Water Technologies & Solutions
application note

Sievers* total traceability

certified reference materials & vials for TOC analysis

importance of traceability

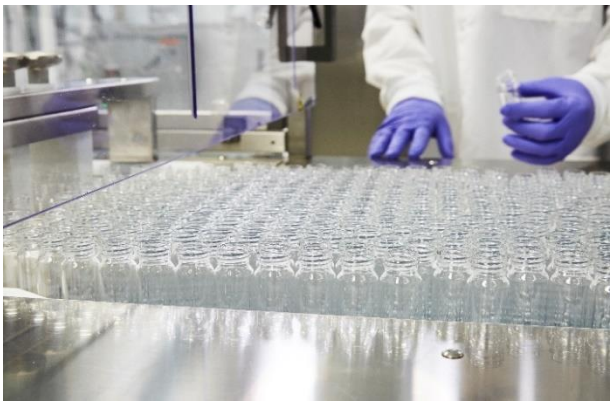
In the pharmaceutical industry, traceability is increasingly vital to the integrity of pharmaceutical products. By providing end-to-end visibility into pharmaceutical supply chains, companies can better trace serialized products from wholesalers to end customers and ensure product integrity. The Drug Supply Chain Security Act will eventually require serialization and item-level traceability of prescription drugs, enabling supply chain partners to track product ownership to the manufacturer or re-packager.

Beyond supply chain, nearly every functional area within a pharmaceutical facility is beginning to emphasize traceability—both for quality control and to improve operations. For example, traceability requirements in cleaning validation studies and water quality monitoring help ensure the accuracy, performance, and reliability of critical total organic carbon (TOC) measurements. The use of TOC instruments, like the Sievers* M9 TOC Analyzer, has become a widespread best practice throughout the pharmaceutical industry, providing a simple yet effective way to ensure processes are in control.

Measurement traceability, as applied to TOC analysis, refers to an unbroken chain of comparisons to a known standard, and is important to validate the pharmaceutical user's TOC data. Calibration and verification are the most commonly used methods to align a TOC instrument with a traceable standard for determining precision and accuracy.

measurement failures and out-of-specification results

Out-of-Specification (OOS) results refer to test results that fall outside established specifications. When an OOS result occurs, FDA regulations require that an investigation be conducted to determine the cause and that a written record of the investigation be made, including conclusions and follow-up. Whether a sample



preparation or an actual process issue, there is a limited amount of time before costs begin to rise as the root cause investigation is conducted.

Improved traceability can shorten the resolution of an OOS investigation, and details or reports supplied by vendors to help quickly close out non-conformances are invaluable. Sievers' Failure Analysis Report (FAR), available to any customer using both a Sievers instrument and consumables, is an important tool in traceability.

For example, an OOS investigation would be triggered if a pharmaceutical company reports a TOC value exceeding its limit for a cleaning validation (CV) study. The company may troubleshoot this measurement and investigate if the instrument is flawed, the vial is contaminated, or if the sample does indeed have a higher TOC concentration. If components of the measurement system are supplied by Sievers, there is the ability to cross reference the lot numbers of:

- Vials used to collect the CV samples;
- Standards bracketing the TOC samples against any other reports covering the same lot (providing full visibility into the quality checks associated with empty vials);
- Other certified reference materials such as system suitability tests; and

- TOC instrument health.

If these elements are validated through a FAR, then the end user can be confident that the measurement does accurately reflect an increase in TOC, which can help resolve the OOS investigation efficiently.

why do accreditations matter?

ISO 17034 and ISO/IEC 17025 accreditations ensure that Sievers reference materials used for calibration and verification are consistently produced, controlled, and audited to robust quality standards. ISO 17034 provides the highest level of quality assurance and certifies that a manufacturer's processes comply with strict guidelines and include all contributing factors to uncertainty. ISO/IEC 17025 certifies the reliability of the testing performed in conjunction with reference material production and confirms the manufacturer's ability to produce precise and accurate test and calibration data with the instruments used to qualify each production lot.

With these accreditations, pharmaceutical manufacturers can be confident in the consistency and, thus, the traceability of Sievers standards.

Sievers: full in-house traceability

Pharmaceutical companies face mounting pressures for increased traceability within their supply chains. This includes the need to close out non-conformances and OOS investigations quickly. Because of this, traceability of every material and instrument used in processes becomes important. Sievers addresses these concerns by offering:

- The **highest combined accreditation standard in the industry** (ISO 17034 and ISO/IEC 17025 accredited for the production and testing of TOC and conductivity standards).
- **Full traceability of both standards and vials** (due to in-house cleaning of vials used in standards production).
- Full visibility and analysis of instrument health, including the **availability of Failure Analysis Reports**.

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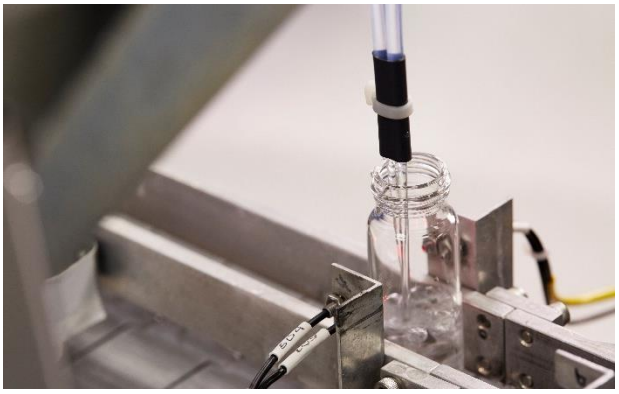
ANAB ACCREDITED ISO/IEC 17025 TESTING LABORATORY
AT-2118 & AT-2131

ANAB ACCREDITED ISO 17034 REFERENCE MATERIAL PRODUCER
AR-2119 & AR-2132



Sievers' complete traceability of reference materials, vials, and analytical instruments helps pharmaceutical companies efficiently "close the loop" on TOC out-of-specification investigations; reducing risks, increasing data quality, and ensuring a reliable and accurate total TOC measurement solution.

Find a contact near you by visiting www.sieversinstruments.com and clicking on "Contact Us".

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