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March 9, 2018

VIA CalSAFER WEBSITE (https://calsafer.dtsc.ca.gov/cms/commentpackage/?rid=12737)

California Department of Toxic Substances Control
1001 I Street
Sacramento, CA 95814
calsafer@dtsc.ca.gov

Re: Draft 2018-2020 Priority Product Work Plan

Dear Madam or Sir:

These comments of the Basic Acrylic Monomer Manufacturers, Inc. (BAMM) address the Safer Consumer Products Draft 2018-2020 Priority Product Work Plan (Draft Work Plan) of the California Department of Toxic Substances Control (DTSC).[1] BAMM members are producers of acrylic acid and basic acrylate monomers (acrylic acid and the alkyl esters: specifically, methyl acrylate, ethyl acrylate, iso-butyl acrylate, n-butyl acrylate, t-butyl acrylate and 2-ethylhexyl acrylate).[2] In these comments, we use the term "acrylates" to refer to these basic monomers, but note that the statements herein may apply to many other acrylates as well. Please visit http://www.bamm.net/ for further information on BAMM and the acrylates.

One of the product categories in the Draft Work Plan is "Building Products and Materials Used in Construction and Renovation." In the accompanying Table 4, giving examples of Candidate Chemicals, the Draft Work Plan lists "Acrylate" with a functional use of "Acrylic Coatings".[3] BAMM strongly believes that acrylic coatings or other acrylate-based products should be deleted from the final 2018-2020 Priority Product Work Plan. As explained below, consumer exposure to acrylates is low to non-existent. Further, the weight of scientific evidence does not support classifying acrylates as asthmagens – the primary health hazard cited for the Table 4 listings.

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[1] R. Brushia, Safer Consumer Products Draft Three Year Priority Product Work Plan (2018-2020) (Feb. 2018), ID #12737, Safer Consumer Products Branch, Department of Toxic Substances Control, Sacramento, CA, http://www.dtsc.ca.gov/SCP/upload/Draft_2018-2020_Priority_Product_Work_Plan.pdf (hereinafter "Draft Work Plan").

[2] BAMM addresses safety, health and environment regulatory activities involving the basic acrylic monomers. The members of BAMM are: Arkema, Inc.; BASF Corporation; and The Dow Chemical Company.

[3] Draft Work Plan at 15, Table 4.

Consumer Exposure to Acrylates in Coatings is Low to Non-Existent

Acrylates are monomers used in the production of copolymers for a variety of surface coatings. They are widely used in water-based paints and coatings where they provide good water resistance, low temperature flexibility, and excellent weathering and sunlight resistance. Because they are water-based, acrylic coatings provide an environmental advantage over the prior oil-based coatings that contributed relatively high amounts of volatile organic chemicals (VOCs) to the air, and thus have been restricted in California to assist in meeting tropospheric ozone standards.

It is important to understand that the copolymers in acrylate coatings are manufactured so as to fully react the acrylate monomers. The copolymers made with acrylics are very large molecules that, like other polymers, are of low toxicity.[4] Consumer exposure to acrylate monomers via contact with coatings and other building materials, if occurring, would be limited to the very low residual monomer levels.

Therefore, potential exposures do not support listing acrylates as Candidate Chemicals.

The Draft Work Plan Does Not Provide Credible Support for Including Acrylates in the Table 4 List of Candidate Chemicals

Acrylates Are Not Detected in Biomonitoring or House Dust

In explaining the basis for inclusion of chemicals in the Table 4 examples of Candidate Chemicals, the Draft Work Plan (p. 15) states:

> Biomonitoring studies show that people are exposed to some of the Candidate Chemicals in these products and that human exposure is widespread. The presence of other Candidate Chemicals has been demonstrated by the fact that they have been detected in indoor air and house dust.

To BAMM's knowledge, no acrylate has been detected via biomonitoring,[5] nor in indoor air or house dust, and such would not be expected given the very low levels of residual monomer. There have been some reports of indoor dust created by cutting or filing acrylate or methacrylate polymeric materials, but in such cases any associated respiratory effects may be attributable to physical irritation by the polymeric dust particles, versus inherent toxicity of the polymer.

