Actions on the Draft NTP Technical Reports Peer Reviewed on July 13, 2017

The NTP convened the NTP Technical Reports Peer Review Panel ("the Panel") on July 13, 2017, to peer review the draft NTP Technical Reports on dietary zinc, 2,3-butanedione, and *p*-chloro- α , α , α -trifluorotoluene. Information for the meeting, including the draft reports, are available at the NTP website (<u>http://ntp.niehs.nih.gov/go/36144</u>). Summary minutes will be prepared and posted to the NTP website when completed. The Panel peer reviewed each report and provided its opinion on the draft NTP conclusions regarding the levels of evidence of carcinogenic activity for the substances tested. The Panel's recommendations do not necessarily represent the opinion of NTP. NTP will consider the input from the Panel in finalizing the technical reports. When completed, the technical reports will be published on the NTP website (<u>http://ntp.niehs.nih.gov/go/reports</u>).

Technical Report TR 592: Dietary Zinc

The Panel voted to accept unanimously (6 yes, 0 no, 0 abstentions) the conclusions as written.

Abbreviated format presenting the main science findings that support the draft NTP's conclusions:

Male Hsd:Sprague Dawley SD rats

- Equivocal evidence of carcinogenic activity of diets deficient in zinc
 - Higher incidences of adenoma of the pancreas and increased incidences of animals with multiple pancreatic adenomas

Female Hsd:Sprague Dawley SD rats

• No evidence of carcinogenic activity of diets deficient in zinc (3.5 or 7 ppm)

Male Hsd:Sprague Dawley SD rats

• No evidence of carcinogenic activity of diets containing excess zinc (250 or 500 ppm)

Female Hsd:Sprague Dawley SD rats

• No evidence of carcinogenic activity of diets containing excess zinc (250 or 500 ppm)

Exposure to diets containing excess zinc resulted in increased incidences of nonneoplastic lesions of the pancreas in male and female rats. Exposure to diets deficient in zinc resulted in increased incidences of nonneoplastic lesions of the testes in male rats.

Technical Report TR 593: 2,3-Butanedione

The Panel voted to accept (4 yes, 2 no, 0 abstentions) the conclusions as written. Panelists who voted "no" recommended *clear evidence of carcinogenic activity* for male rats and *some evidence of carcinogenic activity* for female mice.

Abbreviated format presenting the main science findings that support the draft NTP's conclusions:

Male Wistar Han rats

- Some evidence of carcinogenic activity
 - Combined incidences of squamous cell papilloma and squamous cell carcinoma of the nose

Female Wistar Han rats

- Some evidence of carcinogenic activity
 - Incidences of squamous cell carcinoma of the nose

Male B6C3F1/N mice

• No evidence of carcinogenic activity exposed to 12.5, 25, or 50 ppm

Female B6C3F1/N mice

- Equivocal evidence of carcinogenic activity
 - o Occurrences of adenocarcinoma of the nose

Exposure to 2,3-butanedione resulted in increased incidences of nonneoplastic lesions of the nose, larynx, trachea, lung, and eye in male and female rats and mice.

Technical Report TR 594: *p*-Chloro-α,α,α-trifluorotoluene

The Panel voted to accept unanimously (6 yes, 0 no, 0 abstentions) the conclusions as written.

Abbreviated format presenting the main science findings that support the draft NTP's conclusions:

Male Hsd:Sprague Dawley SD rats

- Some evidence of carcinogenic activity
 - Increased incidences of C-cell adenoma in the thyroid gland
- May have been related to treatment (equivocal evidence)
 - Combined occurrences of alveolar/bronchiolar adenoma or carcinoma in the lung

Female Hsd:Sprague Dawley SD rats

- Some evidence of carcinogenic activity
 - o Increased incidences of C-cell adenoma in the thyroid gland
 - o Increased incidences of benign pheochromocytoma in the adrenal medulla
 - Increased incidences of adenocarcinoma in the uterus
 - Increased incidences of stromal polyp in the uterus

Male B6C3F1/N mice

- Clear evidence of carcinogenic activity
 - Increased incidences of hepatocellular carcinoma and hepatoblastoma in the liver

Female B6C3F1/N mice

- Clear evidence of carcinogenic activity
 - Increased incidences of hepatocellular adenoma, hepatocellular carcinoma, and hepatoblastoma in the liver
- Related to treatment (some evidence)
 - Combined incidences of adenoma or adenocarcinoma in the Harderian gland

Exposure to *p*-chloro- α, α, α -trifluorotoluene caused increased incidences of nonneoplastic lesions in the lung and liver of male and female rats and mice, in the nose of male rats, in the adrenal medulla and uterus of female rats, in the forestomach of male and female mice, and in the larynx in male mice. Exposure to *p*-chloro- α, α, α -trifluorotoluene caused increased severity of nonneoplastic lesions in the kidney of male rats.