Response to the Comments by Snodin on Our Article "Approaches to Assessment, Testing Decisions, and Analytical Determination of Genotoxic Impurities in Drug Substances" [*Org. Process Res. Dev.* Web publication November 13, 2008; DOI: 10.1021/op8002129; 2009, *13*, 285−291.]

Dear Editor:

We would like to acknowledge David Snodin's Letter to the Editor in which he comments on our recent *Org. Process Res. Dev.* (OPRD) paper ("Approaches to assessment, testing decisions, and analytical determination of genotoxic impurities in drug substances"). Three specific topics relating to the need for specification limits, risk assessment and need for routine testing were discussed in the letter, and we find his comments to be consistent with our paper.

As stated in the paper, avoidance of genotoxic impurities (GTIs) as reagents, starting materials, synthetic intermediates and byproducts in chemical processing is an initial consideration in designing appropriate synthetic routes, but is not always feasible. The focus of our paper was not the establishment of acceptable levels of GTIs, but how to develop effective control strategies for GTIs when unavoidable. Establishing an impurity control strategy which combines appropriate scientific rationale, supporting data and analytical testing is essential. The more general question of whether the current EMEA and draft FDA regulatory guidance supports an integrated GTI assessment based on chemical processing and toxicological considerations deserves continued discussion, and we would encourage further dialogue and support.

Regards,

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