The Draft Work Plan (p. 15) also states:

> The combination of lower ventilation rates and the increased use of synthetic building materials has resulted in elevated levels of certain chemicals in the indoor environment, including some Candidate Chemicals [12].

[4] For this reason, acrylate copolymers generally qualify for the exemption from Toxic Substance Control Act premanufacture notification requirements at 40 CFR § 723.250.

[5] Fluorotelomer acrylate is one of a number of perfluoroalkyl and polyfluoroalkyl substances (PFASs) designated by Biomonitoring California (https://biomonitoring.ca.gov/sites/default/files/downloads/DesignatedChemicalsList_October2017.pdf), but, in this case, the moiety of concern for biomonitoring is the fluorotelomer.

Citation 12 given to support this statement makes no mention of acrylates whatsoever.[6]

Thus, biomonitoring, dust, and indoor air data do not support including acrylates as Candidate Chemicals.

Acrylates Are Not Asthmagens

The rationale for listing Candidate Chemicals in Table 4 also cites to a document by Lott and Vallente titled "Full Disclosure: A Strategy to Prevent Asthma Through Building Product Selection."[7] This document is not a peer-reviewed journal article nor a government agency document subject to notice and comment. Rather, it is an advocacy piece by a non-profit group. Its sources in turn are lists or databases maintained by non-profit organizations – again, not peer reviewed or subject to notice and comment. These sources largely "cherry-pick" the literature rather than provide a balanced and comprehensive evaluation of the available data, and in some cases the conclusions are so lacking transparency that it is not even possible to rationally comment on those conclusions.[8] In short, the support on which DTSC relies to list acrylates is a very thin reed that should not meet the standards of a governmental agency.

One of the Lott and Vallette sources (published in 2013) is the Association of Occupational and Environmental Clinics (AOEC) Exposure Code List. AOEC has subsequently removed acrylic acid from its list of asthmagens.[9] No BAMM acrylate has been classified as an asthmagen or respiratory sensitizer under regulations of the European Commission, the United States EPA, or other major governmental bodies.

Thus, acrylates do not pose an asthma hazard and should not be included in Table 4 on such basis.

Acrylates Are Not Carcinogens

The Draft Work Plan (p. 15) lists as hazards, "Carcinogenicity, respiratory toxicity, dermatotoxicity, neurotoxicity." No support is given for assigning these effects to acrylates, other than the asthma citation discussed above. BAMM is aware that ethyl acrylate has been included on the list of Candidate Chemicals because it is listed on the Proposition 65 list of

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[6] Zhang, J.J. and K.R. Smith, Indoor air pollution: a global health concern. British Medical Bulletin, 2003. 68(1): p. 209-225, available at http://coep.pharmacy.arizona.edu/HOPE/maureen/Indoor%20air%20pollution.pdf.

[7] Lott, S. and J. Vallette, Full Disclosure: A Strategy to Prevent Asthma Through Building Product Selection. 2013, Healthy Building Network, https://healthybuilding.net/uploads/files/full-disclosure-required-a-strategy-to-prevent-asthma-through-building-product-selection.pdf

[8] For example, the Collaborative on Health and the Environment (CHE), which is cited by Lott and Vallette, lists simply "acrylates" without specifying which acrylates are included. It cites only to general references and states, "NOTE: Not all the references are currently available, but they will be added as soon as possible." https://www.healthandenvironment.org/our-work/toxicant-and-disease-database/?showcategory=&showdisease=&showcontaminant=2578&showcas=&showkeyword= The given CHE reference we were able to review, Casarett & Doull's 6th Edition, mentions "acrylic monomers" only as "contact allergens" with no assertion they are asthmagens and no distinction among various acrylic monomers (pp. 659-660). As another example, the Commission de la santé et de la sécurité du travail (CSST), also cited by Lott and Vallette, lists "triacrylate (unspecified)" with no citation. http://www.csst.qc.ca/en/prevention/reptox/occupational-asthma/Pages/bernsteinang.aspx

