

Evaluation of NovaSeptum[®] Sampling Products for Cleaning Validation

This study aims to assess the baseline Total Organic Carbon (TOC) levels in NovaSeptum[®] sampling devices to ensure compliance with USP cleanliness standards, specifically USP <1231> regarding Water for Pharmaceutical Purposes, including Water for Injection (WFI). The objective is to conduct a thorough analysis of the TOC levels in various NovaSeptum[®] sampling products to evaluate their effectiveness and suitability for collecting cleaning validation samples in pharmaceutical applications.

Background

Cleaning validation is critical in ensuring that pharmaceutical manufacturing equipment is free from contaminants. The United States Pharmacopeia (USP) cleanliness claim (USP <1231> Water for Pharmaceutical Purposes, specifically WFI requests that TOC levels must be below 0.5 ppm (0.5 mg C/L).

Methodology:

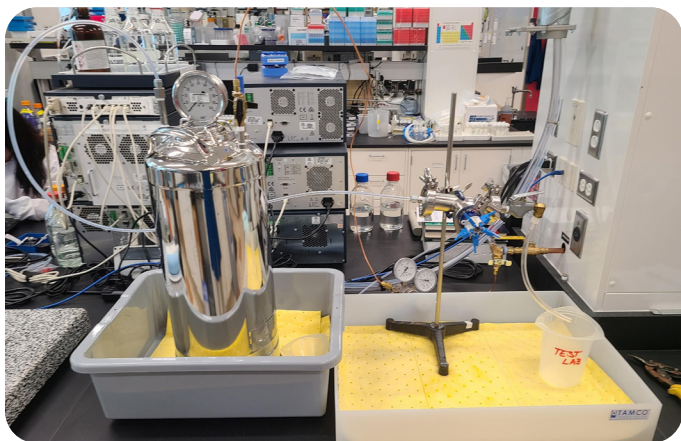
Sample Selection

The following devices were tested:

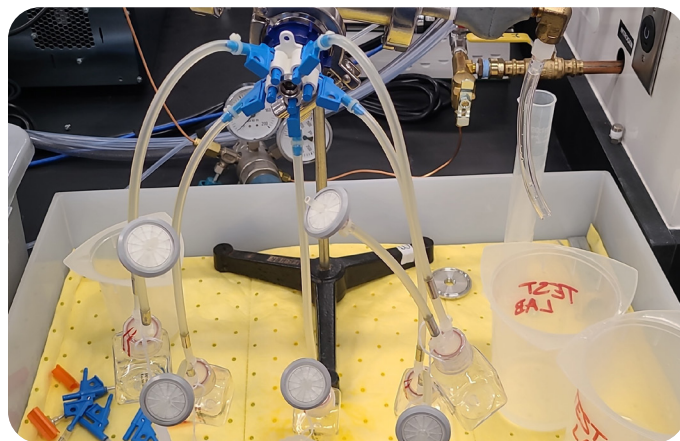
Item	Cat. No.	Lot No.	Sterilization
20 mL Syringes	E461-90020	190801-504	E-Beam (31.7–61.9 kGy)
100 mL Bags	E711-10100	200925-553	E-Beam (26.7–64.0 kGy)
60 mL Bottles	E871-80060	190802-504, 210113-502	Gamma (31.0–38.1 kGy)
15 mL Conical Tube	EC71-80015	210902-502	Gamma (28.0–39.7 kGy)
50 mL Conical Tube	5D41-80050	220609-501	Gamma (28.0–39.7 kGy)

Extraction procedure

- Test apparatus consisted of (i) pressure pot, (ii) 5-port NovaSeptum[®] manifold, and (iii) PFA tubing. The test apparatus was flushed until background TOC levels were below 0.1 mg C/L.
- The devices were filled to target levels one at a time using WFI from the pressure pot.
- Once target levels were reached, the devices were sealed using a NovaSeal[®] crimper.
- All devices were extracted at 60 °C for 6 hours, except the NovaSeptum[®] Syringes, which were extracted at 90 °C for 6 hours.
- Following the extraction the WFI from the devices were analyzed on a Sievers M9 instrument to determine TOC concentrations.
- Ten (10) replicates of each device were tested. (**Note:** for the 15 mL Conical tubes, two devices were pooled to make one replicate.)



