To the co-registrants of ytterbium oxide

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Subject: decision on YbO3
Project number: 30094894
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Dear co-registrants,

On Nov 23th, 2021, ECHA has provided a decision on testing proposal to the registrants of ytterbium oxide (EC 215-234-0, CAS 1314-37-0). This decision contained a request for information on the following endpoints:
Annex VIII

- In vivo somatic cell genotoxicity (Annex VIII)

The in vivo study needs to be considered as there are positive results in one of the in vitro genotoxicity studies performed with the substance.
This decision has been discussed in the Rare Earth Consortium.

The information requested in the decision must be generated using exclusively non-nanoforms of the substance.

The following information is required:

- In vivo mammalian alkaline comet assay (annex VIII, section 8.4, column 2, test method OECD TG 489) in rats, oral on the following tissues: liver, glandular stomach, and duodenum

The original proposed test (in vivo mammalian erythrocyte micronucleus test, OECD TG 474) was rejected by ECHA. The main reason here is, that there is no systemic toxicity observed with the substance, and thus it is highly uncertain whether the substance or its metabolites will reach the target tissue. The in vivo mammalian alkaline comet assay (OECD TG 489) is deemed suitable to follow up the positive in vitro result for chromosomal aberrations. It enables the generation of information regarding potential genotoxic effects at the site of contact. There are no alternative methods which could be used to adapt the information requirement.
The following specifications were described in the decision:

- The test must be performed in rats
- Via the oral route, considering the anticipated routes of human exposure and adequate exposure
- Tissues to be included, liver, glandular stomach, duodenum
- Collection of male gonadal cells from seminiferous tubules to be considered

Multiple testing facilities were contacted and several quotations were compared based on experience, timelines, costs, and expertise. A very limited number of laboratories provides a full service of the in vivo genotoxic study, including the required analytical work; hence, capacity is limited and lead time is significant. The testing facility Charles River Laboratories (Den Bosch, the Netherlands) was selected, and the following study schedule is proposed (not guaranteed):

- Development and validation of the analytical method : mid July 2023
- Comet assay: end of July 2023
- Draft report: end of Oct 2023 (at the latest)

The testing costs, excluding study monitoring and dossier update) are estimated to be approx. € 64k - € 120k (one sex), or € 96k - € 150k (two sexes). The costs will depend on number of sexes (to be determined in the preliminary phase) and the results (in case of positive results, additional investigations are required). The information requested by the ECHA decision will be submitted in an updated registration dossier, as soon as feasible after the requested information is available.

The deadline for submission indicated by ECHA was Nov 30th, 2022.

As the results of the in vivo Comet assay test with the substance were not available, the lead dossier was submitted (annex VIII) (prior to Nov 30th, 2022):

- Including an official communication from the testing facility mentioning the study schedule and confirmation of study placement
- Including updates of general sections 1-3
- Including a quality check of the hazard assessment, and description of the uses

Following submission of the lead dossier, it is expected that ECHA will evaluate the information submitted and then forward the dossier to national authorities. To date, no further feedback or extended submission deadline was received.

Financial Impact on LoA costs (Letters of Access)

Related to the LoA costs, although this test is related to the Annex IX (100-1000 tpy) data requirements, it is also relevant for Annex VIII co-registrants (rationale: As stated in REACH Annex VIII: Appropriate in vivo mutagenicity studies shall be considered in case of a positive result in any of the genotoxicity studies in Annex VII or VIII).

As currently no co-registrant has been identified in the tonnage band 10-100 tpy for ytterbium oxide, should the LoA costs be recalculated in a near future (no recalculation scheduled for the time being), the LOA cost for Annex VII will not be impacted by the costs linked to this additional test (regarding study monitoring and actual study cost).

The costs of the LoA per tonnage band include a provision for future work on the dossier. Part of this provision has already been used. The balance will of course be used to finance the above-mentioned work on the dossier based on the final decision.

Depending on the total cost for complying with ECHA's request, the remaining provision may not be insufficient. In such case, the cost of the LoA shall be adapted accordingly and an additional invoicing to the co-registrants can be deemed necessary.

Because the final decision is not known yet, it is not possible to provide any estimate of such financial impact on the LoAs for the time being.

In the meantime, if there are specific questions, please send an e-mail to the Consortium's mailbox, hosted by Arcadis (see below for the e-mail address).

With kind regards,

Arcadis Belgium nv/sa, on behalf of the members of the Rare Earth Consortium

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