[9] Go to http://www.aoecdata.org/ExpCodeLookup.aspx and search for "acrylic acid". BAMM's critique of AOEC's rationale for having previously listed acrylic acid is provided as Attachment A.

chemicals known to the State of California to cause cancer. The very strong weight of evidence, however, is that ethyl acrylate is not a human carcinogen. High bolus doses administered by gavage cause forestomach tumors in rodents (an organ not present in humans), but there are tumors in no other tissues, and the weight of evidence is that ethyl acrylate is not genotoxic.

In the 1980s, ethyl acrylate was listed as a Proposition 65 human carcinogen, as well as a possible carcinogen by the International Agency for Research on Cancer (IARC) and reasonably anticipated to be a human carcinogen by the National Toxicology Program (NTP). Due to subsequent scientific understanding, NTP removed ethyl acrylate from the Report of Carcinogens in 2000. IARC has not yet changed ethyl acrylate's classification, but its 2003 Technical Publication 39 on forestomach tumors supports the position that ethyl acrylate is not a human carcinogen. Under current case law, ethyl acrylate must remain listed on Proposition 65 as long as the IARC listing continues, but declassification by IARC should lead to delisting from Proposition 65.

Additional information on why ethyl acrylate should not be considered a carcinogen is given in Attachment B. In addition, BAMM is aware that a manuscript has been submitted to the journal *Toxicology* providing a review of the data for methyl acrylate, ethyl acrylate, butyl acrylate, and 2-ethylhexyl acrylate and concluding that they are unlikely to cause human carcinogenicity. We will provide a copy of this publication when in print.

No other acrylate is listed as a carcinogen by Proposition 65, IARC or NTP. Although sufficiently high levels of acrylates can cause irritation, such effects are highly unlikely in consumers due to the very low levels of residual monomer. The fact that acrylates have an unpleasant odor at very low levels further ensures that consumers will avoid exposures to acrylate monomers at levels that would cause adverse effects.[10]

Therefore, health hazards associated with acrylates are not a basis for including acrylates in Table 4.

Conclusion

For the reasons given herein, acrylates in acrylic coatings and other acrylate-based materials do not pose a cognizable health risk. They therefore should not be included in the final 2018-2020 Work Plan.

If you have any questions, please contact me at (757) 903-2194 or e.hunt@comcast.net.

Sincerely,

Elizabeth Hunt

Elizabeth K. Hunt
Executive Director

[10] For example, the odor threshold for ethyl acrylate is 0.0004 ppm, whereas the recommended 8-hour time-weighted average limit is 5 ppm. SCOEL (2004). Recommendation from the Scientific Committee for Occupational Exposure Limits for Ethyl Acrylate. SCOEL/SUM/47, http://ec.europa.eu/social/BlobServlet?docId=3829&langId=en; ACGIH, 2017 TLVs and BEIs. p. 30.

ATTACHMENT A

SUBSTANCE OF BAMM SEPTEMBER 16, 2016 COMMENTS TO AOEC REGARDING LACK OF SUPPORT FOR ASTHMAGENIC DESIGNATION FOR ACRYLIC ACID

Acrylic acid is an unsaturated carboxylic acid. It reacts as a vinyl compound and as a carboxylic acid. It readily undergoes polymerization and addition reactions. Acrylic acid is highly corrosive to skin and eyes and can cause severe burns. Exposure to mists or vapor at levels above the recommended occupational exposure limits can produce eye, nose, or lung irritation. In the literature, irritation to skin and eyes are reported to occur starting at concentrations of about 1 percent.[1]

Although an irritant, and in contrast to many acrylates, acrylic acid itself does not cause sensitization in animal studies.

