

# **Report on the NTP Technical Reports Peer Review Panel Meeting May 22, 2014**

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National Institute of Environmental Health Sciences

**NTP Board of Scientific Counselors Meeting  
December 9-10, 2014**



- 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

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**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

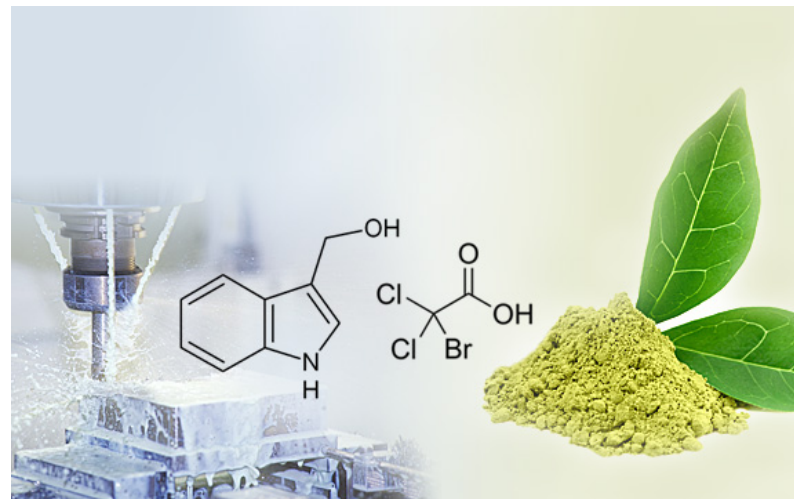
**No evidence:** No chemical related increase in neoplasms

**Inadequate study:** Major limitations preclude interpretation



# Draft Technical Reports Peer Reviewed

- Bromodichloroacetic acid (TR-583)
  - F344/NTac Rats and B6C3F1/N Mice
- Indole-3-Carbinol (TR-584)
  - Harlan Sprague Dawley Rats and B6C3F1/N Mice
- Green Tea Extract (TR-585)
  - Wistar Han Rats and B6C3F1/N Mice
- Cimstar 3800 (TR-586)
  - Wistar Han Rats and B6C3F1/N Mice





# Technical Reports Peer Review Panel

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- Hillary Carpenter III, PhD, Minnesota Department of Health, Retired (Panel Chair)
- Michael W. Conner, DVM, Theravance, Inc
- Michelle V. Fanucchi, PhD, University of Alabama
- Charles R. Mahrt, DVM, MS, PhD, Eli Lilly and Company
- Jon C. Mirsalis, PhD, SRI International
- Gary H. Perdew, PhD, Pennsylvania State University
- Karen Regan, DVM, Research Pathology Services, LLC
  
- Sonya Sobrian, PhD, Howard University (BSC Liaison)



- 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



# Bromodichloroacetic acid (TR-583)

- Drinking water disinfection by-product
- The panel recommended accepting the conclusions (6 yes, 0 no, 0 abstentions) with following changes:
  - Recommended equivocal evidence instead of some evidence based on tumors of the brain and within the oral cavity of male rats
  - Recommended equivocal evidence instead of some evidence based on tumors of the brain in female rats

<b>Sex/Species</b>	<b>Level of Evidence</b>	<b>Neoplastic Lesions</b>
Male Rats	Clear Evidence	Malignant mesothelioma and the combined incidences of epithelial tumors of the skin
Female Rats	Clear Evidence	Fibroadenoma and carcinoma of the mammary gland
Male Mice	Clear Evidence	Hepatocellular carcinoma and hepatoblastoma and increased incidences of adenoma or carcinoma (combined) of the Harderian gland
Female Mice	Clear Evidence	Hepatocellular adenoma, hepatocellular carcinoma, and hepatoblastoma



# Indole-3-Carbinol (TR-584)

- Dietary supplement; Breakdown product from consumption of cruciferous vegetables
- The panel recommended accepting the conclusions as written (4 yes, 2 no, 0 abstentions)

<b>Sex/Species</b>	<b>Level of Evidence</b>	<b>Neoplastic Lesions</b>
Male Rats	No Evidence	75, 150, 300 mg/kg
Female Rats	Some Evidence	Malignant uterine neoplasms (primarily adenocarcinoma)
Male Mice	Clear Evidence	Liver neoplasms (hepatocellular adenoma, hepatocellular carcinoma, and hepatoblastoma)
Female Mice	No Evidence	62.5, 125, 250 mg/kg





# Green Tea Extract (TR-585)

- Botanical dietary supplement
- The panel recommended accepting the conclusions with one edit (5 yes, 1 no, 0 abstentions)
  - Panel recommended that neoplasms of the female mouse tongue were not supportive of equivocal evidence, but were considered no evidence

<b>Sex/Species</b>	<b>Level of Evidence</b>	<b>Neoplastic Lesions</b>
Male and Female Rats	No Evidence	100, 300, 1000 mg/kg
Male and Female Mice	No Evidence	30, 100, 300 mg/kg

Non-neoplastic lesions of the liver, glandular stomach, small intestine (duodenum, ileum, and jejunum), nose, lung, heart, and spleen in male and female rats; bone marrow of female rats; the nose, mandibular lymph node, and bone marrow of male and female mice; and the liver of male mice



- A metal working fluid used as lubricant and coolant
- The panel recommended accepting the conclusions (6 yes, 0 no, 0 abstentions) with one change:
  - Panel recommended the granular cell tumors of the brain to be considered as no evidence instead of equivocal evidence in male rats

<b>Sex/Species</b>	<b>Level of Evidence</b>	<b>Neoplastic Lesions</b>
Male Rats	Equivocal Evidence	Prostate gland adenoma or carcinoma
Female Rats	Equivocal Evidence	Squamous cell papilloma or keratoacanthoma of the skin, Uterine adenocarcinoma or mixed malignant Mullerian tumor
Male Mice	No Evidence	10, 30, or 100 mg/m <sup>3</sup>
Female Mice	Some Evidence	Follicular cell carcinoma of the thyroid, Alveolar/bronchiolar adenoma or carcinoma



# Other Topics from the Review Meeting

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- Change in Rat Stocks
  - F344/NTac to Wistar Han to Harlan Sprague Dawley
  
- Extended Evaluation of the Uterus
  - Indole-3-Carbinol, Green Tea Extract, Cimstar 3800
  
- Molecular Analysis
  - BDCA: Mammary Neoplasms (Female Rat) and Liver Neoplasms (Mice)
  - Indole-3-Carbinol: Liver tissue (Female Rat; 3-months)



- Comments reviewed by NTP staff
- Draft Technical Report edited (with QA report findings)
- NTP Technical Reports to be published in 2015



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# Questions



# Draft Report Review and Publication

