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Innovations in UV Oxidation Direct Conductivity TOC Measurement to Improve Accuracy and Precision

by Roger Schmid and Randy Turner

This article presents innovations to improve the accuracy and reliability of UV oxidation direct conductivity TOC measurement methods.

Total Organic Carbon or TOC is the carbon whose origin is organic in nature. It can originate from naturally occurring organic acids, such as tannic acid, bacteria, and abrasion of valves. The measurement of TOC is critical to the pharmaceutical industry because various regulatory bodies have established limits for TOC in Water for Injection (WFI) and other uses of water in pharmaceuticals. The main regulatory guidelines are incorporated in the following:

1. USP<643>, "Total Organic Carbon," United States Pharmacopoeia 36-NF 31, U.S. Pharmacopeial Convention Inc., Rockville, Md. (2013).
2. USP<645>, "Water Conductivity," United States Pharmacopoeia 36-NF 31, U.S. Pharmacopeial Convention Inc., Rockville, Md. (2013).
3. USP<1231>, "Water for Pharmaceutical Purposes," United States Pharmacopoeia 36-NF 31, U.S. Pharmacopeial Convention Inc., Rockville, Md. (2013).
4. EP 2.2.38, "Conductivity," European Pharmacopoeia, vol. 7.0, Council of Europe, Strasbourg, France (2013).
5. EP 2.2.44, "Total Organic Carbon in Water for Pharmaceutical Use," European Pharmacopoeia, vol. 7.0, Council of Europe, Strasbourg, France (2013).
6. JP 4.5.2, "Monitoring of TOC as the Indicator for Organic Impurities," JP XVI.

To measure TOC, the organic molecules must be reduced to inorganic carbon allowing quantitative measurement of the resultant carbon dioxide CO2. The organic molecule can be decomposed to inorganic carbon by thermal decomposition, UltraViolet (UV)-persulfate oxidation, and direct UV oxidation. The following are common methods of TOC analysis:

1. Thermal decomposition with NDIR detection
2. UV-persulfate oxidation with NDIR detection
3. UV-persulfate oxidation with conductivity detection
4. Direct UV oxidation with conductivity detection

Each process is based on the oxidation of the organic carbon that is present in the water and the subsequent measurement of the carbon dioxide which results from the oxidation. These methods all have advantages and disadvantages depending on how the oxidation and measurements are technically carried out. Therefore, each application has to be first examined as to which of the different methods is the most suitable.

Methods of TOC Analysis

Thermal Decomposition

With this process, the organic particles are destroyed by high temperatures. In this way, the undissolved components (suspended solids or wear debris) are also completely decomposed - *Figure 1*. This is a common method particularly with a high TOC load (e.g., municipal sewage).

UV-Persulfate Oxidation with NDIR or Conductivity Detection

The wet-chemical oxidation with UV light and persulfate is,

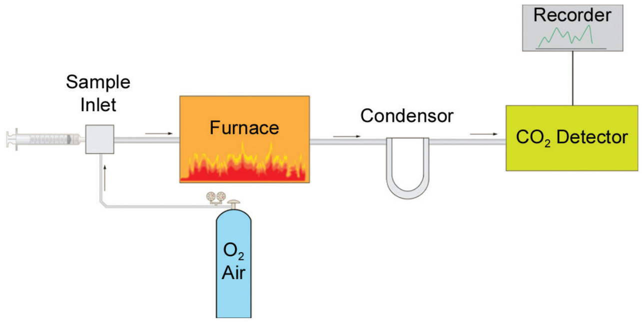

Figure 1. Schematic diagram of thermal decomposition.

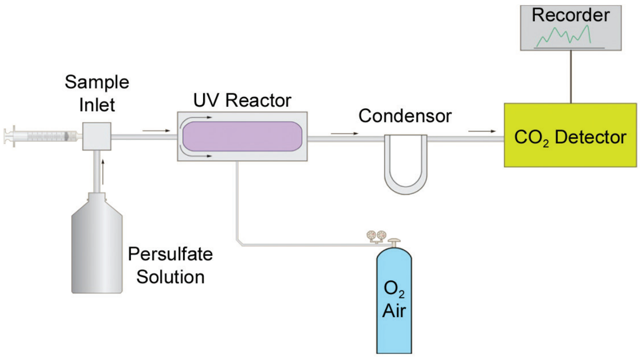

Figure 2. Schematic diagram of UV-persulfate decomposition.

especially with purified water and ultrapure water applications, widely spread and accepted as “the standard.” A great advantage of this method is the large operational range of less than 1 part per billion (ppb) to more than 100 parts per million (ppm) with high accuracy.