We have reviewed the 2012 Review by Dr. Kenneth Rosenman, in which he recommended that acrylic acid be added back to the list of asthmagens, after its removal in 2005.[2] That review cites two case reports in support of that recommendation. These case reports are more than 30 years old and describe the irritating properties of mixtures containing acrylic acid rather than any allergic reaction. There are no other reports that would support designation of acrylic acid as an asthmagen or respiratory sensitizer.

The primary report cited in the 2012 Review (Savonius et al., 1993) describes the case of a 35 year female working in a paper mill.[3] According to the authors, she developed prolonged rhinorrhea, sinusitis, and at a later date asthmatic symptoms when mixing printing inks. After transferring the patient to another task, where she was not exposed to this ink anymore, she stayed "somewhat labile". The authors made their diagnosis based on a challenge with an ink containing acrylic acid, white spirit, ethanol, hydroxy-propanoic acid and bronze powder. No specific challenge with acrylic acid or other ingredients of the ink was made.[4] Only a complex mixture was tested and nothing was reported about the dustiness conditions within the paper mill.

The 2012 Review also states, "There is a case report of urticaria after a skin prick test with acrylic acid," citing to Fowler (1990).[5] In that case, a 36 year old man who handled various chemicals (acrylic resin compounds, acrylic acid, several acid reagents, cyclohexane, methyl

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1 Majka J, Knobloch K, Stetkiewicz J (1974). Evaluation of acute and subacute toxicity of acrylic acid. Medycyna Pracy 25:427-435.

2 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, Unpublished report.

3 Savonius B, Keskinen H, Tuppeainen M, Kanerva L (1993). Clinical and Experimental Allergy 23:416-424, p. 422.

4 The 2012 Review at p. 4 states, "She had a 32% decrease in her peak flow with acrylic acid," but to the extent this is meant to say there was a specific AA challenge it is an incorrect statement. The authors state, "The diagnosis was based on a challenge with *the ink* containing [the five listed ingredients]." Savonius at al. at 422 (emphasis added).

5 Fowler J (1990). Immediate contact hypersensitivity to acrylic acid. Dermatologic Clinics 8:193-195.

isobutyl ketone, phosphoric acid, monobenzyl ether of hydroquinone) developed a recurrent dermatitis. "Immediate hypersensitivity" testing, acrylic acid, 2 % in olive oil, caused itching within 5 seconds and irritation in this dermatitis patient. The author stated that this acrylic acid dilution was "negative" in controls (which did not have pre-damaged skin); he also stated that he had no information about the purity of the acrylic acid he tested. No further evaluations in regard to typical delayed hypersensitivity were performed in this patient. Importantly for purposes of the AOEC A and Rs designations, no respiratory reactions are reported in this publication.

In our opinion these two case reports cited for the recommendation to list AA as a sensitizing asthmagen give no indication that acrylic acid itself has respiratory sensitizing properties in humans. The first study (Savonius et al., 1993) provides no convincing evidence that the asthmatic symptoms in the female worker were due to exposure to acrylic acid. She was exposed to a complex mixture, maybe in combination of dust. There was no specific challenge with acrylic acid; therefore, any conclusion that acrylic acid was the sensitizing agent is speculation. Under these facts, ascribing the observed symptoms to acrylic acid is inappropriate and misleading.

In the second report by Fowler (1990), skin reactions were described in a patient with pre-injured skin, at concentrations already known to be irritating in animal studies. No respiratory reactions were reported. Although characterized by the author as a case of immediate contact urticaria (the only such report associated with acrylic acid), the observed inflammatory reaction more likely was due to the irritation (corrosive) properties of acrylic acid in a patient with pre-damaged skin.

For purposes of designating substances as Occupational Asthmagens on the AOEC List, AOEC has defined occupational asthma as:

> asthma which is acquired de novo from a workplace exposure to a specific substance. This may occur through an immunologic sensitization or by the induction of a chronic asthma state due to an inflammatory response to a non-sensitizing exposure. Although a much broader definition of occupational asthma could include work-aggravated asthma, this working definition focuses on asthma which would not have occurred but for that specific exposure. Work-aggravated asthma will be included only insofar as it refers to a new sensitization or a markedly greater severity of asthma resulting from a new irritant airways response in subjects with previous asthma. Work-aggravated asthma will be excluded where this refers to pre-existing asthma which is not caused, but made symptomatically worse, by inhalation exposures to non-specific substances such as nuisance dust (particles not otherwise classified) or cold, dry air.[6]

Neither an immunologic sensitization nor a direct respiratory reaction based on exposure to acrylic acid is shown by either of the two case reports.

