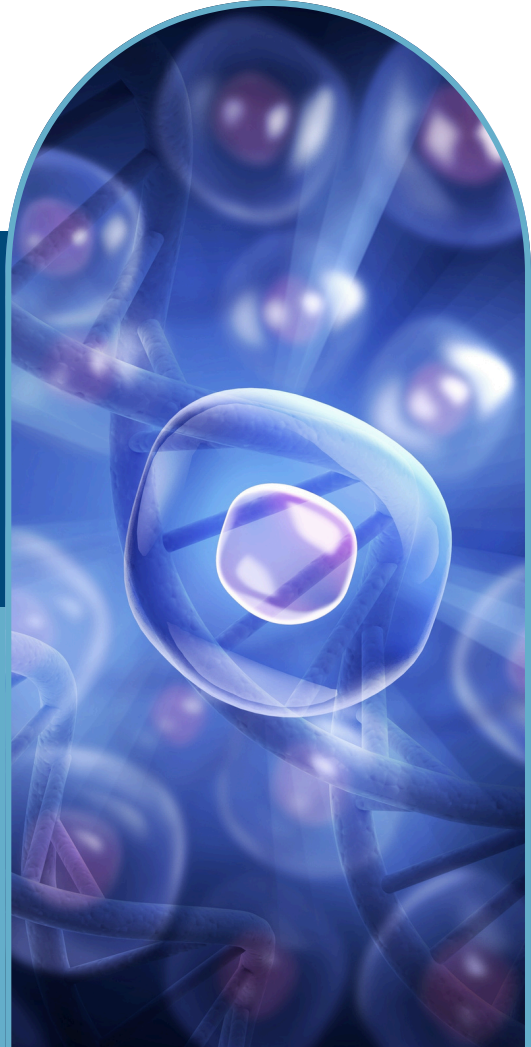


RISK-BASED EXTRACTABLES AND LEACHABLES ASSESSMENT FOR CELL AND GENE THERAPIES

Overcoming CGT-Specific E&L Challenges with Scientifically Justified Study Design

A cell and gene therapy developer preparing for clinical advancement needed to assess extractables and leachables risk across a complex manufacturing and storage workflow. Unlike conventional biologics, the therapy involved living cells, cryopreservation with DMSO, limited available drug product, long-term cryogenic storage, and extensive use of single-use systems. Traditional E&L approaches could not be applied directly. Standard extraction solvents did not fully represent DMSO's strong solvency behavior, accelerated storage studies could misrepresent cryogenic conditions, and limited sample volumes made direct product testing impractical. To move forward with confidence, the developer partnered with Solvias to design a flexible, risk-based E&L strategy tailored to the product, process, and regulatory expectations.



THE CHALLENGES

DMSO-Specific Leachable Risk: DMSO can penetrate polymeric materials and mobilize compounds that may not leach under typical aqueous or organic conditions. Standard solvent systems may therefore miss relevant leachables.

Limited Sample Availability: CGT products are often produced in small, patient-specific batches, leaving little or no excess drug product available for extensive leachables testing.

Cryogenic Storage Conditions: Long-term storage at ultra-low temperatures limits molecular mobility, making traditional accelerated leachables models less predictive. Additional risk may occur during freezing, thawing and post-thaw handling.

Complex Product Matrix: CGT products contain viable cells, metabolites, media components, cryoprotectants, and excipients, creating analytical interference and making complete characterization more challenging.

Evolving Regulatory Expectations: CGT-specific E&L expectations are still developing, requiring clear scientific rationale for solvent selection, simulant use, AET calculations, and study design.



OUR COLLABORATIVE APPROACH

Customized Solvent and Matrix Strategy: Solvias designed extraction and simulation studies around the actual risks of the CGT workflow, including DMSO-containing systems and scientifically justified surrogate matrices where direct product testing was not feasible.

Risk-Based Material Prioritization: The team evaluated single-use components, container closure systems, and high-contact materials based on surface area, contact time, material composition, and likelihood of patient exposure.

Orthogonal Analytical Methods: Solvias applied complementary analytical techniques to improve detection across volatile, semi-volatile, non-volatile, organic, and elemental impurities, addressing the limitations of any single method.

Cryogenic and Post-Thaw Considerations: The strategy incorporated real-time or representative cryogenic conditions, with added focus on thaw and post-thaw hold points where leachable release may be more relevant.

Regulatory-Ready Justification: Solvias supported the study design with clear documentation explaining solvent selection, simulant rationale, AET assumptions, analytical limitations, and risk mitigation.



THE RESULTS

- A CGT-specific E&L strategy developed without relying on unsuitable platform assumptions.
- DMSO-related leachable risks addressed through customized extraction and analytical design.
- Limited product availability managed through scientifically justified simulation studies.
- Cryogenic storage and thaw-related risks evaluated using relevant conditions and timepoints.
- Regulatory confidence strengthened through clear, defensible scientific rationale.



CONCLUSION

This case demonstrated how a flexible, risk-based strategy can help developers overcome these challenges without compromising scientific rigor or patient safety. By combining tailored study design, orthogonal analytical methods, and clear regulatory justification, Solvias helped the customer transform uncertainty into a defensible E&L package suitable for advanced therapy development.

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- 5 centers of excellence

