**Charge**

- 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 NTP’s conclusions regarding the hypothesis under the conditions of this study.

**Study Hypothesis**

- Exposure to 2-hydroxy-4-methoxybenzophenone will induce carcinogenic activity or toxicity when administered in feed to rats or mice through two years of age.

**Charge Questions**

- *Information presentation.*
  - Comment on the clarity, transparency, and presentation of information in the draft report.
    - Identify any information that should be added or deleted.
    - Identify any areas for improvement.
    - Identify any editorial corrections/comments.

- *Study design and conduct.*
  - Comment on the study design and conduct for addressing the hypothesis including:
    - Appropriateness of the dosing regimen and other considerations of dose selection for rats and mice.
    - Any limitations of the study design and conduct that might impact interpretation of the study results for rats and mice.

- *Study findings and draft conclusions.*
  - Comment on whether the study findings support the hypothesis.
  - Comment on whether the study findings support NTP’s draft conclusions regarding the toxicity and carcinogenic activity of 2-hydroxy-4-methoxybenzophenone (presented in bulleted format as will be projected at the meeting for voting on conclusions*):

  **Hsd:Sprague Dawley SD rats, exposed to 2-hydroxy-4-methoxybenzophenone**

  - Male
    - *Equivocal evidence of carcinogenic activity*
      - Occurrence of brain and spinal cord malignant meningiomas
    - Exposure to 2-hydroxy-4-methoxybenzophenone resulted in increased incidences of nonneoplastic lesions of the testis and pancreas in male rats.
**Female**
- **Equivocal evidence of carcinogenic activity**
  - Increased incidence of thyroid C-cell adenomas
  - Increased incidence of uterine stromal polyps
- Exposure to 2-hydroxy-4-methoxybenzophenone resulted in increased incidences of nonneoplastic lesions of the uterus and adrenal cortex in female rats.

**B6C3F1/N mice, exposed to 2-hydroxy-4-methoxybenzophenone**

- **Male**
  - *No evidence of carcinogenic activity at 1,000, 3,000, and 10,000 ppm*
  - Exposure to 2-hydroxy-4-methoxybenzophenone resulted in increased incidences of nonneoplastic lesions of the bone marrow, spleen, kidney, and liver in male mice.

- **Female**
  - *No evidence of carcinogenic activity at 1,000, 3,000, and 10,000 ppm*
  - Exposure to 2-hydroxy-4-methoxybenzophenone resulted in increased incidences of nonneoplastic lesions of the bone marrow, spleen, and kidney in female mice.

☐ Agree:
☐ Agree in principle with the exceptions listed below:
☐ Do not agree with conclusions because:

*Note: Draft NTP Technical Report conclusion as written in the draft report:*

Under the conditions of these 2-year studies, there was *equivocal evidence* of carcinogenic activity of HMB exposure in male Hsd:Sprague Dawley SD rats based on the occurrence of brain and spinal cord malignant meningiomas. There was *equivocal evidence* of carcinogenic activity in female Hsd:Sprague Dawley SD rats based on the increased incidence of thyroid C-cell adenomas and the increased incidence of uterine stromal polyps. There was no evidence of carcinogenic activity in male or female B6C3F1/N mice at exposure concentrations of 1,000, 3,000, and 10,000 ppm.

Increases in the incidences of nonneoplastic lesions of the testis and pancreas in male rats and of the uterus and adrenal cortex in female rats occurred with exposure to HMB. Increases in the incidences of nonneoplastic lesions of the bone marrow (males and females), spleen (males and females), kidney (males and females), and liver (males) in mice occurred with exposure to HMB.