Ames test on APR
20 Jan 2012

Aim

This document aims at summarising the exchanges which have taken place between WCA and PMC secretariat in order to better capture the pros and cons of performing the Ames test on APR or strictly applying the guidelines outlined in the Health Risk Assessment for metals Guide (HERAG; http://www.herag.net).

Pros and cons

Table 1. Summary of exchanges between WCA and PMC secretariat on the pros and cons of performing the Ames test on APR versus strictly following HERAG

	Perform Ames now	**Waive Ames test**
Summary	• Ames test provides information on mutagenic potential of substance using bacteria • Considered to be informative and relevant by Prof. D. Kirkland, expert in genotoxicity, and is a normal requirement of Annex VII • Eurométaux recognises genotoxicity is not a straightforward science and that deviations from HERAG could be required for some metals • Reasonably low cost: ~ 5000 € • Available laboratory capacity at Covance in Mar 2012 • If result positive: it would be necessary to perform an *in vivo* mutagenicity study (Single Cell Gel Electrophoresis assay, also known as Comet Assay, with a cost of up to ~ 50 000 €), REACH dossier can be completed with results of *in vivo* study. However, APR would be classified as a Category 2 mutagen if the *in vivo* study was positive. • If result negative: STOP, full REACH dossier complete • Will be performed for PGM and Au projects, hence performing it for Re project also is more coherent and robust	• Ames test considered to be irrelevant for some metals in HERAG (false negatives) • Assumption: APR unlikely to be genotoxic to bacteria (i.e. positive) since no genotoxicity was observed in mammalian cells during Mouse Lymphoma and Micronucleus assays (reports Nov 2011) • Dossier can be submitted without Ames test on the basis of HERAG rationale/justification • If APR file is subject to Evaluation and authorities believe Ames test is required, it can still be performed then
WCA and PMC secretariat's view	• ECHA guideline-compliant • Regulatory acceptance likely to be 100 % • Minimum to no risk of question or rejection by authorities • Recommendation: perform at least screening Ames test	• ECHA guideline-compliant if waiving is properly justified on the basis of REACH Annex XI rules, ECHA technical guidance and HERAG • Regulatory acceptance will depend on overall acceptance of HERAG guidelines for metals • Risk of being questioned by authorities

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Next steps/actions

Chairpersons of Re WG have agreed to follow the ECHA guideline and perform a screening Ames test which will allow assessing the potential for APR to cause reverse mutations in bacteria (validated by second experiment) as well as identifying most appropriate vehicle and substance concentrations.

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