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

The 2012 Review states, "AA meets major criteria #1 and therefore meets the AOEC criteria for an asthmagen." Major Criteria 1 for designating a substance as an asthmagen reads as follows:

> 1. 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 peer-reviewed study should indicate a response to sub-irritant levels of sensitizing substances. Ideally, a positive challenge will be controlled by negative challenges in asthmatic patients who are not believed to be sensitized to the particular substance, though such a design is not routinely used for specific exposure challenges.[7]

This criterion is not met because the Savonius et al. case report did not involve a specific inhalation challenge with acrylic acid. The challenge was done with an ink mixture. Given this exposure to a mixture, it is not possible to ascribe the worker's symptoms to acrylic acid. And given that there is no other report in the literature associating acrylic acid – a high production volume chemical – with occupational asthma, it is dubious that acrylic acid was the asthmagenic agent in that case.

The Savonius paper is the only publication referring to acrylic acid and asthma. Neither it nor the Fowler paper provides sufficient scientific evidence to designate acrylic acid as A or Rs. Neither paper demonstrates that the AOEC criteria for designation of a substance as an asthmagen are met, nor that acrylic acid caused respiratory sensitization or asthma. The usefulness of the AOEC database to clinicians is dependent on the accuracy of its data and reliability of its evaluation of those data against its criteria. Listing of substances that do not meet the criteria could actually hamper proper diagnosis and treatment.

In conjunction with this, we agree with the Methacrylate Producers Association that 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. Acrylates and Methacrylates are distinct groups. Distinguishing among these groupings will assist clinicians in making accurate assessments and advancing research into the causes of asthma.

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[7] Revised protocol at 6.

ATTACHMENT B

RODENT FORESTOMACH TUMORS ARE NOT A BASIS FOR CLASSIFYING ETHYL ACRYLATE AS A CARCINOGEN

The weight of evidence demonstrates that ethyl acrylate does not pose carcinogenic hazard. No tumors have been observed in carcinogenicity studies in which animals were exposed by routes that might be routes of exposure for humans. While forestomach tumors were observed in rats and mice in a study where high doses were administered by gavage, gavage is not an appropriate route of exposure to evaluate the safety of ethyl acrylate in consumer products, where exposure to humans is not by bolus doses and other studies by more appropriate routes exist.

The following summarizes the database of relevant ethyl acrylate studies and their significance for assessing whether ethyl acrylate poses a cancer risk. The Appendix to this Attachment includes references for studies and reviews cited herein as well as other relevant materials.

Summary of Experimental Results

Ethyl acrylate induced no tumors in chronic drinking water studies in rats and dogs (Borzelleca et al., 1964), nor in a chronic inhalation study in rats and mice (DePass et al, 1984), nor in a chronic dermal study in mice (Miller et al., 1985). Ethyl acrylate also did not induce skin tumors in a short-term carcinogenicity study using a transgenic mouse engineered for predisposition to skin tumors (Nylander-French & French, 1998). In 1986, the National Toxicology Program (NTP) reported forestomach tumors in rats and mice receiving high oral doses of ethyl acrylate by gavage daily for two years (NTP, 1986). The tumors were associated with significant point-of-contact irritation as evidenced by high incidence of inflammation and ulceration of the forestomach. Tumors were not reported at any other tissue site.

