

In Vitro Metabolism Studies with VC and Human Livers

Pros and Cons

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During the collection of data for the preparation of a physiologically-based pharmacokinetic (PB-PK) risk assessment for vinyl chloride (VC), we did not find a systematic comparison of in vitro rates of metabolism in livers obtained from rodents and humans. Such studies have been conducted with other PB-PK based risk assessments (e.g. Reitz et al., (1989) who studied dichloromethane). Consequently, we discussed the possibility of performing some in vitro studies to supplement the VC data already available in the literature. I have listed below some pros and cons associated with the conduct of such studies.

PROS (of doing more studies):

- Existing human in vivo data are for short periods of time with low concentrations of VC. Under these conditions, tissue loading as well as metabolism of VC is occurring. In vitro studies would allow us to evaluate metabolism directly (tissue loading would not interfere).
- Using the existing data from Bolt, the extent of metabolism in humans would likely be overestimated; thus inappropriately high estimates of human risk might be obtained (my rough (!) guess is that the risk estimates would be 2-3 fold too high if we assumed all uptake of VC was related to metabolism when considering the studies conducted by Bolt).

CONS (of doing more studies):

- Waiting for additional studies would delay the preparation of the VC risk assessment. In addition to the time necessary to prepare and implement a research contract, there is always the possibility that the in vitro assay techniques might be difficult to develop and/or implement. If we proceed without these studies, the preparation of the risk assessment can begin immediately.
- Additional funds would be required for the in vitro studies. My guess is that this project might cost \$30,000 - \$40,000; depending upon the scope of the research and the techniques chosen to implement it.

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References

1. Reitz, R.H., Mendrala, A.L. and Guengerich, F.P. (1989). In Vitro Metabolism of Methylene Chloride in Human and Animal Tissues: Use in Physiologically-Based Pharmacokinetic Models. Toxicol. Appl. Pharmacol. **97**, 230-246.