing MMA or MMA residues (polymers etc.) to be labelled "Contains a respiratory sensitizer"). This decision was based upon a conclusion that there is insufficient evidence to regard MMA as a respiratory sensitizer. Accordingly HC has removed MMA from their list of known respiratory sensitizers.[7]

- From 2001 to 2004, an advisory committee for California OSHA considered whether to list several chemicals, including MMA, as airborne contaminants in the workplace and, if so, what should be permissible exposure limits. Minutes for the advisory committee meetings show that the committee reviewed whether the data indicated that MMA was a respiratory sensitizer. Ultimately, however, while sensitization was found to be a concern for other chemicals reviewed by the advisory committee, there was no such finding for MMA, as shown by the Initial Statement of Reasons for the proposed rule,[8] now codified at 8 CCR 5155, Table AC.[9]

In sum, there is a very strong scientific consensus that the current evidence does not support listing of MMA as an asthmagen/respiratory sensitizer. This is the conclusion of various in-depth, expert reviews conducted from 2000 to 2014. Therefore, to enhance the accuracy, credibility and usefulness of the Exposure Code System, AOEC should remove MMA.

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[7] See Health Canada, *Sensitizers*, http://www.hc-sc.gc.ca/ewh-semt/occup-travail/whmis-simdut/sensitizers-sensibilisants-eng.php (listing MMA as a skin sensitizer but not a respiratory sensitizer).

[8] California Occupational Safety and Health Standards Board (2005), Initial Statement of Reasons, Airborne Contaminants, http://www.dir.ca.gov/oshsb/airbornecontaminants2005ISOR.pdf.

[9] http://www.dir.ca.gov/title8/5155table_ac1.html.

APPENDIX C

AOEC Should Be a Leader in Adopting More Precise Nomenclature

We strongly believe that the referral to several different and distinct groups of chemistry under the class "Acrylates" will not aid clinicians to improve their diagnosis of chemical induced respiratory disease. Indeed, we suspect that this may be a major stumbling block to progress in this area. As such we strongly recommend that AOEC takes the lead in adopting a more precise approach to describing the chemistry being listed.

Specifically, we note that in three places (items 1, 20 and 25) in the review of Medical Literature for agents already listed or nominated to be listed on the AOEC dated 2012 the reviewer refers to "*... Esters and salts of acrylic acid are known as acrylates (i.e. methylmethacrylate).*" going on to state "*Various acrylate compounds have previously been reviewed: polymethylmethacrylate, acrylic acid and methylmethacrylate in 2005 and ethyl methacrylate; ethoxylated TMPTA (CAS# 028961-43-5) in 2004 and cyanoacrylate in 2002."*

We would like to point out that the terms "Acrylic" or "Acrylate" and "Acrylic resin," while commonly used in modern language, are not sufficiently precise as to pinpoint any given area of chemistry. Indeed, the term "Acrylic", although originally intended to mean a molecule "containing acryl", has over time and use been broadened to include a wide range of polymers and formulated products, including synthetic fabrics and fibres, polymers formed from acrylonitrile, thermoplastic resins based upon esters of acrylic acid and/or methacrylic acid and even a wide range of paint and decorative products used by artists and industrial and domestic painters. Similarly, in the European Union and elsewhere, the term "Acrylic resin" has been broadened to include any liquid chemical that contains the "Acyl" group.[1] In practice, the presence of other chemical groups adjacent to the "Acyl" group can greatly reduce its chemical and biological reactivity due to stearic hindrance by a +I-effect (Osman et al., 1988).[2] Indeed, this explains the proliferation of this chemistry and the extremely wide range of polymers that are produced. In the case of acrylic/methacrylic polymers, the "Acyl group" is completely incorporated into the polymer backbone rendering it non-reactive, i.e., chemically and biologically inert.

As a consequence of this generalized use of the terms, polymers and chemical substances of wide-ranging physical and chemical properties, chemical reactivity and toxicology are being banded together quite inappropriately. It is evident that this imprecise way of describing the chemistry is leading to confusion among health professionals and consumers alike and potentially frustrating advances in the detection and treatment of chemical induced disease. The

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[1] The "Acyl" group has the general formula R–C(=O)–. "Acryl" refers to an acyl group derived from acrylic acid: H_2C=CH–C(=O)–.

[2] Osman K, Namboodiri, HW, Rabinowitz, JR. (1988). Reactivities of acrylic and methacrylic acids in a nucleophilic addition model of their biological activity. *J. Am. Chem. Soc.*, 110 *(*6), pp 1701–1707 DOI: 10.1021/ja00214a007.

paper by Quirce et al., recently identified in the AOEC review of 2012 illustrates this situation very well by conflating acrylics, methacrylates and cyanoacrylates.[3]

Referring specifically to the chemistry grouped in the 2012 review for AOEC, we would like to make the following points:

First, Cyanoacrylates (which are instant glues such as SuperGlue) are relatively unique in that they are thermoplastic resins that rapidly polymerize in the presence of water (specifically hydroxide ions) and are very distinct from other acrylic resins. Their recognized toxicity reflects their chemical reactivity, particularly with moisture.

Second, in contrast, Acrylates and Methacrylates (Esters of Acrylic Acid and Methacrylic Acid) differ from Cyanoacrylates by the absence of a "Cyano" group and the presence of an alkyl or other side group.[4] This difference in chemical structure is responsible for the reduced chemical and biological reactivity of Acrylates and Methacrylates, and the introduction of the α-methyl group in Methacrylates further reduces the chemical and biological reactivity of Methacrylates (Methacrylic Acid and its esters) over Acrylates (Acrylic Acid and its esters).

We realize that this dive into chemistry may appear of little relevance to AOEC when your objective is to alert clinicians to the possibility of health effects with these chemical types. We suggest, however, that grouping these chemistries together belies important differences in chemical and biological reactivity that clinicians should be cognizant of. In particular, Cyanoacrylate resins have a chemistry and health effect potential that is very distinct from that of Acrylate/Methacrylate resins.[5] In addition, the chemistry and health effect potential of polymers is very different from that of the monomers or liquid resins that are reacted to create the polymers.

We therefore respectfully suggest that you and your reviewers keep Cyanoacrylate resins and polymers in a separate category from Acrylic/Methacrylic resins (comprising Acrylic Acid and its esters and/or Methacrylic Acid and its esters) and Acrylic polymers. Monomers and resins should be categorized separately from polymers. It would be useful to also keep in mind that Acrylates and Methacrylates are distinct groups. This would be useful to clinicians for investigating sources of exposure and understanding their health impacts.

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[3] Quirce S, Baeza ML, Tornero P, Blasco A, Barranco R, Sastre J (2001). Occupational asthma caused by exposure to cyanoacrylate. Allergy 56(5):446-449.

[4] The cyanoacrylate group is: CH_2=C(CN)–C(=O)–O–R.
The acrylate group is: H–C(=R)–C(=O)–O–.
The methacrylate group is: CH_3–C(=R)–C(=O)–O–.

[5] We use "resin" here in the European sense of a liquid comprised of monomers.