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Hazard and risk assessments for impurities, residual solvents, extractables, and leachables.

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HAZARD AND RISK ASSESSMENTS FOR IMPURITIES, RESIDUAL SOLVENTS, EXTRACTABLES, AND LEACHABLES.

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During their life-cycle (i.e., manufacture to end-use), single-use products in the biotechnology industry come in contact with processing equipment, packaging components, and delivery systems. Small amounts of chemicals that may transfer to the single-use product at any step in the life-cycle may subsequently leach into the pharmaceutical drug product and be delivered to the patient along with the dose. It is important that this chemical transfer does not occur in quantities that alter the safety, identity, strength or quality of the drug product. The assessment of potential leachable chemicals begins with a detailed analysis of compounds released from the single-use product under exaggerated conditions (i.e., a chemical extractable analysis). The observed extractables help guide the identification of potential compounds in a subsequent leachables study. This leachable analysis is carried out to identify (and quantify) the compounds that leach into a drug product under normal conditions of use (i.e., production, storage, use, etc). A patient health risk assessment is then performed to address the compounds identified in the leachable study. In addition to a toxicological hazard assessment of individual leachable compounds, the risk assessment includes dose of the drug product, route of administration, dosing frequency, and patient population. Where substance-specific hazard data are inadequate or unavailable, an in silico hazard determination and/or a Threshold of Toxicological Concern (TTC) approach may be utilized. The goal of the risk assessment is to determine whether the inevitable low level migration of chemicals from packaging and processing materials leads to an unacceptable patient risk profile. Specific examples of extractable/leachable studies and subsequent risk assessments will be presented and discussed.