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Reproductive & Developmental Toxicity Guidance on Food Additive

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Stakeholders workshop
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Reproductive & Developmental toxicity

OBJECTIVE

Identify the potential of a food additive, which is systemically absorbed (or crosses the placenta), to impair reproduction and prenatal and postnatal development and function.

Rationale

- Systemic availability of FAs
- Substance crossing the placenta

General Considerations

efsa
European Food Safety Authority

❖ Objectives of reproductive & developmental toxicity testing:

- Identify substances which cause reproductive effects
- Identify substances which cause lethal, teratogenic or other toxic effects on the embryo and foetus
    - prenatal (via the mother) and to FAs
    - postnatal (via maternal milk) exposure to FAs

❖ End-points of interest:

- fertility and reproductive function
- developmental (pre- and postnatal)
- specific (immunotoxicity, neurotoxicity, endocrine disruption)

❖ Tiered approach

Reproduction - Tiered approach

TIER 1 (applicable to all additives)

Identify reproductive and endocrine effects

❖ **End-points of interest:**

- Reproductive effects
- Endocrine effects

❖ **Testing requirements:**

- Extended repeated dose oral toxicity study (90-day) in rats

(OECD TG 408)

Reproduction - Tiered approach

There is no Tier 2 if absorption is negligible

TIER 2 (triggered)

Reproductive (functional) and developmental effects

- **End-points of interest:**
  - Fertility and Reproductive function
  - Developmental toxicity (pre- and postnatal)
  - Developmental neurotoxicity and immunotoxicity, endocrine effects

- **Testing requirements:**
  - Prenatal developmental toxicity in *rabbit* **(OECD TG 414)**
  - Extended One Generation Reproductive Toxicity Study in rats **(OECD TG 443)**

Reproduction - Tiered approach

TIER 3 (triggered by results in Tier 2)

Case-by-case approach (additional studies)

- **End-points of interest:**
  - Endocrine effects
  - Developmental neurotoxicity
  - Developmental immunotoxicity
  - Mode of action

- **Testing requirements:**
  - Developmental neurotoxicity (OECD TG 426)
  - Mode of action studies
  - *Multi-generation study (conditional) for existing FAs (OECD TG 416)*

Reproduction - Tiered approach

Overview

Tier 1 (mandatory)

- 90-Day Extended Toxicity Testing (reproductive, endocrine effects)

Tier 2 (triggered)

- Prenatal Developmental Toxicity Study (rabbit)
- Extended One-Generation Reproductive Toxicity Study (rodent, rat)
  - reproductive, developmental and specific endpoints

Tier 3 (triggered)

- Examine further specific endpoints (case-by-case approach)

Key changes

- **single species** (rodent)
- **EOGRTS replacing multi-generation study**
- **'triggers'** (F2 generation)
- **endocrine activity**