ID HESI.03

Nitrosamine impurity issues and potential resolutions

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Johnson et al., (2021) was a publication from the Health and Environmental Sciences Institute Genetic Toxicology Technical Committee (HESI GTTC), where in vivo mutagenicity dose response data was compared to in vivo cancer bioassay dose response data to calculate benchmark dose confidence intervals and permitted daily exposures (PDE). Certain benefits of the approach were presented, along with some aspects where additional data and refinement were considered on the use of the in vivo mutation data that was available at the time. These include the critical effect size, the uncertainty factors used, as well as justification for using the PDE approach. Nitrosamines have become an important class of impurities within pharmaceuticals, and there are continuing efforts and advancements to ensure patient safety. It is also very important that there is not unjustified withdrawal of marketing authorisation, and precision in the risk assessment approach is paramount to this. During the presentation and discussion, we will focus on the current projects on nitrosamine risk assessment and best practise.

Johnson, G.E., Dobo, K., Gollapudi, B., Harvey, J., Kenny, J., Kenyon, M., Lynch, A., Minocherhomji, S., Nicolette, J., Thybaud, V., Wheeldon, R., and A. Zeller 2021. Permitted daily exposure limits for noteworthy N-nitrosamines. Environmental and Molecular Mutagenesis, 62(5), pp.293-305.