RESORCINOL TASK FORCE

To: *Toxicology Excellence for Risk Assessment (TERA),*
Resorcinol RfD Peer Review Project

AMEC Earth & Environmental

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Subject: AMEC Resorcinol RfD Report, RTF DRF Study

Dear Sirs,

As you may know, the Resorcinol Task Force (RTF) was set up in 1998 to facilitate the filling of relevant data gaps relating to potential hazards and risks posed by resorcinol. The membership of the Task Force includes all three of the major global producers (INDSPEC, Mitsui and Sumitomo) and has strong links with several key user-groups.

Following an initial gap analysis of the International Uniform Chemical Information Database (IUCLID), it emerged that one of the major data gaps existing in the resorcinol dataset was a multi-generation reproductive toxicity test. Since resorcinol has been reported in the literature as having a dose-related, reversible effect on the thyroid through the inhibition of thyroid peroxidaise enzymes, it was recognised that a study of generational effects would be valuable. The RTF felt this information would be particularly useful, among other things, with respect to the European Commission's ongoing evaluation of the potential effect of resorcinol as a thyroid-specific endocrine disrupter.

Responding to this need, the RTF initiated the commencement of a suite of studies in 2001 leading to the conduct of a fully Office of Environmental Compliance and Documentation (OECD)-416 guideline-compliant two-generation drinking water study on Sprague Dawley rats. This study is currently on-going and its conclusions will be reported in the spring of 2005.

In light of the information then available in the database from previous work in this area, the Task Force decided to commission a Dose Range-Finding (DRF) study as a precursor to the main study in order to confirm the appropriateness of the delivery route and to establish relevant dose levels. This study was carried out during late 2002 / early 2003. The fact that this study was conducted to Good Laboratory Practices (GLP) standards by WIL Research and was comprehensive in its approach had the immediate effect of catapulting it to the status of being the most reliable study in the field performed to date, despite the fact that it was never intended to be reviewed on a stand-alone basis.

In the interests of cooperation and full disclosure, the European Commission was informed of the RTF's plans in 2002 and has been kept updated ever since. Some of the information associated with the DRF study and the two-generation study has properly become publicly available through the reporting of Commission proceedings (for example at the EU Stakeholder Forum meetings on Endocrine Disrupters) and this information has inevitably spread to other stakeholders. The RTF has no problem with this, but would wish to stress that the DRF study was never intended to be reviewed on a stand-alone basis, since it was envisaged that its primary function was to support the full two-generation study which followed. Any parties now reviewing the DRF study need to take this fact into

consideration during any assessment of the results of the DRF study. However, with this caveat in place, the RTF sees no reason why the study should in any way be down-graded in its reliability or relevance

The RTF has become aware that AMEC Earth and Environmental has been commissioned to develop a Proposed Reference Dose (RfD) for Resorcinol and has chosen to cite the RTF DRF study as the critical study in its assessment. Again, the RTF can see why AMEC has chosen to take this approach but would wish the above caveats to accompany this selection. RTF has reviewed the assessment of the DRF study in AMEC's recent RfD report, and has no specific concerns about the approach taken even though AMEC's conclusion that a conservative LOAEL may exist at 360 mg/l is a departure from WIL's own assessment of the same data as a NOAEL. We note, with interest, the view of AMEC concerning the possibility that the follicular hyperplasia observed could be artifactual because of the absence of any supporting changes in T_3, T_4 or T_{SH} levels. Although it is still too early to draw any conclusions from the on-going OECD-416 guideline-compliant two-generation study, such an interpretation would be consistent with our current observations.

In conclusion, we support AMEC's decision to make use of the DRF study in the absence of other more reliable, targeted studies. However, we did feel it appropriate and responsible to ensure that those entrusted with reviewing and assessing AMEC's work should be aware of the context of the DRF study and its presentational limitations, since it was never envisaged that it would be considered as a stand-alone study for regulatory purposes at its inception. It will, of course, be our intention to keep all interested stakeholders apprised of the results of the main study once they become available

Should you require any further information on the subjects covered in this letter, please do not hesitate to make contact with the Task Force at the co-ordinates given below.

We request that this letter be provided to any individuals, panels, agencies or other entities that will be reviewing the AMEC report and/or the DRF study.

Yours Faithfully,

Paul Ashford -- Resorcinol Task Force Manager

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