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:**
  Sub-chronic toxicity study (90 day)

- **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 sub-chronic toxicity (90 day) studies available on the substance.
  - Available non-GLP studies
    There are no non-GLP-compliant sub-chronic toxicity (90 day) studies available on the substance.
  - Historical human data
    There are no appropriate historical human data that address the sub-chronic toxicity (90-day) 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 sub-chronic toxicity (90-day). 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 repeat dose toxicity studies on the substance and other similar substances are considered inadequate to meet the REACH standard requirement for sub-chronic toxicity (90 day) because the exposure period is too short.
  - 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 toxicity because of the available data that may be used to design the range-finding study for the 90-day repeat dose 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 animals per category member, which equates to a total of 1120 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.

8.6.2. The sub-chronic toxicity study (90 days) does not need to be conducted if:
— a reliable short-term toxicity study (28 days) is available showing severe toxicity effects according to the criteria for classifying the substance as R48, for which the observed NOAEL-28 days, with the application of an appropriate uncertainty factor, allows the extrapolation towards the NOAEL-90 days for the same route of exposure, or
— a reliable chronic toxicity study is available, provided that an appropriate species and route of administration were used, or
— a substance undergoes immediate disintegration and there are sufficient data on the cleavage products (both for systemic effects and effects at the site of uptake), or
— the substance is unreactive, insoluble and not inhalable and there is no evidence of absorption and no evidence of toxicity in a 28-day 'limit test', particularly if such a pattern is coupled with limited human exposure.

None of the adaptations are applicable to this substance. There is no short-term toxicity study showing severe effects; there is no chronic study available; the substance does not undergo immediate disintegration; 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.