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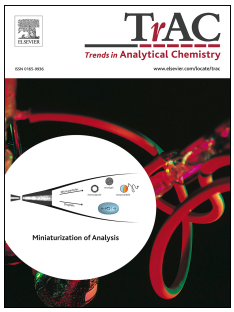

Identification, Analysis and Safety Assessment of Leachables and Extractables

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Identification, Analysis and Safety Assessment of Leachables and Extractables

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Abstract:

Pharmaceutical drug products (DP) can contain foreign impurities due to contact with manufacturing, storage, distribution and administration systems. These foreign impurities (leachables) are leached from these systems by the drug product and can be linked to extractables measured in the systems during laboratory investigations.

Assessing the impact of leachables on the suitability of the DP requires that it be screened to discover, identify and quantify leachables. Given the large number and great chemical diversity of potential leachables, an analytical strategy involving multiple, orthogonal analytical methods is necessary to generate a complete leachables profile.

Once the profile has been delineated, the effect of leachables on the DP's suitability can be established. The potential adverse effect of leachables on patient safety can be established via chemical safety risk assessment, which involves comparing a DP user's (patient) exposure to individual leachables with exposure thresholds which are toxicologically established for the individual leachables.

Key words: extractables; leachables; analytical screening methods; toxicological safety risk assessment; pharmaceutical packaging; container-closure systems; manufacturing component, medical devices; controlled extraction study

Abbreviations:

AET = Analytical Evaluation Threshold
bBtBPP = bis(2,4-di-tert-butylphenyl) phosphate
BHT = Butylated Hydroxytoluene
BW = body weight
C_A = Concentration of the analyte
C_{IS} = Concentration of the internal standard
C_L = Concentration of a leachable in a drug product
CCS = Container-Closure System
CES = Controlled Extraction Study
DP = Drug Product
E&L = Extractables and Leachables
EVA = Ethylene (vinyl acetate)