Accelerating residual solvents analysis in 21 CFR Part 11 compliant settings

through real-time mass spectrometry

Introduction

SIFT-MS is a direct, real-time mass spectrometry (MS) technique which offers revolutionary volatile compound analysis capabilities to Pharma and CDMO labs due to its fast time to data, time efficient workflows, analytical flexibility, and ease of use. It expedites analytical workflows, such as residual solvents analysis, by generating faster results than traditional methods. Syft Tracer Pharm11 is a SIFT-MS-based solution that includes SyftAuditTracer software designed for 21 CFR Part 11 compliant environments. Volatile impurities can be characterized in real-time including nitrosamines, ethylene oxide, and residual solvents.

The real-time mass spectrometry advantage

Syft Tracer Pharm11 provides unmatched ease of use while increasing workflow efficiency through minimal sample preparation requirements, high-throughput capacity, and analytical flexibility. System or column changeover between analytical methods is not required, saving both analyst and instrument time. SIFT-MS eliminates the need for chromatographic separation and achieves selectivity via rapidly switchable reagent ions. Analytes undergo different reactions with each reagent ion, generating product ions via independent ion chemistries that are diagnostic of species identity.

Software designed to unlock real-time workflows and compliance

SyftAuditTracer software is designed to maximize the speed and ease of residual solvents analysis while supporting 21 CFR Part 11 compliant processes. It allows users to easily acquire, process, and report on data while maintaining a traceable account of all user actions, records, and system access within the audit trail. Data processing functions are specific to real-time SIFT-MS analysis, so quantitative results can be generated quickly and intuitively.

Residual solvents analysis with Syft Tracer Pharm11

SIFT-MS is well-suited to residual solvents analysis (USP<467>), with analytical performance previously validated according to USP<1467> (Biba et al. (2021)). Data are generated in real-time during the course of data acquisition, with each SIFT-MS sample analysis completing in several minutes (typically 3 minutes or less). This means sample throughput >200 per day is achievable with the automated solution. Once a sequence starts, additional batches can be queued to run immediately after, even if different methods are used. This is possible because SIFT-MS requires no system or column changes between different methods.

In addition to bringing SIFT-MS analysis into the compliant environment, SyftAuditTracer allows the user to seamlessly process raw analytical data to generate analytical results, culminating in a PDF report. As SIFT-MS is a real-time technique, sample is injected over a long, slow injection, rather than in a tight, fast band. The raw signal data collected over the injection is averaged to obtain a mean intensity (see example shown in Figure 1 of an injection taken over the course of 100 seconds), which is used in downstream data processing. Blank subtraction and calibration (calibration curves or single point calibrations) can also be performed in SyftAuditTracer software. Figure 2 shows an example calibration curve from a study conducted with the Class 2 solvent chlorobenzene, demonstrating excellent linearity across the working range (10-750 ppb in solution).

Conclusion

Syft Tracer Pharm11 accelerates the analysis of volatile impurities such as residual solvents through its high-throughput automation, fast time to data, ease of use, and analytical versatility. Its unique capabilities streamline typical Pharma and CDMO analytical applications, while ensuring 21 CFR Part 11 compliance through the SyftAuditTracer software.

Figure 1. The first step of data processing involves computing a mean intensity across the sample injection profile. The plot illustrates the long, slow injections required for real-time SIFT-MS analysis. In this example, data is collected over the course of 100,000 ms (100 seconds).

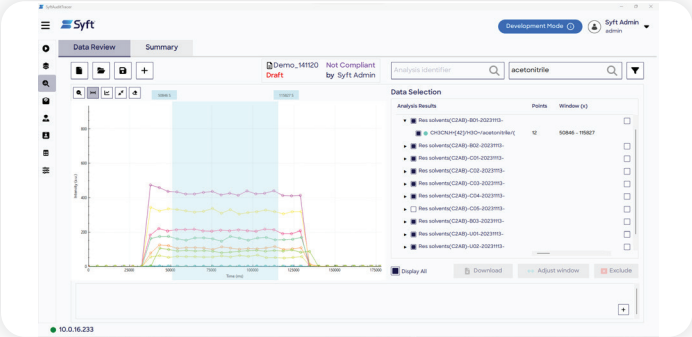
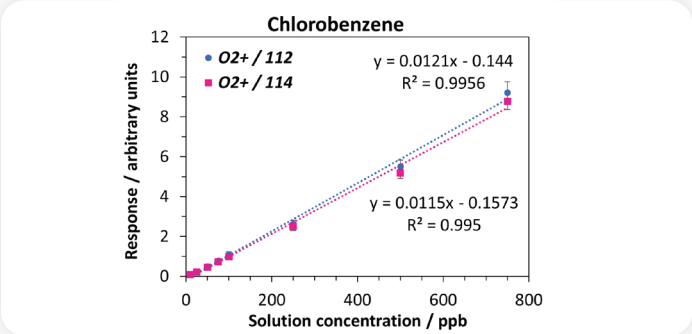


Figure 2. An example calibration curve for the Class 2 residual solvent chlorobenzene, exhibiting excellent linearity across the chosen range.



References

Biba E, Perkins MJ, Langford VS (2021). Stimuli to the Revision Process: High-throughput residual solvent analysis using selected ion flow tube mass spectrometry (SIFT-MS). United States Pharmacopeia. Pharm. Forum 47(6). https://online.usppf.com/usppf/document/GUID-2EE1BF6B-C82B-4F11-8E0B-C5520A4E8C3D_10101_en-US.

Food and Drug Administration (2003). Guidance for Industry Part 11, Electronic Records; Electronic Signatures—Scope and Application.

Food and Drug Administration (1997). 21 CFR Part 11. Electronic Records; Electronic Signatures; Final Rule Electronic Submissions; Establishment of Public Docket; Notice.

United States Pharmacopeia. Residual Solvents <467>

United States Pharmacopeia. Residual Solvents—Verification of Compendial Procedures and Validation of Alternative Procedures <1467>.

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