The Effects of TCDD, PeCDF and TCDF on Reproduction of Mink and Growth and Survivability of Their Offspring

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In the Tittabawassee River basin, the greatest proportion of mammalian exposure to 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD)-like compounds is provided by:

- 2,3,4,7,8-pentachlorodibenzofuran (PeCDF)
- 2,3,7,8-tetrachlorodibenzofuran (TCDF)
Introduction

2,3,7,8-Tetrachlorodibenzo-\(p\)-dioxin (TCDD)

2,3,4,7,8-Pentachlorodibenzofuran (PeCDF)

2,3,7,8-Tetrachlorodibenzofuran (TCDF)
Introduction

- The mink (*Mustela vison*) is an established resident of this environment and is highly exposed to TCDD-like chemicals.
Results from a field study indicated:

- TCDD toxic equivalent (TEQ)-based hazard quotients (HQ) > 1 for both dietary exposure and tissue-based exposure using PCB 126-based mink feeding studies as a comparison.

- However, demographics indicated a healthy, lightly harvested population.
Introduction

- A mink reproduction study was conducted to assess the effects of PeCDF and TCDF relative to TCDD
Objectives

► Determine if TCDD, PeCDF and TCDF affect reproductive performance of female mink and the survival and growth of their offspring
Objectives

- Determine the relative potency of TCDF and PeCDF compared to TCDD based on various endpoints
Methods

117 adult female mink were randomly assigned among 13 treatments

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<th>Control</th>
<th>TCDD</th>
<th>PeCDF</th>
<th>TCDF</th>
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<tbody>
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<td></td>
<td>ng/kg bw/d</td>
<td>ng TEQ/kg bw/d</td>
<td>ng/kg bw/d</td>
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<tr>
<td></td>
<td>2.8</td>
<td>2.8</td>
<td>21</td>
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<td>13</td>
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Methods

Least doses

- Approximated environmentally relevant concentrations
  - Median predicted field exposure
    $\approx 4 \text{ ng TEQ/kg bw/d}$
  - The 95th centile for field exposure
    $\approx 7 \text{ ng TEQ/kg bw/d}$
Methods

Greatest doses

- 8 x greater than the median field exposure
  - 4 ng TEQ/kg bw/d

- 4 x greater than the 95th centile for field exposure
  - 7 ng TEQ/kg bw/d
Methods

- Dietary treatments started
- Initiated breeding
- Breeding completed
- Whelping began
- Dam and kit necropsies
- Gestation (40 – 52 d)
- 11 wks
- 3½ wk
- 3 wks
- 6 wk weights (Weaning)
- 3 wk weights
- Birth weights
- 10 wk weights
- 14 wk weights
- 18 wk weights
- 22 wk weights
- 27 wk weights
- Kit growth period
- Juvenile mink necropsies
Methods

- **Endpoints Assessed**
  - Number of females whelping
  - Litter size
  - Kit body mass at birth and 3 and 6 wks of age
  - Kit survivability through 6 wks of age
Methods

- Endpoints Assessed
  - Body mass of adults and juveniles
  - Organ mass
  - Hepatic chemical concentrations
Methods

Endpoints Assessed

- Morphological and histological alterations
  - Mandibular and maxillary squamous epithelial proliferation in kits and juveniles
Results

- Reproductive Endpoints
  - No significant effect on:
    - # females whelping
    - Litter size
    - Kit survivability through 6 wks of age
Results

- Growth Endpoints
  - No consistent effect on body mass of:
    - Adult females
    - 6-wk-old kits
    - 27-wk-old juveniles
Results

- Organ Mass

  - No consistent effect on organ mass of:
    - Adult females
    - 6-wk-old kits
    - 27-wk-old juveniles
Hepatic Concentrations of TCDD, PeCDF and TCDF in Juvenile Mink

Liver concentration, ng/kg

TCDD
PeCDF
TCDF
Hepatic Bioaccumulation Factors (BAF) for TCDD, PeCDF, and TCDF in Juvenile Mink

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<thead>
<tr>
<th>Chemical</th>
<th>Control</th>
<th>BAF</th>
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<td>TCDD</td>
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<td>PeCDF</td>
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<td>TCDF</td>
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Results

- Morphological and Histological Alterations
  - Kits
    - Evidence of mandibular and maxillary squamous epithelial proliferation in TCDD, PeCDF and TCDF groups
  - Juveniles
    - Mild to severe jaw lesions caused by TCDD, PeCDF and TCDF in a dose-related manner
Incidence of Maxillary and Mandibular Squamous Epithelial Proliferation in Juvenile Mink

Dose (ng chemical/kg bw/d)
Mink exposed to TCDD, PeCDF and TCDF

- Unaffected
  - Reproductive success
  - Survivability of offspring

- When exposure
  - 8 x greater than the Tittabawasee River median field exposure → 4 ng TEQ/kg bw/d
  - 4 x greater than the 95th centile for field exposure → 7 ng TEQ/kg bw/d
Doses resulting in 50% of the animals developing the jaw lesion were:

- 10 ng TCDD/kg bw/d (10 ng TEQ_{TCDD}/kg bw/d)
- 22 ng PeCDF/kg bw/d (6.5 ng TEQ_{PeCDF}/kg bw/d)
- 206 ng TCDF/kg bw/d (21 ng TEQ_{TCDF}/kg bw/d)

Relative potency values

- PeCDF $\approx 0.45$ (WHO TEF = 0.3)
- TCDF $\approx 0.05$ (WHO TEF = 0.1)

See MP 186 for more detail
Conclusions

Current Study

- Doses up to 36 ng TEQ/kg bw/d - no effect on:
  - Reproductive performance
  - Offspring survivability

PCB 126-driven mink feeding studies suggest:

- NOAEL ≈ 4 ng TEQ/kg bw/d
- LOAEL based on kit survivability ≈ 8 ng TEQ/kg bw/d
- LOAEL based on reproductive failure ≈ 36 ng TEQ/kg bw/d

The toxicity of TCDD, PeCDF and TCDF compared to PCB 126 in mink needs further evaluation
Conclusions

- The occurrence of mandibular and maxillary squamous epithelial proliferation in the absence of reproductive and/or survivability effects confirms that this lesion is a more sensitive measurement endpoint.