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When Every Nanogram Matters:

HIGH-RESOLUTION EXTRACTABLES SCREENING FOR PREFILLED SYRINGES

A biopharmaceutical company developing a monoclonal antibody (mAb) in a prefilled syringe (PFS) needed to evaluate potential extractables and leachables from the container closure system. As the product progressed toward commercialization, regulatory expectations required increasingly comprehensive identification of compounds that could migrate into the drug product throughout its shelf life. Traditional extractables studies often relied on aggressive solvent extractions that did not accurately represent the finished product or storage conditions. In addition, the very low analytical evaluation thresholds (AETs) required for higher-dose products demanded analytical sensitivity well beyond conventional screening methods. To generate a realistic, highly sensitive, and regulatory-ready assessment of leachable risk, the company partnered with Solvias.

THE CHALLENGES

Very Low Analytical Evaluation Thresholds
For prefilled syringes delivering larger daily doses, AETs can decrease to the low ng/mL range. Detecting and identifying compounds at these concentrations requires highly sensitive analytical methods without compromising confidence in compound identification.

Conventional Extractables Studies May Overestimate Risk
Traditional extraction approaches frequently evaluate individual packaging components under exaggerated conditions or extract surfaces that never contact the drug product. This can generate extractables profiles that do not accurately reflect the compounds likely to migrate into the finished product during storage.

Unknown Compounds Create Regulatory Risk
Compounds that cannot be identified are typically treated as toxicological unknowns, increasing regulatory uncertainty and often requiring additional investigation. Maximizing identification rates is therefore essential for efficient risk assessment.

Complex Drug Product Matrices
Biologic formulations containing excipients such as polysorbates can complicate extractables analysis by requiring additional sample preparation while maintaining extremely low detection limits.

OUR COLLABORATIVE APPROACH

Simulation-Based Extractables Study Design
Rather than extracting isolated packaging components, Solvias designed a study that evaluated the assembled prefilled syringe using extraction solvents and conditions representative of the intended drug product and storage environment as well as an extraction with enhanced extraction conditions (worst case scenario). Accelerated aging principles were applied to simulate long-term storage while maintaining realistic migration behavior.

Ultra-Sensitive HRAM Screening
High-resolution accurate mass GC-MS and LC-MS/MS workflows were implemented to screen volatile, semi-volatile, and non-volatile extractables at analytical evaluation thresholds as low as 1 ng/mL, enabling detection of trace-level compounds relevant to patient exposure.

Advanced Compound Identification
Compound identification combined commercial libraries with Solvias' proprietary database containing thousands of extractables and leachables reference spectra. Accurate mass measurements, MS/MS fragmentation, and orthogonal confirmation significantly reduced the number of unidentified compounds.

Comprehensive Risk Assessment
The integrated workflow generated both realistic migration estimates and chemically confident compound identifications, providing a robust scientific basis for toxicological assessment and regulatory documentation.

THE RESULTS

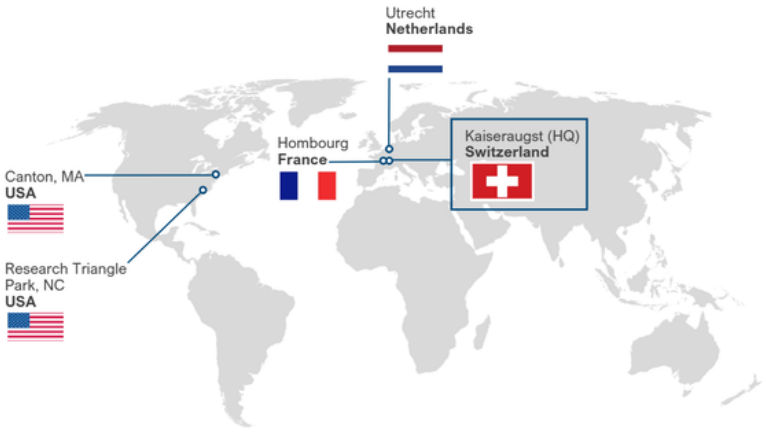
- Untargeted screening sensitivity down to 1 ng/mL to support very low analytical evaluation thresholds.
- Identification rates of 98–100% for detected organic compounds through combined HRAM workflows and proprietary databases.
- Regulatory-ready extractables dataset supporting container closure qualification and product development.

CONCLUSION

This case demonstrates how simulation-based extractables studies, combined with high-resolution accurate mass spectrometry and advanced compound identification strategies, enable comprehensive characterization of potential leachables while minimizing analytical uncertainty. By integrating realistic extraction conditions with ultra-sensitive HRAM screening, Solvias helped the customer generate a scientifically robust, regulatory-ready assessment of container closure compatibility.

WHY PARTNER WITH US?

- CRO
- Founded in 1999
- 800+ team members
- 175+ PhD-level scientists
- GMP, GLP, ISO9001 certified
- 23K m^2 of lab capacity
- 700+ customers worldwide
- 5 centers of excellence



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