Analysis of Clean-in-Place (CIP) Alconox® Swab Samples Using the Teledyne Tekmar Fusion UV/Persulfate TOC Analyzer

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Summary

Clean-in-place (CIP) is a process for cleaning pharmaceutical manufacturing equipment with minimal manual intervention and without disassembly. The procedure is accomplished by using solvents or detergents in the manufacturing apparatus, in combination with controlled flow, pressure, temperature and time variables. Through this process, manufacturing equipment can be successfully and consistently cleaned and afterward, validated to be clean. The detergent Alconox is commonly used in CIP operations. After the equipment is cleaned with the detergent and rinsed, swabs are used to collect any residual detergent or contamination in the cleaned equipment. These swabs are then analyzed for Total Organic Carbon (TOC) to determine if the equipment is truly clean and ready for the next manufacturing process.

This application note will demonstrate the analysis of Alconox swab samples for total organic content (TOC) to validate both swab sample testing and the Teledyne Tekmar Fusion UV/Persulfate TOC analyzer as a suitable instrument for TOC analysis and CIP validation.

Method Parameters

To optimize the instrument, the Fusion's TekLink software default TOC "Pharmaceutical Water" method was modified slightly to reduce the small amount of foaming produced by the 1.0 ppm Alconox sample. Method modifications included:

- Reagent Volume was increased from 0.6 mL to 0.8 mL to ensure complete oxidation of Alconox swab samples.
- Pre-Sparge Time was set at 0.20 minutes to allow the 10% Sodium Persulfate ($Na_2S_2O_8$) with 5% Phosphoric Acid (H_3PO_4) reagent to interact with sample and assist in reducing sample foam.
- Baseline Stabilization Time was increased from 0.50 minutes to 1.60 minutes to allow the baseline to completely stabilize for sample analysis of two repetitions.

Note: When analyzing three (3) repetitions with the Fusion TekLink TOC "Pharmaceutical Water" method, each repetition is sparged in the IC sparger individually and the default 0.50 minutes provided for Baseline Stabilize Time is adequate.

When analyzing two (2) repetitions, both sample aliquots are sparged simultaneously, resulting in analysis of the second repetition before the baseline has completely stabilized. Consequently, 1.60 minutes is needed to allow the baseline to stabilize prior to analysis of the second repetition.

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Calibration

The Fusion TOC analyzer was calibrated using a stock standard of 5.0 parts per million carbon (ppmC), prepared from potassium hydrogen phthalate (KHP). The Fusion's auto-calibration feature was used to automatically create a calibration curve of 0.0, 0.10, 0.25, 0.5, 1.0, 2.5 and 5.0 ppmC calibration standards.

Procedure

1. A stock standard of Alconox was prepared at 125 ppmC.
2. 40 mL of TOC grade water was added to each of three 40 mL VOA vials, after triple rinsing them with TOC grade water.
3. 1.0 ppm Alconox swab samples were prepared by spotting 320 µL of the 125 ppmC Alconox stock standard onto stainless steel coupons. The coupons were air dried and then swabbed individually with separate swabs.
4. Each used swab tip was broken off and placed in a separate VOA vial which had been previously filled with 40 mL of TOC grade water.
5. Five swab blanks were prepared in the same manner, omitting the Alconox swabbing step.
6. Vials were placed on a shaker table and shaken for 15 minutes.

Results

Table I Results

Sample ID	TOC Result (ppm)	Percent Recovery[1]
Calibration Check Standard (1.0 ppm C)	0.9928	99.3%
Swab Blank 1	0.2979	-
Swab Blank 2	0.2435	-
Swab Blank 3	0.2615	-
Swab Blank 4	0.3130	-
Swab Blank 5	0.2933	-
Swab Blank Average	0.2818	-
1.0 ppm Alconox Swab 1	1.2430	96.1%
1.0 ppm Alconox Swab 2	1.2212	93.9%
1.0 ppm Alconox Swab 3	1.2930	101.1%
Calibration Check Standard (1.0 ppm C)	1.0060	100.6%

1. Percent recovery of swabs was calculated after blank subtraction.

Conclusion

The results of this study demonstrate that the Teledyne Tekmar Fusion UV/Persulfate TOC analyzer is well-suited to validate the CIP process. The system generated reliable quantitative TOC data when analyzing Alconox swab samples at a level as high as 1.0 ppmC.