

**STATE OF MICHIGAN**  
**Rick Snyder, Governor**



**DEPARTMENT OF ENVIRONMENTAL QUALITY**  
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September 19, 2017

**Response to Public Comments for**  
**Propylene (CAS # 115-07-1)**

**Summary:**

Based on public comments, the Michigan Department of Environmental Quality (MDEQ), Air Quality Division (AQD) has reviewed the Initial Threshold Screening Level (ITSL) for propylene. Based on that review, the AQD agrees with the commenter that the ITSL basis needs to be updated. Therefore, the ITSL is changed from 1,500  $\mu\text{g}/\text{m}^3$  (annual averaging time) to 8,600  $\mu\text{g}/\text{m}^3$  (8-hour averaging time).

**Background:**

Revisions to the Air Pollution Control Rules<sup>1</sup> were promulgated December 22, 2016. Subsequently, AQD published toxic air contaminant screening levels and their basis as required by Rule 230(1). Pursuant to Rule 230(2), the AQD solicited and received public comments on these screening levels for 60 days: February 14 through April 14, 2017. The AQD must respond to these comments within 180 days; the latest date for response is October 11, 2017.

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<sup>1</sup> Air Pollution Control Rules in Michigan Administrative Code promulgated pursuant to Article II Pollution Control, Part 55 (Sections 324.5501-324.5542), Air Pollution Control, of the Natural Resources and Environmental Protection Act, 1994. PA 451, as amended (NREPA).

## **Comments and Responses:**

### ***Comment:***

The 1985 National Toxicology Program (NTP) study that is the basis of the proposed propylene ITSL (1,500 µg/m<sup>3</sup>) is out of date and MDEQ should consider more recent scientific information. Moreover, MDEQ should recognize the relatively mild nature of the nasal lesions, in addition to the relatively few animals affected in the NTP study. Finally, MDEQ should recognize the significant differences in nasal physiology and breathing patterns between rats and humans.

MDEQ should include scientific information available subsequent to the 1985 NTP study in its evaluation. This scientific information includes: 1) findings from Drs. Jack Harkema and Gordon Hard regarding the critical effects (i.e., increased incidence of squamous metaplasia of the respiratory epithelia of the nasal cavity in male and female rats and increased incidence of chronic focal inflammation of the kidney in male and female mice) identified in the NTP study; and 2) scientific research evaluated under the Organization for Economic Co-operation and Development (OECD) Screening Information Data Set (SIDS) program.

Drs. Harkema and Hard conducted independent peer reviews of the microscopic archived tissue slides from the NTP study and provided robust summaries of these expert reviews (Harkema, J. 2002. Histopathology Report: Evaluation of Nasal Cavity Slides from NTP Inhalation Studies of Propylene in Rats and Mice for the American Chemical Council, and Hard, G. 2001. Expert report on renal histopathology changes in mouse and rat inhalation studies with propylene). These reviews are provided as attachments to these comments.

The 2002 Harkema report clearly described that there was no obvious dose-response relationship in either the rats or mice exposed by chronic inhalation to propylene (5,000 or 10,000 ppm). The nasal histopathology review indicates that this chemical agent induces mild rhinitis (nasal inflammation) and associated epithelial alterations suggesting chronic, low-grade irritation in these rodents without any obvious dose-response relationship. This may suggest a possible threshold effect at the low dose (5,000 ppm) for most of the observed nasal lesions.

The 2001 Hard report concludes that the inflammatory changes observed in the mouse kidney represent a spontaneous lesion without any toxicological significance. The presence of perivascular and cortical infiltrates of lymphoid cells in propylene exposed mice of both sexes was confirmed by histopathology re-evaluation. However, the background of similar change in the control mice was almost as high as for the exposed groups. Propylene did not cause exacerbation of spontaneous chronic progressive nephropathy and there was not any evidence of renal tubule toxicity.

The studies under the OECD SIDS program include: 1) a GLP OECD 414 guideline developmental toxicity study, 2) a GLP OECD 474 guideline micronucleus study, 3) a

GLP-compliant cell proliferation study, 4) two GLP OECD 471 guideline Ames studies and 5) an in vivo mutagenesis hprt assay. These studies were reviewed for scientific quality and reliability by an international scientific body as part of the OECD High Production Volume Chemical Program. In addition, the robust study summaries and other SIDS documents were approved by the international community at the SIDS Initial Assessment Meeting in May 2003.