A substantial body of studies, most performed after the 1986 NTP bioassay, clearly demonstrates that the tumors reported in the NTP study are merely a portal-of-entry effect limited to gavage dosing of the rodent forestomach. As later noted by the NTP, the weight of the evidence is that ethyl acrylate is not genotoxic *in vivo*, and metabolic and pharmacokinetic data indicate that ethyl acrylate is rapidly and completely detoxified in the body (NTP, 1998). Lists of mechanistic and genotoxicity studies are provided in the Appendix to this Attachment, and consideration of these studies is included in the various reviews discussed in the next section of this letter.

Recent studies further support a conclusion that ethyl acrylate-induced forestomach tumors in rodents occur via a non-genotoxic mechanism, consistent with disruption of metabolic detoxification and chronic inflammation resulting in continued induction of cell proliferation, hyperplasia, and ultimately carcinomas. One such study was a Good Laboratory Practice (GLP) OECD TG-488 gene mutation assay using gpt Δ transgenic mice with analyses in liver and forestomach. This model is capable of detecting point mutations and deletions in separate targets. The results demonstrated no direct mutagenic activity of ethyl acrylate in mouse forestomach or liver (Masumori, 2015; Ellis-Hutchings et al., 2016, 2018). In another recent study, ethyl acrylate

was shown to deplete mouse forestomach glutathione at concentrations less than or equal to the tumorigenic dose level (Ellis-Hutchings et al., 2018).

History of Ethyl Acrylate Carcinogenicity Classifications

Following the 1986 study finding forestomach tumors in rodents, the International Agency for Research on Cancer (IARC) classified ethyl acrylate as Group 2B ("possibly carcinogenic to humans") (IARC, 1986), and NTP listed ethyl acrylate as a substance "reasonably anticipated to cause cancer in humans" (NTP, 1989). Since then, various scientists and scientific bodies have questioned the relevance of forestomach tumors to cancer risks in humans, and a general consensus has developed that where tumors are observed in no other tissues and the substance is not genotoxic, then the observation of forestomach tumors is not relevant to human cancer risk assessment (e.*g.*, PCC 1997; IARC, 2003; Proctor et al., 2007; Williams & Iatropoulos, 2009).

In 1998, NTP evaluated the body of data of for ethyl acrylate, including studies it had conducted after its 1986 bioassay. NTP concluded that ethyl acrylate should be considered non-genotoxic in humans, and formally recognized that the forestomach tumors reported in the 1986 study were induced by a mechanism not relevant to human carcinogenesis (NTP, 1998). On that basis, NTP removed ethyl acrylate from its Report on Carcinogens (NTP, 2000).

Similarly, an IARC Working Group in 1999 found that rodent forestomach tumors following gavage dosage are of little relevance to humans where the tumors are not accompanied by evidence of genotoxicity or tumors at other sites (IARC, 2003).[1] The Working Group report included a specific review of ethyl acrylate. Its conclusions, matched with the general IARC conclusions and in line with NTP's conclusions, indicated that ethyl acrylate is an agent for which forestomach tumors should not be used for human hazard assessment (Boorman & Sills, in IARC, 2003).

Subsequent to the IARC Working Group, a 2007 peer-reviewed article concluded that forestomach tumors associated with factors such as those seen for ethyl acrylate should not form the basis for a carcinogenicity classification (Proctor et al., 2007). A 2009 recent peer-reviewed article by two participants in the 2003 IARC Workshop similarly concludes that the forestomach tumors in rodents exposed to ethyl acrylate via gavage are not relevant to assessment of human carcinogenicity (Williams & Iatropoulos, 2009). This is in line with findings of the Presidential/Congressional Commission on Risk Assessment and Risk Management, which in 1997 had included ethyl acrylate forestomach cancer by gavage as a rodent tumor mechanism that may not be relevant to human cancer risk if forestomach tumors are the only responses observed, and those responses are due to local hyperplasia (PCC, 1997, p. 65, Table 4.2).

