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Small Molecule Bioanalysis Basics

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Introduction

Small molecule drugs have been a mainstay for drug developers for decades. Although a larger percentage of growth is expected in the large molecule arena, small molecules still make up 90% of the marketing of pharmaceutical drugs. The toxicokinetics and pharmacokinetics of small molecule drugs are critical components of regulatory submissions. The concentrations of these small molecule drugs in biological matrices, or bioanalysis, are largely conducted by LC-MS (liquid-chromatography interfaced with mass spectrometry). The validation of these methods is governed by international guidelines and regulations. The US FDA issued its final guidance on Bioanalytical Method Validation in 2018 and the International Council on Harmonization (ICH) is expected to issue its final guidance in 2022. This talk will focus on key components of bioanalysis in toxicology studies, for example, sample size and volume, limits of quantitation, dynamic concentration range, incurred sample reproducibility (ISR), use of stable label internal standards, sensitivity, and stability of the small molecule in bioanalytical fluids and also areas of potential failure like cross-contamination, incorrect anticoagulants, sample clotting, and sample storage conditions. Additionally, there will be a discussion on the translation and use of the nonclinical bioanalytical methods to clinical methods and the continuity of the bioanalytical method development process between drug development phases. Microsampling as new technology will be introduced. Finally, case studies will be presented for discussion.