The Hard and Harkema reports were also peer-reviewed by the OECD SIDS Initial Assessment Meeting (SIAM) participants and were accepted in the OECD SIDS dossier and the Screening Information Assessment Report (SIAR), which provides further evidence of their acceptance as valid and important expert reviewers of specific findings in the NTP studies. Propylene was determined to be a “low priority” for further work in the SIDS Initial Assessment Meeting (SIAM 16).<sup>[2]</sup>

In 2003, ACGIH proposed a Threshold Limit Value (TLV) for propylene based in part on the NTP’s 1985 study. The Panel submitted comments to ACGIH (Price, C. 2003), which revised the TLV documentation for propylene accordingly. In addition, NTP, in a 2002 letter to the Panel, agreed with Dr. Hard’s comments from the new research and to the rationale provided by the independent peer reviews by Drs. Harkema and Hard (Hailey, 2002).

**Response:**

The AQD reviewed the submitted comments and recommended articles for propylene. AQD agrees with the commenter that the ITSL was based on older information and the more recent ACGIH TLV may be a more appropriate ITSL basis. The ITSL was based on an NTP (1985) study that found an increased incidence of chronic focal inflammation in the kidney in male and female mice and an increased incidence of squamous metaplasia of the respiratory epithelia of the nasal cavity in female rats. The review of NTP renal histopathology slides by Hard (2001) and nasal cavity slides by Harkema (2002) revealed new information of the respective lesions. The ACGIH (2006) review is more recent and accounts for the Hard (2001) and Harkema (2002) information as well as other more recent studies. ACGIH used the NTP (1985) study LOAEL of 5,000 ppm as a key study in their determination of the TLV-TWA of 500 ppm (860 mg/m<sup>3</sup>). The AQD agrees with the information and with the commenter that the ACGIH TLV-TWA of 500 ppm (860 mg/m<sup>3</sup>) is an appropriate basis for deriving the ITSL. Therefore, the ITSL is changed from 1,500 µg/m<sup>3</sup> (annual averaging time) to 8,600 µg/m<sup>3</sup> (8-hour averaging time). The ITSL was derived according to Rule 232(1)(c) as (occupational exposure level) ÷ 100, for the protection of the general population including sensitive subgroups from lifetime exposure.

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<sup>[2]</sup> See Summary Conclusions of the SIAR (May 2003), available at <http://webnet.oecd.org/hpv/UI/handler.axd?id=05bca44c-4720-4926-843d-6539599b3de4>.

### **Summary and Conclusions:**

Based on the public comments, the AQD has reviewed the Initial Threshold Screening Level for propylene. The AQD agrees with the commenter that the ITSL basis was outdated and not the most appropriate. Therefore, the ITSL is changed from 1,500  $\mu\text{g}/\text{m}^3$  (annual averaging time) to 8,600  $\mu\text{g}/\text{m}^3$  (8-hour averaging time).

The primary AQD reviewer for these comments was Doreen Lehner, AQD Toxicologist. The secondary (peer) reviewer was Bob Sills, AQD Toxics Unit Supervisor.

### **References:**

ACGIH. 2006. Propylene. TLVs and BEIs Based on the Documentation of the Threshold Limit Values for Chemical Substances and Physical Agents & Biological Exposure Indices. ACGIH Worldwide Signature Publications.

Hard. 2001. Expert Report on Renal Histopathologic changes in mouse and rat Inhalation Studies with Propylene. Prepared for American Chemistry Council Olefins Panel, 1300 Wilson Boulevard, Arlington, VA 22209.

Harkema. 2002. Histopathology Report: Evaluation of Nasal Cavity Slides from NTP Inhalation Studies of Propylene in rats and mice for the American Chemical Council. 1300 Wilson Boulevard, Arlington, VA 22209.

NTP. 1985. Toxicology and Carcinogenesis studies of propylene (CAS No. 115-07-1) in F344/N rats and B6C3F1 mice (inhalation studies). National Toxicology Program. U.S. Department of Health and Human Services. Public Health Service. National Institute of Health. NTP TR 272. NIH Publication No. 86-2528.

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