Direct UV Oxidation

Direct UV oxidation is applied only in ultrapure water and pharmaceutical applications where chemicals are not necessary. These instruments have been increasingly in use over the last few years. This article demonstrates the possibilities and limitations of modern TOC instruments by means of concrete examples. Details of the characteristics of direct UV on-line monitors will be presented to show the latest developments (e.g., functional test) which simplify daily routines and ensure safety. All the above mentioned methods have their particular advantages and disadvantages according to the systems’ limitations. For this reason, it is important to choose the instrument exactly for its application and environment.

Direct UV Oxidation with Conductivity Detection

Why is direct UV oxidation often selected to monitor TOC in the pharmaceutical industry? This method is fast and very reliable. Chemicals are not necessary and the maintenance is simple and easy which allows simple and compact analyzers. After the first conductance measurement, the sample flows into the UV-reactor. In this SWAN design, the water is directly channelled over the surface of the UV lamp to the second conductance measurement cell. The TOC concentration is calculated from the different values of the two sensors - *Figure 3.*

TOC = TC – TIC

- **TIC Total Inorganic Carbon**
  The component that originates from inorganic sources, e.g., CO_2
  The values are determined by the first sensor
- **TC Total Carbon**
  The sum of inorganic and organic carbon (TIC plus TOC), the value of which is determined by the second sensor
- **TOC Total Organic Carbon**
  The component that originates from biological sources, e.g., biofilm or cells

TIC in ultra-pure water and pharmaceutical applications is almost solely CO_2 from atmospheric CO_2. In most pharmaceutical production plants, the TIC is greater than the TOC. As with every other system, the direct UV method also has its limitations.

1. Limited range
   a. Conductivity – < 2 microsiemens per centimeter (< 2 µS/cm) at 20°C
   b. TOC – < 1 parts per million (ppm)
2. Reproducibility of UV-oxidation
3. Thermal effects
4. Accuracy

To avoid the mentioned disadvantages, we focused on achieving a complete oxidation by:

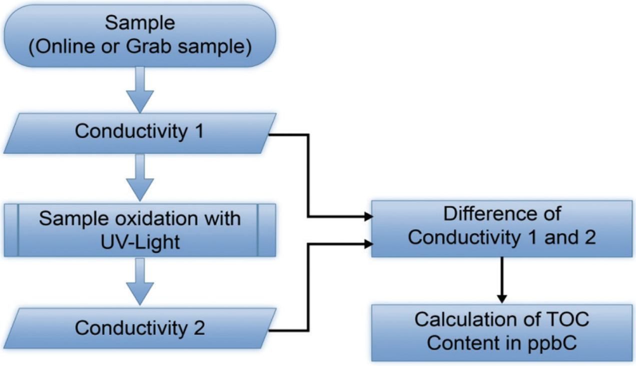

Figure 3. Schematic diagram of direct UV oxidation.

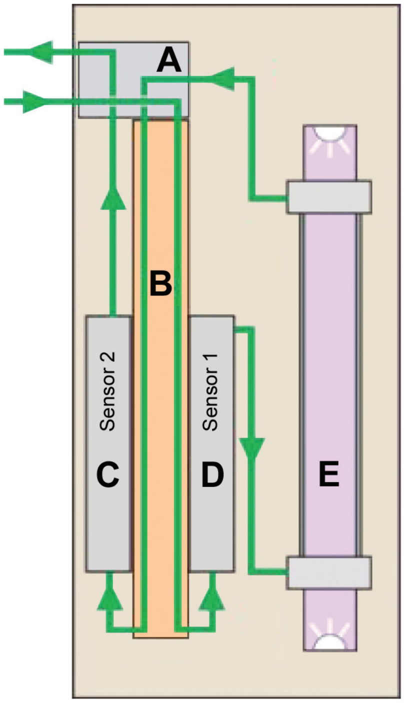

Figure 4. Reactor with a heat exchanger.

