Extractable and Leachable Studies

New regulatory expectations

Extractable and leachable (E&L) studies are an essential part of the pharmaceutical drug development process. Regulatory agencies are requesting more and more early phase E&L studies, especially for drugs using non-standard or parenteral clinical applications. Because E&L studies can cost up to 750.000 € and span multiple years, the classical (standard) approach (Figure 1) is not feasible in early project phases.

Figure 1: Classical E&L approach

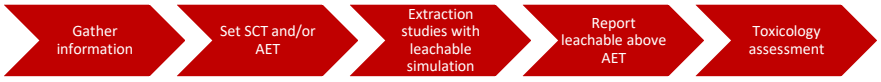

Figure 2: Accelerated E&L approach

A modern Quality by Design process

Both the classical approach and the accelerated (early-phase) approach (Figure 2) are based on Quality by Design (QbD) principles. Both start with an information gathering phase. Depending on the information available (material qualification program, vendor supplied extractable data, lack of extractable data, parental dosing devices) a risk analysis is carried out and a study plan is developed. The correct safety concern threshold (SCT) is selected and an analytical evaluation threshold (AET) is calculated from the SCT, the container parameters and the dosing regimen.

In the accelerated study design for early phases, the next three steps are conducted in parallel. An extraction study using an automated solvent extractor (ASE) is conducted in parallel with method adaptions for the specific set-up.

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ASE extractors (Figure 3) use organic and aqueous liquid solvents at elevated temperatures and pressure to increase the efficiency of the extraction process. Increased temperature accelerates the extraction kinetics, and elevated pressure keeps the solvent liquid above its boiling point, thus ensuring safe and rapid extractions. Additionally, the pH-hardened pathway allows the extraction of matrices that are pretreated with acids or bases.

Figure 3: Automated solvent extractor device

Additionally, either a simulated leachable study or a leachable study with available R&D material is carried out. Potential leachables are reported if they are above the AET.

Conclusion

Depending on the phase of the product development and regulatory expectations, classical and accelerated approaches for conducting E&L studies are available.

Modern technologies, such as an ASE, high-resolution mass spectroscopy and gas chromatography coupled to a mass spectrometer can be used to generate the necessary data for your product depending on your needs.

Give us a call and discuss with our experts!