

Comments from the American
Chemistry Council to the
EDMVAC on the Amphibian
Metamorphosis Tier 1 Screen

April 27, 2005

Technical Comments on the Amphibian Screen Development

- Differences in phase 1 protocols used (three labs in three different countries) make it difficult to compare endpoint variability and reproducibility between labs
- Resolution needed on length of screen (14 v 21d?) and stage at initiation (stage 51 v 54)
- No non-thyroid active toxicant has been included in either phase 1 or the proposed phase 2 plan
 - Necessary to gauge specificity and relevance of the endpoints

Is an Amphibian Thyroid Screen Redundant?

- The amphibian metamorphosis study was recommended by EDSTAC as a thyroid screen since metamorphosis is a process governed by the thyroid hormone axis
- Thyroid activity also assessed in the pubertals and 15d intact male
- Sensitivity comparison should be made between these three assays to determine if the amphibian assay adds value as a screen
- In order to make this comparison, same chemicals need to be tested in the assays
 - Comparison available for thyroid antagonist, PTU
 - No comparison appears available for a thyroid agonists

Recommendations for Consideration

- Resolve length of assay and larval stage at initiation considerations for protocol
 - Harmonization with OECD
- Add a non-thyroid active toxicant to phase 2
- Include a sensitivity comparison between the frog, pubertal assays and 15-d intact male
 - Ensure compounds necessary for comparison have been included in the phase 2 amphibian proposal
 - Use the above information to determine if amphibian screen is redundant