

Response to the Comments by Bercu and Callis on our communication “Controlling the Genotoxins Ethyl Chloride and Methyl Chloride Formed During the Preparation of Amine Hydrochloride Salts from Solutions of Ethanol and Methanol” [Org. Process Res. Dev. 2009, 13, 786–791; DOI: 10.1021/op9000737]

Dear Editor:

We acknowledge the Letter to the Editor from J. P. Bercu and C. M. Callis regarding our recent paper “Controlling the Genotoxins Ethyl Chloride and Methyl Chloride Formed During the Preparation of Amine Hydrochloride Salts from Solutions of Ethanol and Methanol.” We find their comments to be consistent with the discussion in our paper.

We absolutely support using toxicology data to establish specifications for residual impurities and minimizing impurities to levels as low as reasonably practicable. Our paper focused on minimizing residual EtCl and MeCl in two drug candidates, and controlling the parameters determined to be key in these crystallizations may be helpful to minimize the inclusion of potentially genotoxic impurities in other drug candidates. The limits for the

two impurities mentioned in our paper may be considered conservative; such conservative limits may be adopted by those advancing a drug candidate to increase the ease of approval by regulatory agencies, or may be required by regulatory agencies based on information from within their databases. When carcinogenicity data are available, we believe such data should be used to establish limits on genotoxic impurities.

Best regards,

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