The Office of Environmental Health Hazard Assessment (OEHHA) has determined that TRIM® VX meets the criteria for listing under Proposition 65 via the authoritative bodies mechanism. This determination is based on conclusions by the National Toxicology Program (NTP) that TRIM® VX causes cancer, and on the scientific evidence relied on by NTP. NTP is designated as an authoritative body for purposes of listing chemicals as causing cancer pursuant to Title 27, Cal. Code of Regs., section 25306. TRIM® VX will therefore be added to the Proposition 65 list as a chemical known to cause cancer.

OEHHA made this determination after reviewing public comments on the proposed listing of TRIM® VX. On January 26, 2018, OEHHA issued a Notice of Intent to List (NOIL) “TRIM® VX” under Proposition 65 as a chemical known to the state to cause cancer. The action was based on Proposition 65 statutory requirements and on the authoritative bodies provision of the Proposition 65 implementing regulations, Section 25306. This document responds to public comments received on the Notice of Intent to List TRIM® VX under Proposition 65.

Under Section 25306, a chemical has been “formally identified” as causing cancer by an authoritative body if: (1) the chemical has been included in a list of chemicals causing cancer published by the authoritative body; is the subject of a report which is published by the authoritative body and which concludes that the chemical causes cancer; or has been “otherwise identified” as causing cancer by the authoritative body in a document that indicates that the identification is a final action; and (2) if the list, report, or document meets specified criteria in Section 25306(d)(2).
OEHHA has reviewed the conclusions and statements in the 2016 NTP Technical Report on the Toxicology and Carcinogenesis Studies of TRIM® VX in Wistar Han [Crl:WI (Han)] Rats and B6C3F1/N Mice (Inhalation Studies). OEHHA has determined that these conclusions and statements satisfy the Section 25306(d)(1) requirements. Specifically, TRIM® VX is the subject of a report published by the authoritative body that concludes that TRIM® VX causes cancer; and that the report meets the Section 25306(d)(2) requirements, thus satisfying the formal identification criteria in the Proposition 65 regulations. NTP’s conclusions in the report on which OEHHA relies include the following:

NTP states in the Conclusion section of the report’s Summary (page 6):

“We conclude that exposure to aerosols of TRIM VX caused tumors of the lung in male and female mice.…”

NTP states in the Conclusion section of the report’s Abstract and main body of the report (pages 9 and 71, respectively):

“Under the conditions of these 2-year inhalation studies… There was clear evidence of carcinogenic activity of TRIM VX in male B6C3F1/N mice based on the increased combined incidences of alveolar/bronchiolar adenoma or carcinoma of the lung.”

“There was clear evidence of carcinogenic activity of TRIM VX in female B6C3F1/N mice based on the increased combined incidences of alveolar/bronchiolar adenoma or carcinoma (primarily carcinoma) of the lung.” (Emphasis in original)

The evidence cited by NTP in support of these conclusions was reviewed by OEHHA with regard to the sufficiency of evidence criteria in Section 25306(e)(2). Based on NTP’s conclusions and the data relied on by NTP in reaching those conclusions, OEHHA has determined that TRIM® VX meets the sufficiency of evidence criteria in Section 25306.

The January 26, 2018 notice initiated a 30-day public comment period. Comments on the Notice of Intent to List were submitted by the following organizations:

- Independent Lubricant Manufacturers Association (ILMA)

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6 NTP (2016). Full citation provided in footnote 2.
7 Ibid.
OEHHA reviewed all of the comments and accompanying materials submitted in the context of the regulatory criteria for listing chemicals under the authoritative bodies mechanism in Section 25306.

Comments relevant to the NOIL are summarized, grouped, and numbered by topic, and responses follow below.

1. Concerns regarding dose selection and test material

Comment 1a:
ILMA expressed concerns about the doses tested in the NTP studies, concluding that the studies fail to meet the criteria in Section 25306. MFS agrees with ILMA’s comments.

“…NTP erroneously selected an inappropriate dose level…The highest dose level of 100 mg/m³ selected for two-year study was too high because fibrosis was seen in both male and female rats and mice at that level in the 90-day study; 50 mg/m³ would have been the more appropriate choice.”

“Dr. Brock also questioned the selection of 100 mg/m³ dose level during his comments at the Panel meeting…”

“…the exposure concentrations used in these studies were considerably higher than those encountered in an occupational setting.” (quoted by ILMA from its February 6, 2016 letter to NTP, commenting on the NTP Draft Technical Report)

“From ILMA’s perspective, the NTP’s election to choose a dose level of 100 mg/m³ when the 50 mg/m would have provided an appropriate level is tantamount to disregarding scientifically valid data… the NTP study fails to meet the objective criteria OEHHA uses to list chemicals under its Authoritative Bodies listing mechanism.”

Response:
ILMA submitted comments on the same dose selection issues to NTP, both in written form and in oral form at the NTP Technical Reports Peer Review Panel meeting on February 16, 2016. The NTP Technical Reports Peer Review Panel discussed these

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8 ILMA submitted written comments to NTP on February 6, 2016 on the Draft NTP Technical Report on Trim® VX.
issues at their meeting, and accepted the Draft Technical Report’s conclusions as written (See Appendix K of the NTP Technical Report\textsuperscript{9} for a summary of the meeting). Appendix K also documents that “Dr. Elwell, the first [peer] reviewer, stated that overall the report was well written and the results supported the conclusions.”

