

SOP Title: Solutions and Standard Preparation for TOC Analyzer

SOP Number: 22919

Revision: 07

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1. PURPOSE

This procedure defines how to make accurate stock standard solutions of organic and inorganic compounds in reagent water that are traceable to certified materials. Working standard solutions are then prepared by accurately diluting these stock solutions with reagent water. This procedure also defines how to make accurate solutions necessary for TOC analysis by USP <643> method.

2. SCOPE

The scope of this procedure includes preparation of solutions used in TOC analysis and of standards ranging in concentrations from 0.2 ppm of organic carbon through 5.0 ppm of organic carbon in the stock solution. The working standards can be used to directly calibrate Ranges 1, 2, 3, 4 and 5 of the Total Organic Carbon Analyzer.

3. RESPONSIBILITIES

3.1 Director / Process Analytics/Quality Control (PA/QC)

- Defines procedure

3.2 PA/QC personnel

- Trains laboratory personnel
- Performs procedure
- Reviews data

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3.3 Biopharmaceutical Quality Assurance

- Provides quality oversight

4. DEFINITIONS

- **Stock Calibration Solutions** – A concentrated solution of a known amount of organic compound in water H₂O made from a certified reference material. Ideally, the final concentration of the stock solution is at least 100 times more concentrated than the background carbon present in the reagent water used to make this standard.
- **Working Calibration Solutions** – A quantitative spike of a stock calibration solution into reagent water. These solutions and the amount of carbon added to the reagent water are to be used to develop the calibration curve for the TOC Analyzers. The working solutions are also used to test the analyzer for performance and system suitability as per USP <643> on TOC.

5. MATERIALS AND REAGENTS

Part Number	Description	BDP Approved Substitution Permitted?
30005	1,4 - Benzoquinone C ₆ H ₄ O ₂ Grade: USP reference Standard <11> or equivalent Molecular Weight: 108.09 % Carbon: 66.67	<input type="checkbox"/> YES <input checked="" type="checkbox"/> NO
30134	Sodium Persulfate Na ₂ S ₂ O ₈ Grade: ACS Reagent Grade ≥95% Use: 10% in reagent	<input type="checkbox"/> YES <input checked="" type="checkbox"/> NO
30430	Sucrose C ₁₂ H ₂₂ O ₁₁ Grade: USP Reference Standard <11> or equivalent Molecular Weight: 342.30 % Carbon: 42.10	<input type="checkbox"/> YES <input checked="" type="checkbox"/> NO
30536	Phosphoric Acid H ₃ PO ₄ Grade: ACS Reagent Grade ≥85% Use: 5% (by weight) in persulfate reagent and 21% (by weight) in acid reagent	<input type="checkbox"/> YES <input checked="" type="checkbox"/> NO
N/A	Reagent Water - The reagent water used must be of the highest quality deionized, distilled or reverse osmosis water available, containing no more than 0.1 ppm C for low-level analysis.	<input type="checkbox"/> YES <input checked="" type="checkbox"/> NO
N/A	Blank Water - Reagent water that has been treated and manipulated as if it were a standard but contains "0" (no) added carbon from known sources.	<input type="checkbox"/> YES <input checked="" type="checkbox"/> NO

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6. EQUIPMENT

- Glassware

All volumetric glassware and pipettes that are used in this procedure must be serialized, certified, and Class A quality. The surface must be as free of carbon as possible and be cleaned using **SOP 22918 Glassware Cleaning for Trace TOC Analysis**. The glassware must be dedicated for TOC analysis to minimize carbon contamination.

Volumetric flasks are recommended for all concentration standards. The pipette volumes will range from 1 to 50 milliliter depending on the concentrations being prepared. The pipettes must be of the type that are calibrated “to deliver” their volume. Volumetric pipettes must be used for the large volumes.

- Analytical Balance, within calibration, accurate to 0.1 milligram.

7. PROCEDURE

Label each flask with the name of the solution including the concentration, date prepared, expiration date, and initials of the preparer.

