

Acetoacet-o-anisidide – Comments of Environmental Defense

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Environmental Defense appreciates this opportunity to submit comments on the robust summary/test plan for acetoacet-o-anisidide.

The Color Pigments Manufacturing Association (CPMA) proposes that no additional testing is necessary for acetoacet-o-anisidide (AaoA). According to the robust summary, the sole use of this compound is as a chemical intermediate in the production of pigments, and it is used and transported in closed systems. Therefore, the exposure circumstances are limited to the potential for occupational exposures and, except in the case of accident, there should not be exposure to the general population.

The CPMA contends that data from acetoacetanilide (AAA) and acetoacet-o-toluidide (AaoT) can be used to fill missing data for repeat dose, developmental and reproductive endpoints for AAoA. The basis for this contention is that AAoA, AAA, and AAoT have similar but not identical physiochemical properties and acute toxicities, and they all induce methemoglobinemia. No evidence on metabolism, changes in gene expression, or biological effects other than methemoglobinemia are presented. While the findings, to date, suggest that the three chemicals have some common toxicological properties, the data are too limited to conclude that AAoA does not possess a mechanism of toxicity distinct from AAA and AAoT.

AAoA was tested in a 14-day but not a 28-day repeat dose study. In addition, this study has several limitations including incomplete methods description and incomplete histological evaluation, so this study cannot be regarded as adequate. The combined repeat dose and reproduction/development screen for AAoT appears to be a good study but the complete report is not available for review and, as stated above, the results cannot be assumed to predict the results for AAoA.

In short, the evidence for establishing a toxicological category for AAoA, AAA, and AAoT is inadequate at this time. Accordingly, a developmental toxicology study should be conducted on AAoA. Since AaoA is used and transported in closed systems with little or no opportunity for consumer or environmental exposures, except in the case of accident, no reproductive study is needed. Given the entire set of circumstances and available data for AAoA, the need for a 28-day repeat dose study is borderline. Given that a developmental toxicology study is needed, however, it should be possible to incorporate appropriate repeat-dose analyses into that study.

Thank you for this opportunity to comment.

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