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06/22/2004 03:28 PM

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Subject: Environmental Defense comments on 2-Oxetanone, 4-methylene (CAS# 674-82-8)

(Submitted via Internet 6/22/04 to oppt.ncic@epa.gov, hpv.chemrtk@epa.gov, boswell.karen@epa.gov, chem.rtk@epa.gov, lucierg@msn.com and Jlr@cpma.com)

Environmental Defense appreciates this opportunity to submit comments on the robust summary/test plan for 2-Oxetanone, 4-methylene (CAS# 674-82-8).

The test plan and robust summaries for 2-oxetanone, 4-methylene (diketene) was submitted by the Color Pigments Manufacturing Association. Diketene is used as a chemical intermediate in the manufacture of a wide array of products, including dyes, color pigments, pharmaceuticals, food preservatives and insecticides. The sponsor claims that diketene is highly unstable in biological media because it is rapidly hydrolyzed to acetoacetic acid. It is also stated in the test plan that the chemical is manufactured and transported in closed systems and that there is no known direct or consumer use of the chemical where exposure to the general population may occur. However, no monitoring data are provided for diketene or its degradation product, acetoacetic acid. Since acetoacetic acid is a natural product, monitoring data might be difficult to interpret but information on waste stream levels would be helpful. The sponsor claims that diketene exposure in the workplace is self-limiting because it is extremely irritating to the eyes and mucous membranes. Are there monitoring data to support this claim? Is there a short-term exposure level that has been established in the workplace?

There are no available data for diketene on mammalian health endpoints, and the only data available for ecological endpoints have been derived from ECOSAR and other models. Nevertheless, the sponsor plans to conduct no new studies for two main reasons. First, surrogate data from another HPV chemical, methyl acetoacetate (MAA), is proposed to be used to fulfill all mammalian health endpoints with the exception of acute toxicity. Use of the surrogate data is said to be justified on the basis that MAA, like diketene, is converted to acetoacetic acid. While this may be true, the sponsor offers no experimental evidence to demonstrate that this conversion actually occurs. In addition, acetoacetic acid is formed via a hydrolysis pathway for diketene and a presumed enzymatic step for MAA. The enzymatic step could be quite slow and not necessarily quantitative, so the use of the surrogate data has significant potential flaws. At the very least, the sponsor needs to provide experimental data demonstrating similar rates of common metabolite formation before the surrogate data can be accepted. We also suggest that the sponsor consider generating gene expression data in an appropriate biological system to either support or refute the contention that MAA and diketene exert the same biological effects. In addition, if the chemicals' behavior is so similar we ask why the sponsor did not attempt to place MAA and diketene in the same category, since both are HPV chemicals? Finally, the sponsor needs to explain why the acute toxicity of diketene appears to be at least five times greater than that of MAA.

The second reason why no new studies are proposed is that diketene is

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apparently also sponsored by Wacker-Chemie as part of the ICCA Initiative under the OECD SIDS program; the sponsor argues that because studies could be proposed as part of that initiative, the sponsor does not want to conduct duplicate studies. While the avoidance of duplicate studies is desirable, the sponsor needs to propose appropriate studies or provide information now regarding the studies to be performed by Wacker-Chemie and also ensure that the results of such studies are made publicly available when they are completed.

For the above reasons, we do not concur, at this time, that no new studies are needed. We must recommend, based on the information provided in the test plan and robust summaries, that data be generated on all mammalian health endpoints except for acute toxicity. We would be glad to reconsider this recommendation if the sponsor provides a more substantial justification for the use of surrogate data.

Thank you for this opportunity to comment.

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