7.1 Preparation of Sodium Persulfate Solution

7.1.1 Weigh 25 g of sodium persulfate and put it in the bottle labeled sodium persulfate.

7.1.2 Add 9 mL of phosphoric acid and add it to the persulfate.

7.1.3 Add 213 mL of reagent water and cap and mix thoroughly.

7.1.4 Sonicate for 10 minutes.

7.1.5 Record preparation in the reagent logbook, **Form 22702-01**.

7.1.6 This solution is good for 1 week and stored at room temperature

7.1.7 Label with Solution Name, Log ID, Volume, Storage Temperature, and 1-week expiration date. Initial and date.

7.2 Preparation of Acid Reagent

7.2.1 Measure 376 mL of reagent water.

7.2.2 Add 74 mL of phosphoric acid and swirl for at least 10 seconds to mix.

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- 7.2.3 Record preparation in the reagent logbook, **Form 22702-01**.
- 7.2.4 This solution is good for 6 months and stored at room temperature.
- 7.2.5 Label with Solution Name, Log ID, Volume, Storage Temperature, and 6-month expiration date. Initial and date.
- 7.3 Preparation of 0.05N Phosphoric Acid Solution for Soaking Swabs
 - 7.3.1 Measure 500 mL of reagent water.
 - 7.3.2 Add 570 μ L of phosphoric acid and swirl for at least 10 seconds to mix.
NOTE: 40 mL of 0.05N Phosphoric Acid Solution per swab sample is required for soaking.
 - 7.3.3 Record preparation in the reagent logbook, **Form 22702-01**.
 - 7.3.4 This solution is good for 1 month and stored at room temperature.
 - 7.3.5 Label with Solution Name, Log ID, Volume, Storage Temperature, and 1-month expiration date. Initial and date.
- 7.4 Preparation of Stock Calibration Solutions
 - 7.4.1 Sucrose/H₂O 40 ppm
 - 7.4.1.1 Weigh 95 mg \pm 4.0 mg of sucrose on a weigh boat and record the exact weight.
 - 7.4.1.2 Transfer the sucrose to a 1000 milliliter volumetric flask which is half full of reagent water.
 - 7.4.1.3 Squirt the weigh boat with reagent water, from a squirt bottle, until all of the crystals have been transferred to the flask.
 - 7.4.1.4 Invert the flask to dissolve the sucrose. Sonicate if needed.
 - 7.4.1.5 Fill the flask to the 1000 milliliter mark with reagent water.
 - 7.4.1.6 Seal the container with a flask stopper of appropriate size and invert the flask 10 times to equilibrate the solution.
 - 7.4.1.7 The 40 ppm C solution is good for 1 month and stored at 2^o-8^oC.

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- 7.4.1.8 Record the preparation of the Stock Calibration Solutions in the reagent logbook, per **SOP 22702 Solutions Used in BQC.**
- 7.4.2 1, 4 - Benzoquinone/H₂O 40 ppm C 1000 milliliter
(Stock System Suitability/Calibration Solution routine analysis)
 - 7.4.2.1 Accurately weigh 60 mg ± 3 mg of 1, 4 - Benzoquinone on a weigh boat and record the exact gross weight.
 - 7.4.2.2 Transfer the 1, 4 - Benzoquinone to a clean, dedicated 1000 milliliter volumetric flask which is half full of reagent water.
 - 7.4.2.3 Squirt the weigh boat with reagent water from a squirt bottle until all of the crystals have been transferred to the flask.
 - 7.4.2.4 Swirl, and invert the flask to dissolve the 1, 4 - Benzoquinone. If required, sonicate to dissolve.
 - 7.4.2.5 Fill the flask to the 1000 milliliter mark with reagent water.
 - 7.4.2.6 Seal the container with a flask stopper of appropriate size and invert the flask 10 times to equilibrate the solution.
 - 7.4.2.7 This 40 ppm C solution is good for 1 month and stored at 2^o-8^oC.
 - 7.4.2.8 Record the preparation in the reagent logbook, per **SOP 22702 Solutions Used in BQC.**
- 7.5 Preparation of Working Calibration Solutions (WCS)
 - 7.5.1 Preparation of the 5 ppm WCS
 - 7.5.1.1 Fill a 200-milliliter volumetric flask approximately half full with reagent water.
 - 7.5.1.2 Transfer 25 mL of stock calibration solution into the flask with volumetric pipettes.
 - 7.5.1.3 Swirl the flask a minimum of 10 seconds to mix.
 - 7.5.1.4 Fill the flask to the 200-milliliter mark with reagent water.

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- 7.5.1.5 Seal the container with a flask stopper of appropriate size and invert the flask 10 times to equilibrate the solution.
- 7.5.1.6 This is a 5 ppm solution.
- 7.5.1.7 This 5 ppm solution is good for 1 week and is to be stored at 2°-8°C.
- 7.5.1.8 Record preparation on **Form 22919-01**.
- 7.5.2 Preparation of 2 ppm WCS
 - 7.5.2.1 Fill a 500-milliliter volumetric flask approximately half full with reagent water.
 - 7.5.2.2 Transfer 25 mL of the stock calibration solution into the flask with a volumetric pipette.
 - 7.5.2.3 Swirl the flask a minimum of 10 seconds to mix.
 - 7.5.2.4 Fill the flask to the 500-milliliter mark with reagent water.
 - 7.5.2.5 Seal the container with a flask stopper of appropriate size and invert the flask 10 times to equilibrate solution.
 - 7.5.2.6 This is a 2 ppm solution.
 - 7.5.2.7 This 2 ppm solution is good for 1 week and is to be stored at 2°-8°C.
 - 7.5.2.8 Record preparation on **Form 22919-01**.
- 7.5.3 Preparation of 1 ppm WCS
 - 7.5.3.1 Fill a 2.0-liter volumetric flask approximately half full with reagent water.
 - 7.5.3.2 Transfer 50 mL of the stock calibration solution with a volumetric pipette.
 - 7.5.3.3 Swirl the flask a minimum of 10 seconds to mix.
 - 7.5.3.4 Fill the flask to 2.0-liter mark.

