Actions

Peer Review Meeting of the Draft NTP DART Reports on 2-Hydroxy-4-Methoxybenzophenone and 2-Ethylhexyl p-Methoxycinnamate

Webcast
October 14, 2021

The National Toxicology Program (NTP) virtually convened the NTP Developmental and Reproductive Toxicity (DART) Reports Peer-Review Panel ("the Panel") on October 14, 2021, to peer review the *Draft NTP DART Reports on 2-Hydroxy-4-Methoxybenzophenone and 2-Ethylhexyl p-Methoxycinnamate*. Meeting information, including the draft reports, is currently archived under NTP's "Past Events."[1] A meeting report will be prepared and posted to the NTP website when completed.

The Panel[2] peer reviewed the draft reports and provided its opinion on NTP's preliminary conclusions regarding the level of evidence of the developmental and reproductive toxicity of 2-Hydroxy-4-Methoxybenzophenone and 2-Ethylhexyl p-Methoxycinnamate. The Panel's recommendations do not necessarily represent NTP's opinion. NTP will consider the Panel's peer-review comments in finalizing the reports. When complete, the reports will be published on the NTP website.[3]

DART Report 05: Draft NTP Developmental and Reproductive Toxicity Technical Report on the Modified One-Generation Study of 2-Hydroxy-4-methoxybenzophenone (CASRN 131-57-7) Administered in Feed to Sprague Dawley (Hsd: Sprague Dawley® SD®) Rats with Prenatal and Reproductive Performance Assessments in F_1 Offspring

Reproductive Toxicity

The Panel voted to accept unanimously (4 yes, 0 no, 0 abstentions) the level of evidence conclusion as written.

- *Equivocal evidence of reproductive toxicity* in Hsd:Sprague Dawley® SD® rats based on a decrease in F_2 litter size in both the prenatal and reproductive performance cohorts.

Developmental Toxicity

The Panel voted to accept unanimously (4 yes, 0 no, 0 abstentions) the level of evidence conclusion as written.

- *Some evidence of developmental toxicity* in Hsd:Sprague Dawley® SD® rats based on the observed postnatal growth retardation. The relationship of the increased occurrence of diaphragmatic and hepatodiaphragmatic hernias in F_1 adults and F_2 pups to 2H4MBP exposure is unclear.

Other Effects

The Panel voted to accept unanimously (4 yes, 0 no, 0 abstentions) the level of evidence conclusion as written.

- Exposure to 2H4MBP was not associated with signals consistent with alterations in estrogenic, androgenic, or antiandrogenic action. Exposure to 2H4MBP was associated with lower F_1 and F_2 mean body weights; this effect on body weight contributed to the apparent 2H4MBP-related decreases in male reproductive organ weights. Mating and littering were not significantly affected by 2H4MBP exposure. Exposure to 2H4MBP was associated with nonneoplastic kidney lesions in the F_0, F_1, and F_2 generations. Expected estrogenic responses were observed in the ethinyl estradiol (EE) group.

[1] https://ntp.niehs.nih.gov/go/meeting
[2] https://ntp.niehs.nih.gov/ntp/about_ntp/trpanel/2021/october/rostertrprp20211014_508.pdf
[3] https://ntp.niehs.nih.gov/go/750897

DART Report 06: Draft NTP Developmental and Reproductive Toxicity Technical Report on the Modified One-Generation Study of 2-Ethylhexyl p-Methoxycinnamate (CASRN 5466-77-3) Administered in Feed to Sprague Dawley (Hsd: Sprague Dawley® SD®) Rats with Prenatal, Reproductive Performance, and Subchronic Assessments in F_1 Offspring

Reproductive Toxicity

The Panel voted to accept unanimously (4 yes, 0 no, 0 abstentions) the level of evidence conclusion as written.

- *No evidence of reproductive toxicity* in Hsd:Sprague Dawley® SD® rats at 1,000, 3,000, or 6,000 ppm. Mating and littering were not affected significantly by EHMC exposure.

Developmental Toxicity

The Panel voted to accept unanimously (4 yes, 0 no, 0 abstentions) the level of evidence conclusion with the following marked changes.

- *Equivocal evidence of developmental toxicity* in Hsd:Sprague Dawley® SD® rats based on the observed postnatal effects on body weight that showed some indication of recovery by study end, delays in postnatal day 28-adjusted vaginal opening and balanopreputial separation, which could have been influenced by the apparent transient effects on body weight, and time in estrus was slightly longer in EHMC-exposed females relative to that of the control group.

Other Effects

The Panel voted to accept unanimously (4 yes, 0 no, 0 abstentions) the level of evidence conclusion as written.

- No other signals consistent with alterations in estrogenic, androgenic, or antiandrogenic action were observed. EHMC exposure did not induce any specific fetal malformations.