1. Stabilization of the thermal conditions
2. Increase of radiation flux
3. Optimization of the sample flow

A few measures and modifications had to be developed to reach this goal. All the presented changes had a huge effect on the method presented below.

Stabilization of the Thermal Conditions

The direct UV-method is strongly influenced by temperature effects. Due to the energy transfer from the UV-lamp, the sample temperature will be increased up to 10°C from conductivity sensor 1 to 2. The conductivity has to be compensated for this temperature difference. Unfortunately, the compensation is only an approximation depending on temperature and conductivity resulting in a potential error in measurement. As a result of our research, the reactor is fitted upstream with a heat exchanger where the outgoing water warms the counter current incoming water. With this, we can minimize the temperature difference between sensor 1 and sensor 2 to below 0.2°C. Particularly, on samples with low TOC values, this modification minimizes measurement errors. The achieved results are considerable stable and have lower variability's than before - *Figure 4.*

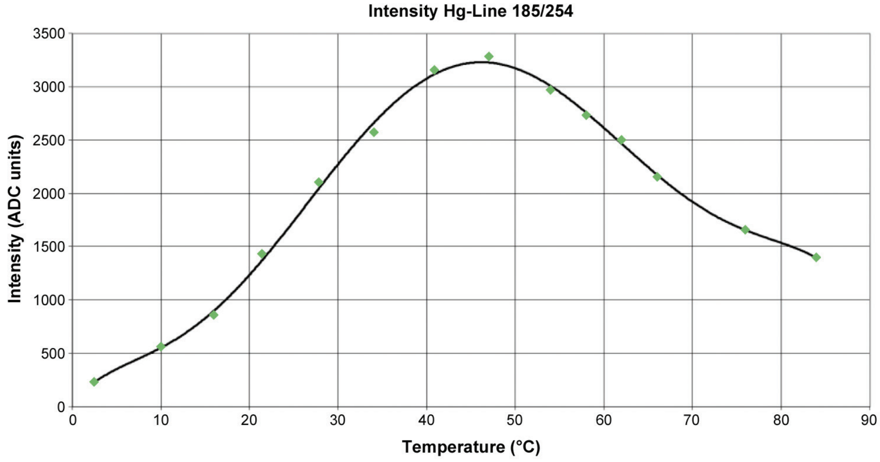

Figure 5. Intensity curve of a mercury low-pressure lamp.

Increasing Radiation Density during UV-Oxidation

The UV-lamps (Hg low pressure quartz bulb) employed, have a narrow temperature band where they produce the maximum energy output. This peak point is between 40°C and 50°C. Figure 5 shows the summary spectrum (185 and 254 nm) of an Hg lamp. The 185 nm UV wavelength exhibits a more pronounced impact by temperature.

From the Figure 5, the importance of keeping the temperature of the lamp within the optimal range is clear. Outside influences (environmental temperatures, location) and the sample water itself (changing sample temperatures) can lead to lamp temperatures outside the optimal range.

The heat exchanger solution minimizes the difference between the two conductivity sensors to less than 0.2°C. However, in order to maintain the temperature in the optimal range between 40°C and 50°C, further measures are necessary. An additional heating cartridge or sample cooler as seen in Figure 6 enable a target temperature of 42°C to be precisely sustained. Thus, the maximum radiation efficiency is achieved, resulting in optimal and consistent oxidation.

Optimization of the Sample Flow Through the UV Lamp

The aforementioned measures already show a substantial improvement to the system. The full potential is only

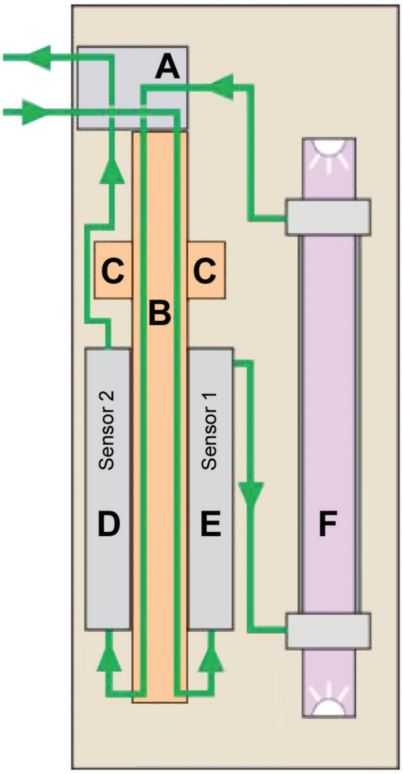

Figure 6. Reactor with heat exchanger and a heating cartridge.

realized in combination with an optimized sample flow. The classic design of a UV lamp and the sample is flowed around the light source. Divergence loss and reflection are practically unavoidable. The formation of deposits on the directly radiated surface, which decreases radiation density, cannot be fully eliminated in long running operations. This side effect can only be avoided by establishing a direct contact between the UV lamp and the sample.

