BASIC ACRYLIC MONOMER MANUFACTURERS, INC.

IARC Has Acknowledged that the Cancer Classification for Ethyl Acrylate Warrants Reevaluation

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Disclaimer

IARC listed ethyl acrylate in 1986 based on the NTP studies showing forestomach tumors in rats and mice. BAMM has asked IARC on multiple occasions to reevaluate its cancer classification, taking into consideration the extensive science that caused NTP to reverse its cancer classification decision. In 2007, the Head of IARC's Carcinogen Identification and Evaluation Group expressly acknowledge that BAMM members "make a good case that a re-evaluation of ethyl acrylate may result in a different classification," but IARC has not yet undertaken that reevaluation because of competing priorities.

In 1999, an IARC Working Group reviewed ethyl acrylate and other animal forestomach carcinogens to determine their predictive value in assessing carcinogenic risks to humans. Describing the ethyl acrylate situation, the Working Group concluded generally that:

> the relevance [of rodent forestomach tumors] for humans is probably limited for agents that have no demonstrable genotoxicity and that are solely carcinogenic for the forestomach squamous epithelium in rodents after oral administration, since the exposure conditions are quite different between the experimental animals and humans. (IARC 2003, p. 13).

With respect to ethyl acrylate, the Working Group stated further that it "appears to be clastogenic to mammalian cells *in vitro* but not *in vivo*" and described it as:

> an example of a chemical that induces forestomach tumours in both sexes of two species of rodents when given by gavage, but only after prolonged exposure. When delivered by inhalation, in the drinking-water or by skin application, ethyl acrylate does not increase the incidence of tumours at any site. (IARC 2003, p. 11).

Accordingly, ethyl acrylate matched the Working Group's description of an agent of little relevance to human carcinogenicity. The Working Group cited a review by two National Institutes of Environmental Health Sciences (NIEHS) researchers, which concluded:

> There is no evidence of carcinogenicity of ethyl acrylate when given by inhalation to rats and mice. There is no evidence of carcinogenicity of ethyl acrylate in skin painting studies in outbred or transgenic mice. Ethyl acrylate is clastogenic *in vitro* but not *in vivo*. Ethyl acrylate does not bind to deoxyribonucleosides *in vitro*. Ethyl acrylate is not mutagenic in bacteria. Ethyl acrylate reacts spontaneously with glutathione and protein sulfhydryl groups in many tissues including the forestomach. Ethyl acrylate at doses that produce forestomach tumours also produces evidence of toxicity. Further, it appears that a certain time of sustained hyperplasia of the forestomach is required for effective tumorigenesis of ethyl acrylate in the forestomach of rats. (Boorman and Sills, 2003).

The IARC Working Group's conclusions indicate that the rodent forestomach tumors induced by ethyl acrylate are not relevant to humans.

BAMM will continue to encourage IARC to reevaluate its cancer classification of ethyl acrylate. The extent and magnitude of human exposure is an important criterion for IARC when setting priorities. Because human exposure to ethyl acrylate is very limited, it is difficult to predict when IARC might reconsider its outdated cancer classification of ethyl acrylate.

References:

1. Letter from Vincent Cogliano, PhD, Head, Carcinogen Identification and Evaluation Group, 5 April 2007.

2. International Agency for Research on Cancer (1986). Ethyl Acrylate: 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.

3. International Agency for Research on Cancer (1999). IARC Monographs on the Evaluation of Carcinogenic Risks to Humans, Vol. 71, Re-evaluation of Some Organic Chemicals, Hydrazine, and Hydrogen Peroxide, Summary of Data Reported and Evaluation, Lyon, IARC Press.

4. International Agency for Research on Cancer (2003). Summary Report: Predictive value of rodent forestomach and gastric neuroendocrine tumours in evaluating carcinogenic risks to humans, Technical Publication No. 39, pp 7-14.

5. Boorman G.A. and R.C. Sills. (2003). Ethyl Acrylate. Environmental Toxicology Program, National Institute of Environmental Health Sciences. Research Triangle Park, N.C.