«Forced Degradation Studies: an overview on current best practices & regulatory environment»

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Stress testing (also known as forced degradation) of pharmaceutical products has long been recognized as a critical part of the drug development process, providing foundational information related to intrinsic stability characteristics and to the development of stability-indicating analytical methods. The presentation will cover an overview of current best practices and regulatory environment with a focus on special requirements of ANVISA (Brazilian Health regulatory Agency). A benchmarking study undertaken by nine pharmaceutical companies and ANVISA with a goal of understanding the utility of various stress testing conditions for producing pharmaceutically-relevant chemical degradation of drugs will be presented.

Main focus of the study was to determine whether solution phase stress testing of solid drug products produced degradation products that were both unique when compared to other stress conditions and relevant to the formal drug product stability data. The results from studies of 62 solid dosage form drug products were compiled. A total of 387 degradation products were reported as being observed in stress testing studies, along with 173 degradation products observed in accelerated and/or long-term stability studies for the 62 drug products. Among these, 25 of the stress testing degradation products were unique to the solution phase stress testing of the drug products; however, none of these unique degradation products were relevant to the formal stability data. The relevant degradation productswere sufficiently accounted for by stress testing studies that included only drug substance stressing (in solution and in the solid state) and drug product stressing (in the solid state). Based on these results, it is the opinion of the authors that for solid dosage form drug products, well-designed stress testing studies need not include solution phase stress testing of the drug product in order to be comprehensive.

[1] John M. Campbell, Chris Foti, Chloe Wang, Neal Adams, Leonardo R. Allain, Gabriela Araujo, Renan Azevedo, Jucara Ribeiro Franca, Simon R. Hicks, Steven Hostyn, Patrick J. Jansen, Dorina Kotoni, Andreas Kuemmell, Stacey Marden, Gregory Rullo, Ana Claudia O. Santos, Gregory W. Sluggett, Todd Zelesky, Steven W. Baertschi, *Journal of Pharmaceutical Sciences*, **2022**, 111 (2), 298-305