

Peer Review of NTP Technical Reports on Antimony Trioxide and TRIM[®] VX

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National Institute of Environmental Health Sciences

NTP Board of Scientific Counselors Meeting



National Toxicology Program Technical Reports

- NTP conducts rodent toxicity and cancer studies on agents of public health concern to identify potential hazards for human health
- NTP technical reports describe the methods, results, and NTP conclusions as “levels of evidence” for carcinogenic activity under the specific conditions of the study



Levels of Evidence of Carcinogenic Activity

Clear evidence: Dose-related (i) increase of malignant neoplasms, (ii) increase of a combination of malignant and benign neoplasms, or (iii) marked increase of benign neoplasms if there is an indication from this or other studies of the ability of such tumors to progress to malignancy

Some evidence: Chemical-related increased incidence of neoplasms in which the strength of the response is less than that required for clear evidence

Equivocal evidence: Marginal increase of neoplasms that may be chemical related

No evidence: No chemical related increase in neoplasms

Inadequate study: Major limitations preclude interpretation



- Review and evaluate the scientific and technical elements of the study and its presentation
- Determine whether the study's experimental design, conduct, and results support the NTP's conclusions regarding the carcinogenic activity and toxicity of the substance tested



Technical Report Peer Review Panel

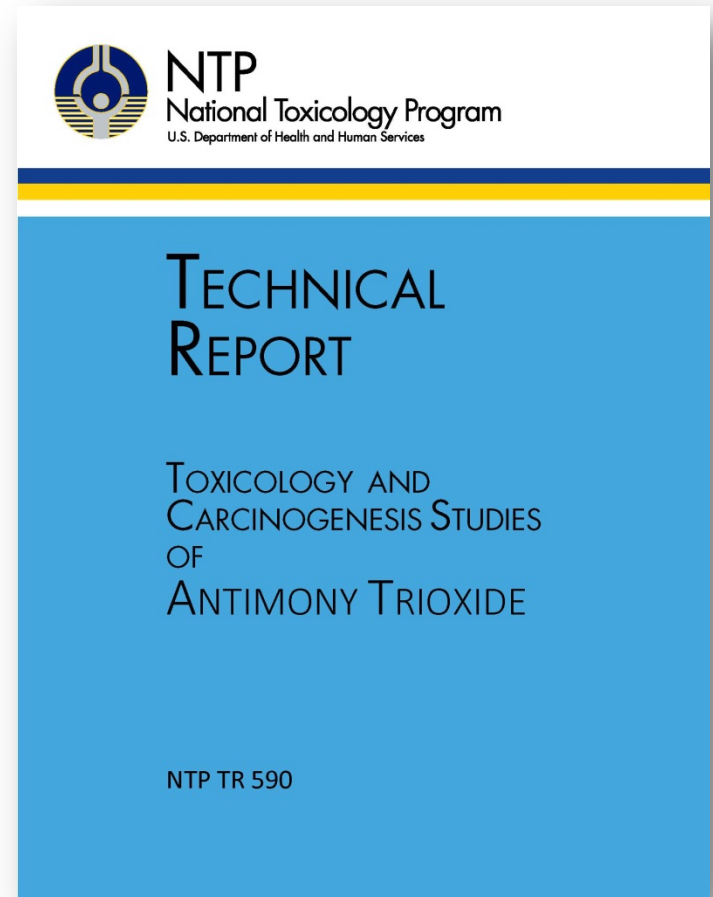
- Jon C. Mirsalis, PhD, SRI International (Panel Chair)
- William J. Brock, PhD, DABT, Brock Scientific Consulting, LLC
- Michael R. Elwell, DVM, PhD, Covance Laboratories, Inc.
- Kent E. Pinkerton, PhD, University of California
- Michael V. Pino, DVM, PhD, Consultant
- Tara Sabo-Attwood, PhD, University of Florida
- Madhuri Singal, PhD, DABT, Reckitt Benckiser

- George B. Corcoran, PhD, ATS, Wayne State University (BSC Liaison)



Draft Technical Reports Peer Reviewed

- Antimony Trioxide
 - Primary form of antimony in the atmosphere
 - Most commercially significant form of antimony
 - Primarily used as a flame retardant
 - NTP conducted inhalation studies in rats and mice





Antimony Trioxide (TR-590)