According to Section 25306(f),

\begin{quote}
“The lead agency shall find that a chemical does not satisfy the definition of “as causing cancer” if scientifically valid data which were not considered by the authoritative body clearly establish that the chemical does not satisfy the criteria of subsection (e), paragraph (1) or subsection (e), paragraph (2).”
\end{quote}

Section 25306(f) does not apply here, since NTP, as well as the NTP Technical Reports Peer Review Panel, considered the issues raised by ILMA regarding the doses tested in the NTP studies, and concluded that the studies in male and female mice each provide “clear evidence of carcinogenic activity”, based on increased combined incidences of alveolar/bronchiolar adenoma or carcinoma of the lung.

The issues raised in this comment do not call into question the sufficiency of evidence in the NTP report. Instead, they find fault with NTP’s dose selection for these studies. These issues were considered and rejected by NTP.

OEHHA cannot substitute its scientific opinion, or the opinions of private parties, for that of NTP. The law, regulations, and legal cases that have interpreted the Authoritative Bodies listing process under Proposition 65 clearly delineate OEHHA’s role in the listing process. See for example, Exxon Mobil Corp. v OEHHA\textsuperscript{10}, which discusses in depth the role of OEHHA in reviewing the evidence relied on by the authoritative body when it identifies a chemical as a carcinogen or reproductive toxicant. The Exxon case dealt directly with the issue of what constitutes “substantial evidence” in the context of authoritative body listings. OEHHA finds the NTP report meets the sufficiency of evidence criteria in Section 25306. OEHHA’s decision to list TRIM® VX based on the NTP Technical Report designation is consistent with the decision in the Exxon case.

\textbf{Comment 1b:}

ILMA expressed concerns about the test substance used in the NTP studies, concluding that the studies fail to meet the criteria in Section 25306. ILMA raised issues about the 12-month recommended shelf life for TRIM® VX, the changes that occur in the

\textsuperscript{9} NTP (2016). Full citation provided in footnote 2.

composition of TRIM® VX over time, storage conditions, and the NTP’s use of samples of TRIM® VX that were 30.5 months old at the conclusion of the 2-year studies. MFS agrees with ILMA’s comments.

“ILMA commented extensively in written submissions to NTP on its Draft and Final Technical Report and made oral presentations during the Peer Review Panel that reviewed the draft conclusions. The Association expressed concerns with the manner in which the NTP study was conducted and the conclusions reached.”

“The NTP Peer Review Panel also expressed serious reservations about the sample and its treatment…” (ILMA)

“Neither the ‘Materials and Methods’ section nor the ‘Chemical Characterization and Generation of Chamber Concentration’ section adequately addressed the concerns ILMA raised multiple times.” (ILMA)

Response:
ILMA submitted comments on the same test substance-related issues to NTP, both in written form\(^1\) and in oral form at the NTP Technical Reports Peer Review Panel meeting on February 16, 2016. The NTP Technical Reports Peer Review Panel discussed these issues at their meeting, and accepted the Draft Technical Report’s conclusions as written (See Appendix K of the NTP Technical Report\(^2\) for a summary of the meeting). Appendix K also documents that “Dr. Elwell, the first [peer] reviewer, stated that overall the report was well written and the results supported the conclusions.”

NTP, as well as the NTP Technical Reports Peer Review Panel, considered the issues raised by ILMA regarding the test substance used in the NTP studies, and concluded that the studies in male and female mice each provide “clear evidence of carcinogenic activity”, based on increased combined incidences of alveolar/bronchiolar adenoma or carcinoma of the lung\(^3\).

As noted in response to Comment 1a, OEHHA cannot substitute its scientific opinion, or the opinions of private parties, for that of NTP. OEHHA must act based on NTP’s determination that a chemical causes cancer if the NTP relied on sufficient evidence as defined under the regulation. The issues raised in this comment do not call into

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\(^1\) ILMA submitted written comments to NTP on February 6, 2016 on the Draft NTP Technical Report on Trim® VX.

\(^2\) NTP (2016). Full citation provided in footnote 2.

\(^3\) *Ibid.*
question the sufficiency of evidence in the NTP report. Instead, they find fault with NTP’s methodologies. These issues were considered and rejected by NTP.

2. Other comments

Comment 2a:
MFS requests that OEHHA withdraw the Notice of Intent to List TRIM® VX because the listing is unnecessary, since TRIM® VX is no longer in production, and it cannot be ordered or obtained from any source worldwide.

Response:
OEHHA acknowledges the comment. However, consideration of the production and availability of a chemical for purchase is not part of the criteria for listing a chemical under Proposition 65. If there are no exposures in California to significant amounts of the chemical, no warning is required and the discharge prohibition does not apply.

Comment 2b:
ILMA states, “If OEHHA proceeds with its Prop 65 listing for the discontinued product TRIM® VX, it must carefully articulate that it is only listing that product.” MFS agrees with ILMA’s comments.

Response:
OEHHA’s Notice of Intent to List TRIM® VX clearly indicates that the sole chemical substance that is the subject of that notice is TRIM® VX. As stated above, OEHHA has determined that TRIM® VX meets the sufficiency of evidence criteria in Section 25306, and TRIM® VX will therefore be listed as known to cause cancer under Proposition 65.