Sampling Apparatus

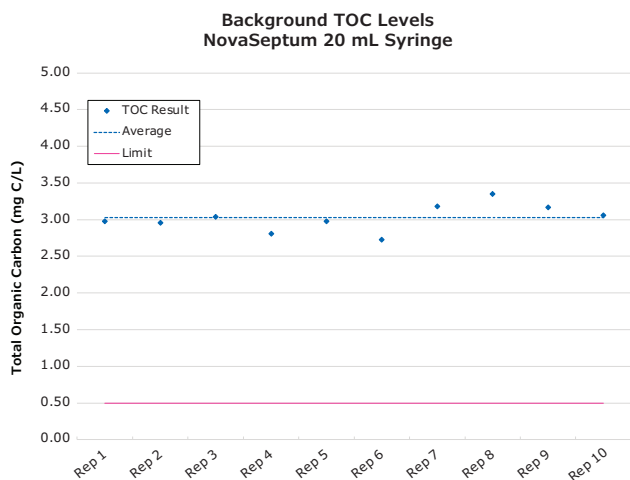


60 mL Bottle Set-Up

Results

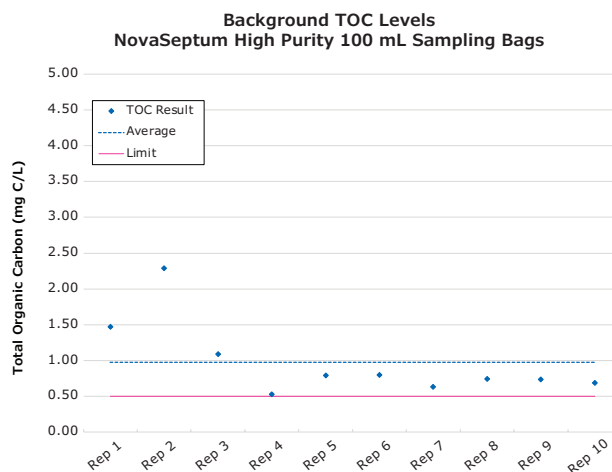
20 mL NovaSeptum® Syringes

- The syringes are made of polycarbonate (PC).
- The syringes had a target fill volume of 20 mL. The actual fill volume ranged from 19.1 mL–20.8 mL, with an average 19.7 mL.
- The TOC results ranged from 2.73 mg C/L to 3.35 mg C/L, with an average of 3.03 mg C/L.
- The background TOC levels were significantly higher the USP cleanliness (USP <1231> Water for Pharmaceutical Purposes, specifically Water for Injection (WFI)) limit of 0.5 mg C/L.



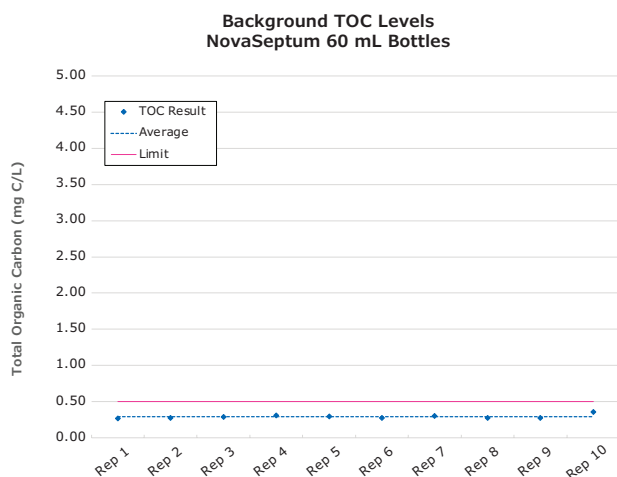
100 mL NovaSeptum® PureFlex™ Bags

- The bags are made from a multilayer film. The fluid contact layer is made from ULDPE. The inner layers contain EVA and EVOH.
- The bags had a target fill volume of 30 mL. The actual fill volume ranged from 14.0 mL–86.6 mL, with an average 54.0 mL.
- The TOC results ranged from 0.53 mg C/L to 2.29 mg C/L, with an average of 0.98 mg C/L.
- The background TOC levels varied significantly, with an inverse relationship to the fill volume. (The more volume collected the lower the TOC value.)