[1] Since its 1986 listing decision, IARC has reviewed its ethyl acrylate classification once, in 1998 (published in 1999), and retained the Group 2B designation (IARC, 1999). However, this review, which was not a plenary review, took place before NTP had completed its re-evaluation of ethyl acrylate in 1999/2000 and before the IARC Working Group found rodent forestomach tumors following gavage dosing to be of little relevance to human carcinogenicity. In 2007, IARC recognized that BAMM had made "a good case that a re-evaluation of ethyl acrylate may result in a different classification than the most recent evaluation done in 1998" (IARC, 2007).

In 2014, IARC's Advisory Group recommended that ethyl acrylate be re-evaluated as a high priority (IARC, 2014). It concluded (p. 22):

> Cancer studies using other routes of exposure [than gavage] gave negative results. There have been many mechanistic studies carried out over the years suggesting that the forestomach-tumour response may be related to irritation and the proliferative cellular response to deposition of the material in the stomach, calling into question the relevance of this finding to human health hazards.

Other authoritative bodies have completed a full review of ethyl acrylate since 2000, and have delisted the chemical as well. The Michigan Department of Environmental Quality withdrew its classification of ethyl acrylate as a possible carcinogen in 2008 (MDEQ, 2008).[2] Health Canada declined to list ethyl acrylate as "CEPA Toxic" in 2011, indicating it had found ethyl acrylate not to pose a carcinogenic risk to humans (Health Canada, 2011).

Like IARC and NTP, the State of California listed ethyl acrylate as a Proposition 65 carcinogen shortly after the 1986 NTP study.[3] Despite the evidence since then that the forestomach tumors induced by ethyl acrylate are not relevant to humans, California is constrained by judicial and administrative interpretations of the "Labor Code mechanism" from removing ethyl acrylate unless and until IARC changes its classification.[4] IARC has scheduled re-review of ethyl acrylate in June 2018; a determination that ethyl acrylate cannot be classified as a carcinogen would be consistent with IARC's technical publication on forestomach tumors.

Conclusion

The lack of tumors in the drinking water studies and at any site other than the forestomach in the gavage studies, the lack of tumors in chronic inhalation and dermal studies, the weight of evidence that ethyl acrylate is not genotoxic, and the extensive body of mechanistic data together demonstrate that the forestomach tumors seen in the NTP gavage study were due to portal-of-entry effects and not due to any inherent carcinogenicity of ethyl acrylate. Thus, the NTP gavage studies are not appropriate for the evaluation of the safety of ethyl acrylate in human exposure settings.

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[2] Michigan currently has an ITSL air quality standard, which is the standard used for non-carcinogenic air pollutants. *See* Mich. Dep't Envtl. Qual., Air Quality Division, List of Screening Levels, http://www.michigan.gov/documents/deq/deq-aqd-toxics-ITSLALPH_244167_7.pdf.

[3] *See* OEHHA (2016), which shows ethyl acrylate to have been listed July 1, 1989.

[4] *See, e.g., Styrene Information and Research Center v OEHHA*, 210 Cal.App. 4th. 1082 (2013).

APPENDIX

STUDIES AND REVIEWS RELEVANT TO EVALUATION OF ETHYL ACRYLATE CARCINOGENICITY

Reviews

ECETOC (1994). Joint Assessment of Commodity Chemicals No. 28, Ethyl Acrylate, CAS No. 140-88-5. European Centre for Ecotoxicity and Toxicology of Chemicals, http://www.ecetoc.org/wp-content/uploads/2014/08/JACC-028.pdf.

Health Canada (2011). Screening Assessment for the Challenge 2-Propenoic acid, ethyl ester (Ethyl acrylate), http://www.ec.gc.ca/ese-ees/default.asp?lang=En&n=21358CCD-1.

IARC (1986). Ethyl Acrylate *in* IARC Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans: Some Chemicals Used in Plastics and Elastomers, Vol. 39, pp. 81-98, International Agency for Research on Cancer, Lyon, France, http://monographs.iarc.fr/ENG/Monographs/vol1-42/mono39.pdf.

