Using Sievers 800 TOC Analyzer in Cleaning Validation Applications

An increasing number of pharmaceutical and biopharmaceutical companies are realizing the benefits of using total organic carbon (TOC) over more traditional methods for cleaning validation applications. As companies begin their method development process, some applications-related questions have arisen. The questions range from how to get started with method development to how to optimize analysis conditions. This technical note offers a few suggestions to help you optimize the performance of your Sievers 800 TOC Analyzer for cleaning validation applications.

Verify Solubility of the Solution When pH 2

The Sievers 800 is designed to measure the TOC of aqueous solutions and as part of the measurement process an adjustment of the sample pH is made to achieve a pH of approximately 2. Altering the pH of an aqueous solution can affect the solubility of the target compounds. For example, acidification of a basic or neutral solution may cause precipitates to form. At the time of acidification within the analyzer, precipitation can occur resulting in a clogging of the instrument's flow path. Therefore, it is important to verify that the target compounds are soluble in acidic conditions. To verify the solubility, place a small aliquot (1-2 mL) of the solution to be analyzed into a test tube or vial. Then acidify the sample with 6 M phosphoric acid until it is pH 2 (2-3 drops). Visually inspect the acidified aliquot for evidence of precipitate formation. This will simulate the environment within the analyzer and ensure compatibility.

If no precipitate has formed, then the solution may be analyzed directly. If a precipitate has formed, then prepare dilutions of the test solution. Acidify and observe these dilutions using the technique described above. When the precipitation no longer occurs upon acidification, the solution may be analyzed using TOC testing.

Ensure that the Instrument's Effluent is pH 2

Use a strip of pH paper to verify that the effluent (waste stream) of the analyzer has a pH of 2. When analyzing buffered solutions, the acid flow rate may need to be adjusted to ensure this low pH.

Analysis of Basic Solutions

Some cleaning applications may require basic conditions. When using concentrations greater than 0.03 M NaOH or KOH, a neutralization (or acidification) step prior to analysis is necessary. Also, basic solutions have the tendency to absorb high concentrations of CO_2, and therefore, the ratio of IC:TOC may exceed 10:1. This issue is discussed in further detail in the Sievers 800 User's Manual.

Refer to Case Study

For general ideas concerning how to get started with method development for your cleaning validation application, refer to the application note, *TOC Analysis of Compounds with Low Water Solubility; Evaluation of Swab Recoveries for Cleaning Validation Applications.* For further questions regarding your particular application, please contact Ionics Instruments for application support.