

Peer Review of Draft NTP Technical Reports

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National Toxicology Program (NTP) 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
 - p-Chloro- α,α,α -trifluorotoluene (PCTFT)
 - 2,3-Butanedione
 - Dietary Zinc



Levels of Evidence (LOE) of Carcinogenic Activity

- **Clear evidence of carcinogenic activity**
 - 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 of carcinogenic activity**
 - Chemical-related increased incidence of neoplasms in which the strength of the response is less than that required for clear evidence
- **Equivocal evidence of carcinogenic activity**
 - Marginal increase of neoplasms that may be chemical related
- **No evidence of carcinogenic activity**
- **Inadequate study**



Factors for Consideration in Applying LOE Categories

- Statistics
- Dose-relationship
- Common versus uncommon lesions
- Concurrent and historical control data
- Multiplicity
- Latency
- Progression: benign to malignant and metastases
- Pre-neoplastic lesions
- Survival
- Body weight effects
- Structure-activity correlations
- Genetic toxicology
- Findings in the other sex or species
- Combinations of neoplasms in the same tissue



- Wistar Han [Crl:WI (Han)] Rat
 - 2,3-Butanedione: last of seven recent studies with this rat

- Hsd:Sprague Dawley SD Rat
 - PCTFT: one of two recent studies using NTP-2000 diet
 - Dietary Zinc: used a unique diet of AIN-93M in this study



LOE Guidelines for Stating Conclusions

- LOE determinations are made independently for each sex and each species
- Doses are not included in the call except for “no evidence” calls
- The top call for each sex/species is made and the remaining calls are written in narrative text as:
 - “... were also related to chemical exposure.” (Some evidence)
 - “... may have been related to chemical exposure.” (Equivocal evidence)



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