Figure 7 demonstrates the sample flow in the newly engineered UV reactor. The sample flows directly along the lamp. The furthest distance from the middle of the lamp is 8 mm and the sample layer is only 0.5 mm thick. Divergence loss and ozone production is prevented because of the enclosed construction. This optimization leads to a distinct increase of radiation density, resulting in complete oxidation of the carbon compounds present in the sample. The UV lamp forms a single unit with the reactor case. The entire reactor can be replaced in the case of a failure and is recyclable. Maintenance is easier and faster.

Stable temperatures and a consistent, intense radiation are the foundations for exact and reliable measurement values. Equally important, however, is the compensation method, i.e., how the measured values are converted to the standard temperature.

The Conductivity Measurement

Temperature Compensation

Stable temperature conditions are the basic principles of accurate and reliable test results; however, the compensation method is equally important. This is how the measured conductance is converted to a comparative temperature. The conversion to a common reference temperature can be based on different algorithms; however, these formulas are not absolute. For this reason, SWAN uses two different compensation methods, depending on the chosen application range.

Carbon Dioxide (CO_2) Model

Water for pharmaceutical applications can by definition contain no salt. It can contain traces of organic carbon compounds (TOC) and dissolved carbon dioxide (TIC) from the atmosphere. Atmospheric CO_2 should be the only source of TIC. Below is an actual example with rounded figures:

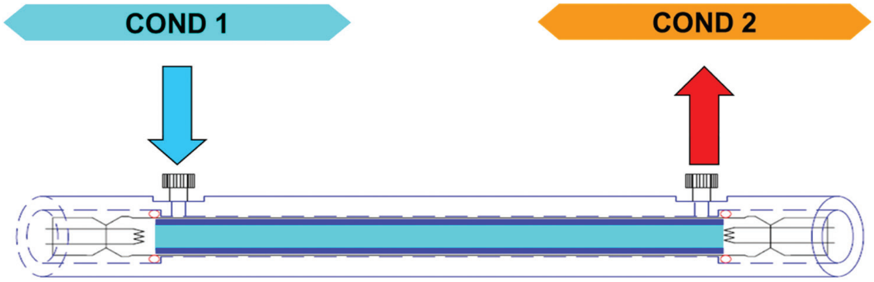

Figure 7. Cross section of a UV reactor.

- Conductivity of the water before oxidation at the first sensor (COND 1) – 0.6 µS/cm at 42°C
- Conductivity of water after UV oxidation at the second sensor (COND 2) – 0.8µS/cm at 42°C
- The absolute conductance of pure water void of CO_2 at 42°C is about – 0.12 µS/cm.

The difference in between the theoretically conductivity of pure water (0.12 µS/cm) and the conductivity at the first sensor (0.6 µS/cm), which in this example is 0.48 µS/cm, must therefore come from CO_2. TIC can be calculated from the definite correlation between conductivity and the carbon dioxide concentration. The corresponding values for the various temperatures are tabulated and stored in the instrument. The organic constituents in our example are converted to CO_2 by the UV lamp resulting in a conductivity of 0.8 µS/cm after oxidation at the second sensor. Consequently, the value at sensor 2 is higher than sensor 1. The difference between the conductivity value at sensor 2 and sensor 1 (due to the oxidation of organic carbon to form CO_2 thereby increasing the conductivity) is converted to ppb TOC an algorithm.

[CONDUCTIVITY 2] – [CONDUCTIVITY 1] = 0.2 µS

Calibration

The calibration is performed with a 1 ppm solution. If the results deviate more than expected from the target value, certain requirements have not been fulfilled, the operating parameters are wrongly adjusted, or the instrument has malfunctioned. This determination of TIC and TOC under the conditions described is an absolute method. The extent of a possible divergence is specified in the menu "installation" and an adjustment cannot be made.