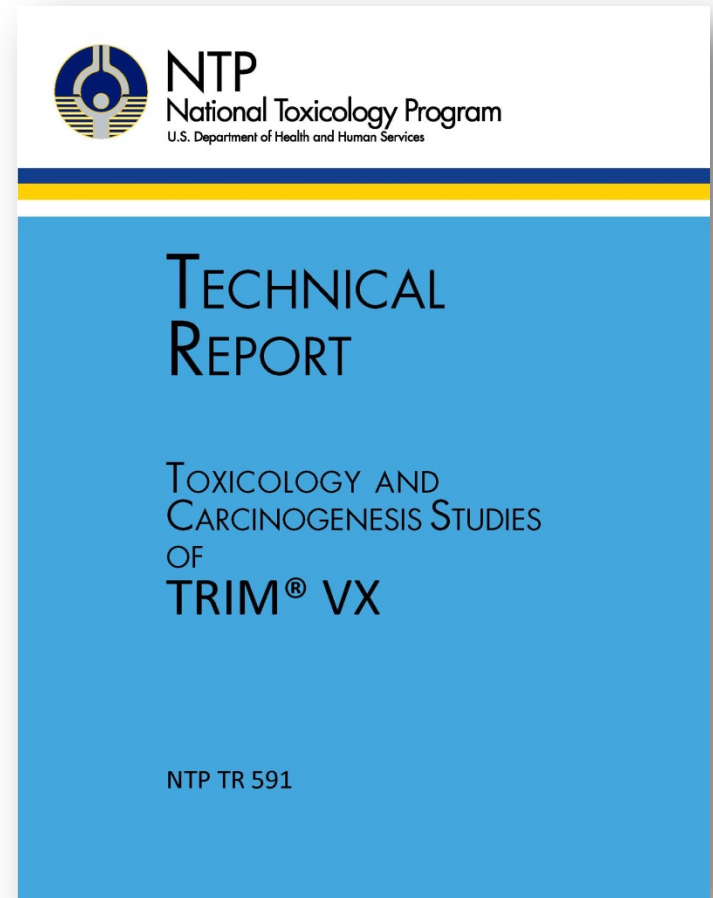
- Male Rats: Some Evidence
 - Increase in combined incidences of alveolar/bronchiolar adenoma or carcinoma of the lung
 - Increase in benign pheochromocytoma of the adrenal medulla
- Female Rats: Some Evidence
 - Increase in alveolar/bronchiolar adenoma of the lung
 - Increase in combined incidences of benign or malignant pheochromocytoma of the adrenal medulla
- Male Mice: Clear Evidence
 - Increase in alveolar/bronchiolar carcinoma of the lung
- Female Mice: Clear Evidence
 - Increased alveolar/bronchiolar adenoma and carcinoma of the lung
 - Increased incidence of malignant lymphoma

Unanimous vote to accept



Draft Technical Reports Peer Reviewed

- Trim[®] VX
 - A metal working fluid (MWF) used in machining processes
 - One of four MWFs studied by the NTP
 - Within the soluble oil class of MWFs
 - Complex mixture of various components (oils, detergents, surfactants, biocides, lubricants, and other ingredients)
 - NTP conducted inhalation studies in rats and mice





- Male Rats: Equivocal Evidence
 - Occurrence of alveolar/bronchiolar adenoma or carcinoma of the lung
- Female Rats: Equivocal Evidence
 - Occurrences of alveolar/bronchiolar adenoma of the lung
- Male Mice: Clear Evidence
 - Increased combined incidences of alveolar/bronchiolar adenoma or carcinoma of the lung
- Female Mice: Clear Evidence
 - Increased combined incidences of alveolar/bronchiolar adenoma or carcinoma (primarily carcinoma) of the lung