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- 7.5.3.5 Seal the container with a flask stopper of appropriate size and invert flask 10 times to equilibrate solution.
- 7.5.3.6 This is a 1 ppm C solution.
- 7.5.3.7 This 1 ppm C solution is good for 1 week and is to be stored at 2°-8°C.
- 7.5.3.8 Record preparation on **Form 22919-01**.
- 7.5.4 Preparation of a 0.5 ppm C WCS
 - 7.5.4.1 Fill a 2.0-liter volumetric flask approximately half full with reagent water.
 - 7.5.4.2 Transfer 25 mL of the stock calibration solution with a volumetric pipette.
 - 7.5.4.3 Swirl the flask a minimum of 10 seconds to mix.
 - 7.5.4.4 Fill the flask to the 2.0-liter mark.
 - 7.5.4.5 Seal the container with a flask stopper of appropriate size and invert the flask 10 times to equilibrate solution.
 - 7.5.4.6 This is a 0.5 ppm C solution.
 - 7.5.4.7 This 0.5 ppm C solution is good for 1 week and is to be stored at 2°-8°C.
 - 7.5.4.8 Record preparation on **Form 22919-01**.
- 7.5.5 Preparation of a 0.2 ppm C WCS.
 - 7.5.5.1 Fill a 2.0-liter volumetric flask approximately half full with reagent water.
 - 7.5.5.2 Transfer 10 mL of the stock calibration solution with a volumetric pipette.
 - 7.5.5.3 Swirl the flask a minimum of 10 seconds to mix.
 - 7.5.5.4 Fill the flask to the 2.0-liter mark.

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7.5.5.5 Seal the container with a flask stopper of appropriate size and invert the flask 10 times to equilibrate solution.

7.5.5.6 This is a 0.2 ppm C solution.

7.5.5.7 This 0.2 ppm C solution is good for 1 week and is to be stored at 2°-8°C.

7.5.5.8 Record preparation on **Form 22919-01**.

7.6 Preparation of USP <643> Total Organic Carbon “Standard Solution” and “System Suitability Solution.”

Both of these solutions contain 0.50 mg C/L of their respective compounds.

7.6.1 Standard Solution from Sucrose stock (0.5 ppm C)
Solution as prepared in 7.5.4

7.6.2 System Suitability Solution for 1, 4 - Benzoquinone
Solution as prepared in 7.5.4.

7.7 Cap and store the stock and working calibration solutions in a 2° - 8°C refrigerator; however, they need to be brought to room temperature prior to use.

NOTE: If different sized flasks are to be used, adjust the weights or volumes added accordingly to achieve the required concentration.

8. CALCULATIONS

8.1 Stock Calibration Solutions

Use the following calculation to determine the carbon concentration of the stock solutions.

$$\text{mg C/L} = \frac{[\text{gross weight (mg)} - \text{tare weight (mg)}] \cdot \% \text{ carbon (C)}}{\text{(ppm C)} \quad \text{Final volume (L)}}$$

where % (C)= decimal fraction of carbon in the reference material,

1,4 Benzoquinone = 0.6667

Sucrose = 0.4210

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8.2 Working Calibration Solutions

Use the following calculation to determine the carbon concentration added to the reagent water of the working calibration solutions.

$$\text{mg C/L} = \frac{\text{stock conc. (mg C/L)} \cdot \text{transfer volume (mL)}}{\text{final volume (L)} \cdot 1000}$$

$$(\text{ppm C}) = \text{final volume (L)} \cdot 1000$$

9. DOCUMENTATION AND RECORDS

9.1 Record the solutions preparation in the Process Analytics Solution Log logbook kept in the BQC laboratory, per **SOP 22702 Solutions Used in Process Analytics**.

9.2 Record the calibration standards in the TOC Calibration Solutions logbook kept in the BQC laboratory, per **SOP 22702 Solutions Used in Process Analytics**.

10. REFERENCES AND RELATED DOCUMENTS

Document Number	Title
22702	Solutions Used in Process Analytics
22918	Glassware Cleaning for Trace TOC Analysis
22919-01	Working Calibration Standards Preparation
22922	Preventative Maintenance for the TOC Analyzers
22963	Operation of Shimadzu TOC Analyzer
	Shimadzu User Manual
	USP Method <643> Total Organic Carbon