Linear Compensation

This method is meaningful when there is no clear correlation between TOC content and conductivity.

With such applications, a TOC-conductivity (Λ)-model can be constructed by the production of calibration solutions which cover the concentration range of the relevant components. The temperature dependency of the conductivity of the samples only needs to be taken in consideration when the calibration and the online-monitoring are made at different temperatures. The AMI line TOC stabilizes the sample temperature, not just with online-monitoring, but also with a calibration at 42°C to 43°C. In order to allow readings with deviating temperatures, the conductivity values Λ_{in} and Λ_{out} are converted to 25°C.

A constant temperature performance is assumed over the entire measurement range with a linear compensation. This value can be manually changed.

The calibration in linear mode occurs through the measurement of an exactly defined sample solution (Sucrose 1 ppm). Based on the measurement result, the instrument calculates the effective slope, which it displays. From experience, the values are in the range of 0.15 to 0.3.

Pharmaceutical Application

Measurement Points

In modern WFI and Pure Water (PW) plants, most measurements are made at the points mentioned below:
Typically in pharmaceutical plants, it is after the distillation, in the storage tank, at the entrance and exit of the loops and of course at the point of use - *Figure 8.*

The Functional Check – an Aide

Instruments that are installed in pharmaceutical applications must pass a System Suitability Test (SST) according to the authoritative pharmacopeia (USP 643 / EP 2.2.24). The specifications of the test solution in these monographs are described in detail.

If the test is carried out in plants which produce according to the USP guidelines, the solutions have to be produced with USP certified reagents. Due to the extreme dilution, the storage life of these solutions is limited to only a few weeks. An SST is the only possibility to check a TOC instrument in praxis.

The prevailing UV lamps have a life expectancy of six months in instruments with direct UV oxidation. Every lamp exchange requires an SST, which means a minimum of two tests a year. Many operators also use the certified SST solutions more often than the required validation interval, even up to monthly checks. This involves considerable costs and is logistically very time consuming.

The automatic functional test of the AMI line TOC can effectively simplify this routine. The process is similar to the established SST. Highly concentrated solutions (sucrose and benzoquinone) are used, which last up to three months. The solutions are diluted at the time of the test with sample water by an integrated peristaltic pump. Both stock solutions are measured one immediately after the other. Conclusions can be made about the functions and the conditions of the instrument by the degree of recovery. The basic function of the instrument can be easily proved without intervention or external modification. The operator has the ability to examine the instrument regularly online, reducing the number of expensive and elaborate tests.

The functional test is activated manually or by a programmable timer. The applied solutions are not subject to pharmaceutical guidelines and can be produced by the operators themselves. The substances can be purchased from the local

