

## CIP-100® TOC and conductivity detection using Sievers M-Series

### purpose

This study demonstrates the ability of Sievers\* M-Series TOC Analyzers to detect and quantify low concentrations of CIP-100® (STERIS Life Sciences) using both TOC concentration and conductivity analyses.

### background information

CIP-100 is an alkaline detergent commonly used in the pharmaceutical industry for the cleaning of manufacturing equipment during product changeover. During cleaning validation, it is essential to determine if any residual detergent remains in the final rinse of equipment. CIP-100 is 10-30% potassium hydroxide and 1-5% tetrasodium ETDA<sup>1</sup>, making this detergent highly suitable for analysis on a Sievers M9 Analyzer for both TOC and conductivity.

### experimental test plan

Four concentrations of CIP-100 were tested on the Sievers M9 Analyzer: 0.001%, 0.01%, 0.025%, and 0.05%. These CIP-100 solutions were made from a 1% CIP-100 stock solution. All CIP-100 solutions were made in clean, low-level TOC glassware and transferred immediately into Sievers Dual Use Conductivity and TOC (DUCT) vials for analysis. DUCT vials have been shown to be highly stable for sample conductivity and TOC concentrations even for storage times of up to five days<sup>2</sup>. The TOC concentrations of these solutions were unknown since the exact carbon concentration of the CIP-100® solution was not known exactly. As such, the 0.01%, 0.025%, and 0.05% samples were run on the instrument using the Autoreagent feature so that the instrument could determine optimal reagent flow rates. The 0.001% samples were run with acid = 0.5 µL/min and oxidizer = 0.0 µL/min based on the low expected TOC (<500 ppb). All samples were run with five repetitions and zero rejects on two separate sample aliquots (n=10).

### test equipment

- Sievers M9 Laboratory TOC Analyzer, Serial Number: 1312-0039
- Sievers Autosampler, Serial Number: 10040214
- DataPro2 Software

### calibration and verification

#### Conductivity Calibration

The Sievers M9 Laboratory Analyzer was calibrated for conductivity using a 1409 µS/cm KCl standard as outlined by Sievers protocols<sup>3</sup>. The conductivity calibration was verified with HCl at 25 µS/cm. The data in **Table 1** presents the results of this verification.

**Table 1. Results of the 25 µS/cm HCl conductivity standard after calibration**

Standard Concentration	Expected	Measured	%RSD	%Diff	%Diff ≤±2% and %RSD ≤3%?
25 µS/cm	25.0 µS/cm	25.47 µS/cm	0.73%	1.88%	Yes, Pass

## TOC Calibration

The analyzer was calibrated for TOC using a single-point 10 ppm calibration using KHP and Na<sub>2</sub>CO<sub>3</sub> as outlined in Sievers protocols<sup>3</sup>. This calibration was verified at 500 ppb using sucrose. **Table 2** presents the results of this verification.

**Table 2. Results of the 500 ppb TOC sucrose standard after calibration**

Standard Concentration	Expected	Measured	%RSD	%Diff	%Diff ≤±2% and %RSD ≤3%?
500 ppb TOC	518 ppb	514 ppb	0.67%	-0.77%	Yes, Pass

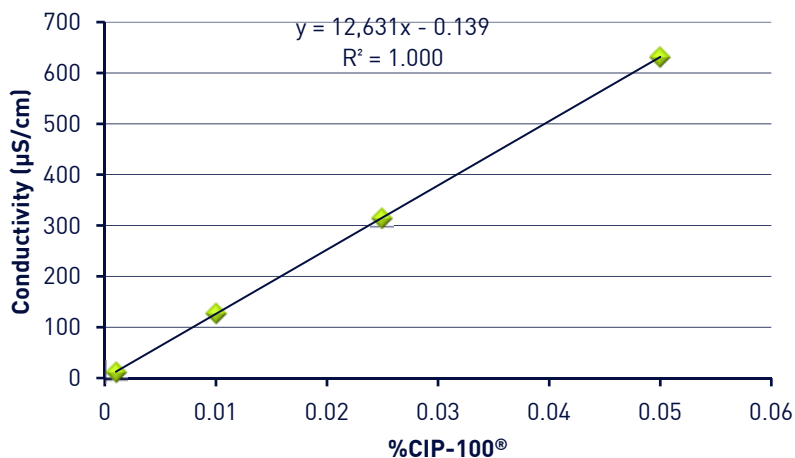
## results and discussion

### Conductivity Results for CIP-100

All conductivity data presented in **Table 3** are temperature corrected conductivity in μS/cm (corrected to 77 °F/25 °C). Linear regression results are shown in **Figure 1**.