IARC (1999). Ethyl Acrylate *in* IARC Monographs on the Evaluation of Carcinogenic Risks to Humans, Re-evaluation of Some Organic Chemicals, Hydrazine, and Hydrogen Peroxide, Vol. 71, pp. 1447-1457, International Agency for Research on Cancer, Lyon, France, http://monographs.iarc.fr/ENG/Monographs/vol71/index.php.

IARC (2003). Views and Expert Opinions of an IARC Working Group, Lyon, 29 Nov.-1 Dec. 1999, IARC Technical Pub. No. 39, International Agency for Research on Cancer, Lyon, France, http://monographs.iarc.fr/ENG/Publications/techrep39/index.php.

IARC (2007). April 5, 2007 letter from V. Cogliano, Head, Carcinogen Identification and Evaluation Group, to C. Farr, regarding the re-evaluation of ethyl acrylate, International Agency for Research on Cancer, Lyon, France.

IARC (2014). IARC Monographs on the Evaluation of Carcinogenic Risks to Humans, Internal Report 14/002, Report of the Advisory Group to Recommend Priorities for IARC Monographs during 2015-2019, https://monographs.iarc.fr/ENG/Publications/internrep/14-002.pdf.

MDEQ (2008). Interoffice Communication from Gary Butterfield to Ethyl Acrylate File re: Screening Level for Ethyl Acrylate (July 22, 2008). Michigan Department of Environmental Quality, Air Quality Division, Lansing MI.

NTP (1989). Report on Carcinogens, 5th ed. U.S. Department of Health and Human Services, Public Health Service, National Institute of Environmental Health Sciences, National Toxicology Program, Research Triangle Park, N.C., https://ntrl.ntis.gov/NTRL/dashboard/searchResults/titleDetail/PB89231914.xhtml.

NTP (1998). Report on Carcinogens: Background document for ethyl acrylate. December 2-3, 1998, Meeting of the NTP Board of Scientific Counselors Report on Carcinogens Subcommittee. US Department of Health and Human Services, Public Health Service, National Institutes of

Health, National Toxicology Program, Research Triangle Park, N.C., https://ntp.niehs.nih.gov/ntp/newhomeroc/other_background/ethylacryl_noapps_508.pdf.

NTP (2000). Report on Carcinogens, 9th ed. U.S. Department of Health and Human Services, Public Health Service, National Institute of Environmental Health Sciences, National Toxicology Program, Research Triangle Park, N.C.

PCC (1997). Risk Assessment and Risk Management in Regulatory Decision-Making, Final Report Volume 2 (1997). U.S. Presidential/Congressional Commission on Risk Assessment and Risk Management, Washington, DC, http://oaspub.epa.gov/eims/eimscomm.getfile?p_download_id=36372.

Proctor, D.M., Gatto, N.M., Hong, S.J. and Allamneni, K.P. (2007). Mode-of-action framework for evaluating the relevance of rodent forestomach tumors in cancer risk assessment. Toxicol. Sci. 98(2):313-326, http://toxsci.oxfordjournals.org/content/98/2/313.long.

Williams, G.M. and Iatropoulos, M.J. (2009). Evaluation of potential human carcinogenicity of the synthetic monomer ethyl acrylate. Regulatory Toxicology and Pharmacology 53: 6-15.

Principal carcinogenicity bioassays

Borzelleca J et al. (1964). Studies on the chronic oral toxicity of monomeric ethyl acrylate and methyl methacrylate. Toxicol. Appl. Pharmacol. 6:29-36.

DePass L et al. (1984). Dermal oncogenicity bioassays of acrylic acid, ethyl acrylate, and butyl acrylate. J. Toxicol. Environ. Health 14:115-120.

Miller R, et al. (1985). Chronic toxicity and oncogenicity bioassay of inhaled ethyl acrylate in Fischer 344 rats and B6C3F1 mice. Drug Chem. Toxicol. 8:1-42.

NTP (1986). Carcinogenesis Bioassay of Ethyl Acrylate. Technical Report Series 259, Publication (NIH) 82-2515. National Toxicology Program, Research Triangle Park, N.C.

Short-term carcinogenesis study

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Mechanistic studies

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