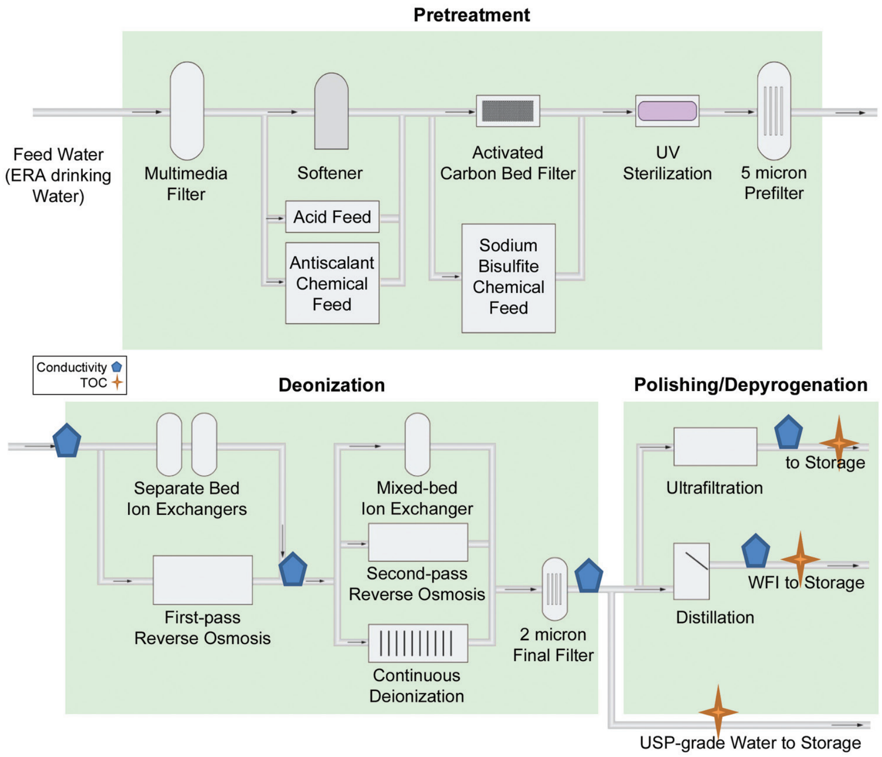

Figure 8. Possible installation in the pharmaceutical water preparations.

Figure 9. TOC analyzer.

chemical distributor as long as they comply with the quality requirements for an analysis.

Simple Grab Sample Testing

An extra benefit of the operating process is the possibility of examining grab samples with the instrument. The sample is drawn through the instrument by a peristaltic pump, regardless of whether it is an SST sample, a functional test or a grab sample - *Figure 9*. Grab samples are easily connected and can be measured immediately by the press of a button. As long as the grab sample measurement mode is active, the signal outpoints of the last value is held to avoid a false alarm.

After the grab sample measurement mode is over, the instrument is rinsed for a set time before the signal points are released to active reporting.

Conclusion

The focus of the development of the TOC analyser concentrated on three areas:

- The stabilizing thermal conditions
- Increasing the radiation density
- Optimizing the sample flow in the system

The technical solutions presented have verifiably improved the precision and accuracy of direct UV oxidation. Moreover, the exacting requirements of the pharmaceutical industry with reference to the standards for calibration and verification were specifically taken into consideration during the development.

Acronyms

PW	Purified Water
TC	Total Carbon
TIC	Total Inorganic Carbon
TOC	Total Organic Carbon
UPW	Ultra-Pure Water
WFI	Water For Injection

Definitions

Adjustment: set of operations carried out on a measuring system so that it provides prescribed indications corresponding to given values of a quantity to be measured.

Note: adjustment of a measuring system should not be confused with calibration, which is a prerequisite for adjustment.

Note: after an adjustment of a measuring system, the measuring system must usually be recalibrated.

Calibration: operation that, under specified conditions, in a first step, establishes a relation between the quantity values with measurement uncertainties provided by measurement standards and corresponding indications with associated measurement uncertainties and, in a second step uses this information to establish a relation for obtaining a measurement result from an indication.

Note: calibration should not be confused with adjustment of a measuring system, often mistakenly called "self-calibration" or with verification of calibration.

Note: often, the first step alone in the above definition is perceived as being calibration.

Validation: the documented act of demonstrating that a procedure, process, and activity will consistently lead to the expected results.

Verification: the process of checking that a product or system meets specifications and that it fulfils its intended purpose.

References

1. USP<643>, "Total Organic Carbon," *United States Pharmacopoeia 36-NF 31,* U.S. Pharmacopeial Convention Inc., Rockville, Md. (2013).

2. USP<645>, "Water Conductivity," *United States Pharmacopoeia 36-NF 31,* U.S. Pharmacopeial Convention Inc., Rockville, Md. (2013).

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6. JP 4.5.2, "Monitoring of TOC as the Indicator for Organic Impurities," JP XVI.

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Randy Turner was a power plant chemist for Southern Company for 17 years and corporate chemist supporting their fleet of fossil plants for 16 years. He became the Technical Director for Swan Analytical USA in January 2012. He holds a BA in chemistry from the University of West Georgia. He has authored and presented numerous papers on power plant chemistry at conferences and has authored or coauthored papers published in industry journals. Turner was the chairman of EPRI's Cycle Chemistry Program. He was awarded the EPRI Technology Transfer Award in 2010 for research in corrosion product transport monitoring and chemical cleaning of supercritical units. He is a member and the first Vice Chair of the ASME Power Plant and Environmental Chemistry Committee. He is a member of the ASME Water Management Committee, the International Properties of Water and Steam Power Cycle Committee, AWWA, and WEF. He can be contacted by email: randy.turner@swan-analytical-usa.com.