Unanimous vote to accept

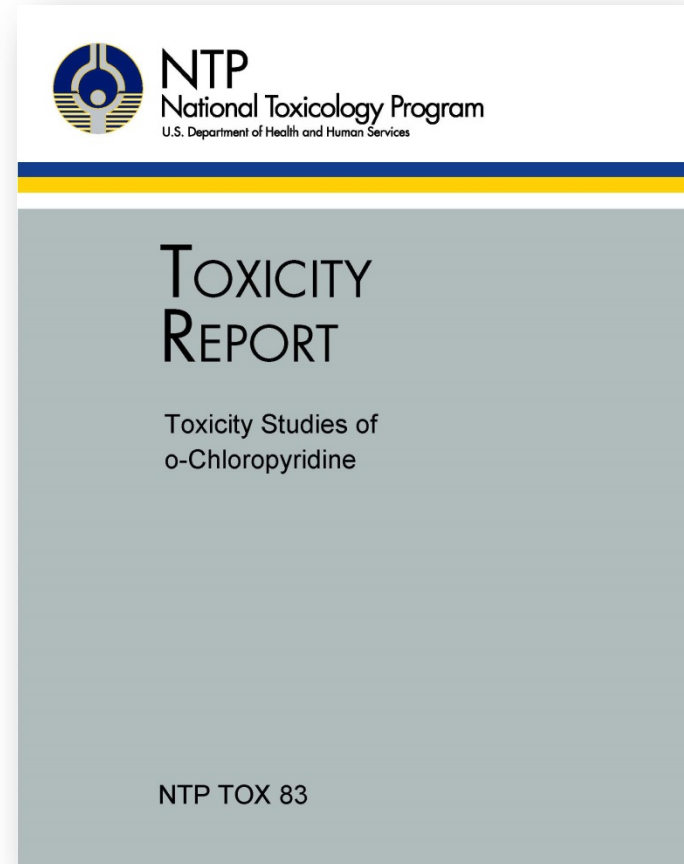


Upcoming Technical Reports

- Next Draft NTP Technical Reports for peer review:
 - Dietary Zinc (TR-592):
 - Element with deficiencies in populations and with potential excesses via dietary supplements
 - Feed studies of zinc deficiency and excess in rats
 - 2,3 Butanedione (TR-593)
 - A butter flavoring agent
 - Inhalation studies in rats and mice
 - p-Chloro-a,a,a-trifluorotoluene (PCTFT) (TR-594)
 - A solvent in paints and coatings and an intermediate in chemical synthesis
 - Inhalation studies in rats and mice



- NTP Toxicity Reports:
 - Typically present the findings for thirteen week studies
 - Lack the level of evidence categories
 - Draft reports are letter reviewed by external experts
 - Final report posted to NTP website

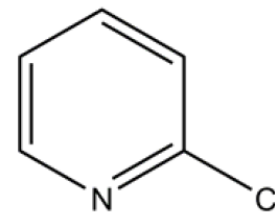




Coming up for Letter Review

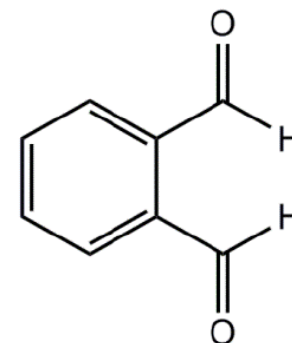
- o-Chloropyridine (TOX-83)

- Intermediate in chemical synthesis
- 2 week dermal study in rats and mice
- 13 week drinking water study in rats and mice



- o-Phthalaldehyde (TOX-84)

- Chemical disinfectant commonly used for dental and medical instruments
- 13 week inhalation study in rats and mice

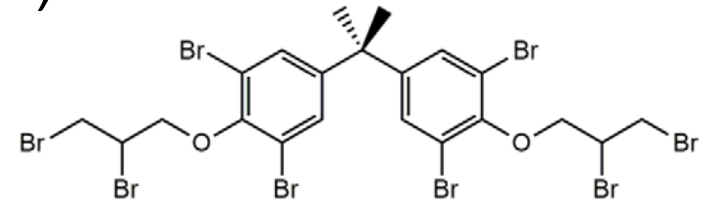




Coming up for Letter Review

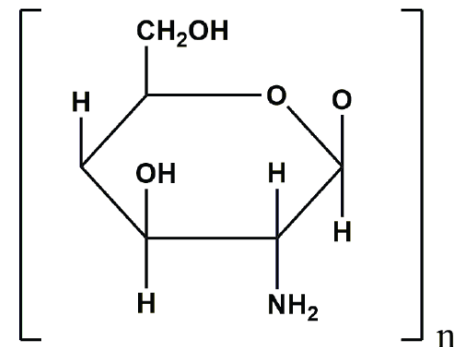
- Tetrabromobisphenol A-bis (2,3-dibromopropyl ether) (TBBPA-DBPE) (TOX-85)

- Used as a flame retardant
- 13 week gavage study in rats and mice



- Chitosan (TOX-93)

- Polymer derived from deacetylation of chitin
- Variety of uses, including as a dietary supplement
- 24 week feed study in rats





Questions