Considerations of Alternative Methods on Testing Proposals

Public substance name: Zinc bis[bis(dodecylphenyl)] bis(dithiophosphate)

EC Number: 259-048-8

CAS Number: 54261-67-5

- **Hazard endpoint for which vertebrate testing was proposed:**
  Pre-natal developmental toxicity study
- **Considerations that the general adaptation possibilities of Annex XI of the REACH Regulation were not adequate to generate the necessary information**
  - Available GLP studies
    There are no GLP-compliant pre-natal developmental toxicity studies available on the substance.
  - Available non-GLP studies
    There are no non-GLP-compliant pre-natal developmental toxicity studies available on the substance.
  - Historical human data
    There are no appropriate historical human data that address the pre-natal developmental toxicity endpoint on the substance.
  - (Q)SAR
    There are no QSAR models available for this higher tier human health endpoint that are sufficiently validated and acceptable (according to OECD Q/SAR validation criteria).
  - In vitro methods
    The registrant has a knowledge of the standard databases and sources of information on in vitro methodologies and is not aware of any validated alternative tests that use in vitro methodologies that could be used to meet the standard requirement of the REACH regulation for pre-natal developmental toxicity. This position is the same as that given in the most current status report of EURL ECVAM (JRC 201, Report EUR 27474).
  - Weight of evidence
    The available screening reproductive toxicity studies on the substance and other similar substances are considered inadequate to meet the REACH standard requirement for pre-natal developmental toxicity because developmental is not sufficiently examined in a screening study.
  - Grouping and read-across
    The substance is a member of a category comprising 15 substances. A category justification and testing proposal have been prepared for the category members. The criteria for selection of the category substance to be tested include low molecular weight, a water solubility and Log Kow that falls within the range for optimal absorption. In addition, it is considered appropriate to use one of the substances which has already been tested for repeat dose and reproductive toxicity because of the available data that

may be used to design the range-finding study for the pre-natal developmental toxicity study and is a category member that is representative of the category as a whole. The testing proposal nominates Phosphorodithioic acid, mixed O,O-bis(iso-Bu and pentyl) esters, zinc salts to be tested and the results read-across to this and the other 14 members of the category. **This approach will save a minimum of 80 adult and approximately 1,000 foetal animals (~12.5 foetuses/female) per category member, which equates to a total of 1,120 adult and 14,000 foetal animals saved.**

- Substance-tailored exposure driven testing [if applicable]
  Not applicable
- Approaches in addition to above [if applicable]
  Not applicable
- Other reasons [if applicable]
  Not applicable
- **CONSIDERATIONS THAT THE SPECIFIC ADAPTATION POSSIBILITIES OF ANNEXES VI TO X (AND COLUMN 2 THEREOF) OF THE REACH REGULATION ARE NOT ADEQUATE TO GENERATE THE NECESSARY INFORMATION**:

Annex IX, column 2 specific rules for adaptation are given below, together with the reason why they are not adequate for this substance.

8.7. The reproductive toxicity studies do not need to be conducted if:
— the substance is known to be a genotoxic carcinogen and appropriate risk management measures are implemented,
or
— the substance is known to be a germ cell mutagen and appropriate risk management measures are implemented,
or
— the substance is of low toxicological activity (no evidence of toxicity seen in any of the tests available), it can be proven from toxicokinetic data that no systemic absorption occurs via relevant routes of exposure (e.g. plasma/blood concentrations below detection limit using a sensitive method and absence of the substance and of metabolites of the substance in urine, bile or exhaled air) and there is no or no significant human exposure.

None of the adaptations are applicable to this substance. The substance is not a genotoxic carcinogenic or germ cell mutagen and the substance is water soluble and there is evidence of local toxicity in a 28-day repeat dose toxicity study on other substances in the category.