**Table 3. Temperature-corrected conductivity results for 0.001%, 0.01%, 0.025%, and 0.05% CIP-100**

% CIP-100	Conductivity (μS/cm)	Standard Deviation (μS/cm)	%RSD
0.001%	11.9	0.2	1.6%
0.01%	127.3	0.2	0.1%
0.025%	315.2	0.6	0.2%
0.05%	631.5	1.4	0.2%



**Figure 1. Linear regression results of temperature-corrected conductivity versus CIP-100 concentration.**

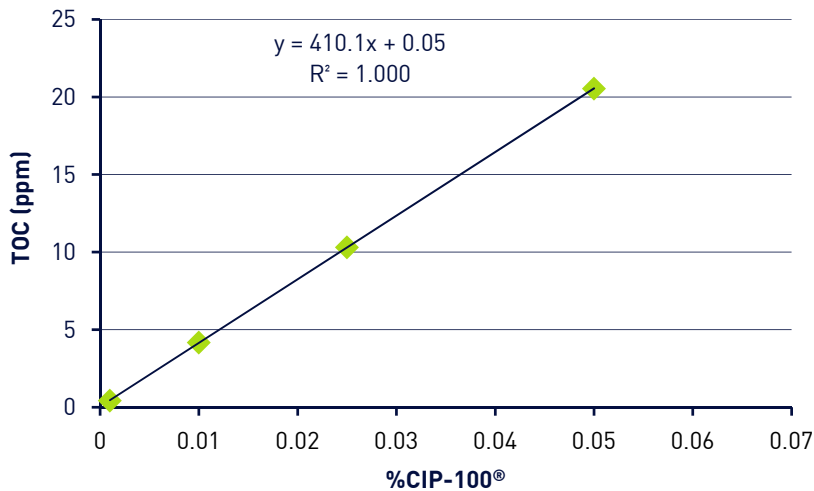
Conductivity levels in CIP-100 were highly linear over the range of 0.001% to 0.05% ( $R^2 = 1.000$ ). At the lowest concentration of CIP-100 (0.001%) the conductivity was still high at  $11.9 \pm 0.2$  μS/cm. The Sievers M9 Analyzers can measure conductivity well below 1 μS/cm, indicating that CIP-100 concentrations below 0.0001% can be reliably detected using conductivity.

## TOC results for CIP-100

TOC measurements for the various concentrations of CIP-100 are presented in **Table 4** with linear regression results shown in **Figure 2**.

**Table 4. TOC results for 0.001%, 0.01%, 0.025%, and 0.05% CIP-100**

% CIP-100	TOC Concentration (ppm)	Standard Deviation (ppm)	%RSD
0.001%	0.43	0.004	0.9%
0.01%	4.17	0.03	0.7%
0.025%	10.3	0.1	1.1%
0.05%	20.5	0.1	0.4%



**Figure 2. Linear regression results of TOC versus CIP-100 concentration.**

Similar to conductivity levels, TOC concentrations of CIP-100 were highly linear ( $R^2=1.000$ ) over the 0.001-0.05% concentration range. The TOC concentration of 0.001% CIP-100 was  $430.8 \pm 0.4$  ppb, which is over 5,000 times higher than the 0.03 ppb limit of detection for the Sievers M9 Analyzer. Therefore, CIP-100 at trace concentrations would be detected using TOC measurements on the Sievers M9 Analyzer.

## conclusions

The ability to measure both TOC concentrations and conductivity levels on the Sievers M9 Analyzer is useful for detecting any residual cleaning agent during the cleaning validation process. CIP-100 is a common alkaline cleaning agent that is easily detected at trace concentrations (<0.001%) using both TOC and conductivity on the Sievers M9 Analyzer. The data indicated a highly linear response ( $R^2 = 1.000$ ) between 0.001% and 0.05% for both TOC and conductivity.

### References

1. Ebers, M., *MSDS for CIP-100: Alkaline Process and Research Cleaner*. (2010).
2. Sievers Instruments: Test Report: DUCT Vial Performance and Stability. (2015).
3. Sievers M9/M9<sup>+</sup> TOC Analyzers Operation and Maintenance Manual. 1.4Rev10 Firmware. DLM 77000-01 EN Rev D. (2014)

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