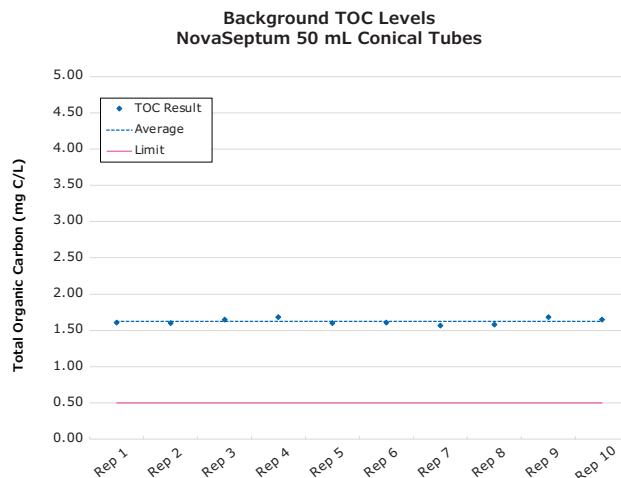
60 mL NovaSeptum® Bottles

- The bottles are made of Polyethylene Terephthalate Glycol (PETG).
- The bottles had a target fill volume of 60 mL. The actual fill volume ranged from 60.2 mL–69.2 mL, with an average 64.7 mL.
- The TOC results ranged from 0.27 mg C/L to 0.36 mg C/L, with an average of 0.30 mg C/L.
- The background TOC levels were below the USP Cleanliness limit of 0.5 mg C/L.



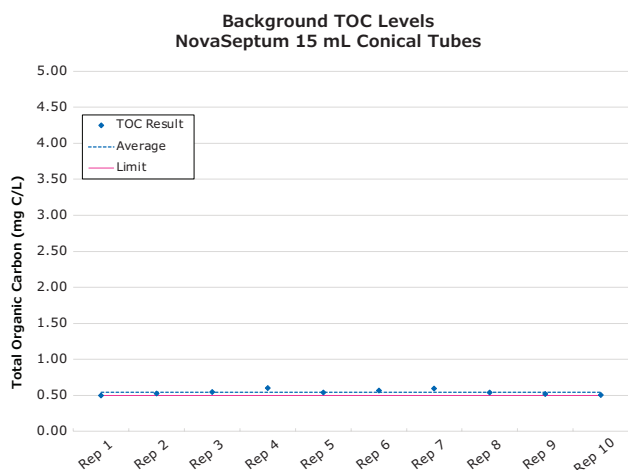
50 mL NovaSeptum® Conical Tubes

- The 50 mL conical tubes are made of polypropylene (PP).
- The conical tubes had a target fill volume of 50 mL. The actual fill volume ranged from 45.4 mL–50.6 mL, with an average 48.7 mL.
- The TOC results ranged from 1.57 mg C/L to 1.68 mg C/L, with an average of 1.62 mg C/L.
- The background TOC levels were above the USP Cleanliness (USP <1231> Water for Pharmaceutical Purposes, specifically Water for Injection (WFI)) limit of 0.5 mg C/L.



15 mL NovaSeptum® Conical Tubes

- The 15 mL conical tubes are made of polystyrene (PS).
- The bags had a target fill volume of 30 mL (as sum of the two devices to generate the replicate). The actual fill volume ranged from 29.7 mL–34.8 mL, with an average 31.1 mL.
- The TOC results ranged from 0.50 mg C/L to 0.60 mg C/L, with an average of 0.55 mg C/L.
- The background TOC levels were just at the USP Cleanliness limit of USP 643 gives 0.50 mg/L carbon. This means 0.55 mg/L exceeds 0.50 mg/L.



Conclusion

Cleaning validation ensures that pharmaceutical manufacturing equipment is free from contaminants. The United States Pharmacopeia (USP) cleanliness (USP <1231> Water for Pharmaceutical Purposes, (WFI)) claim requires that TOC levels must be below 0.5 ppm (0.50 mg/L). This study evaluated NovaSeptum® sampling devices to determine their compliance with this standard. Results showed that:

- NovaSeptum® 60 mL Bottles had TOC levels below USP Cleanliness limit of 0.50 mg C/L and are the most suitable containers for sampling in cleaning validations.
- NovaSeptum® 15 mL Conical Tubes can be used for assays, but a drawback is that two tubes are needed per assays due to the ~20 mL sample requirement for TOC. The 100 mL PureFlex™ Bags are also suitable if the fill volume is closer to 100 mL, but this should be verified with a second study. It's important to use Beta irradiated bags, as the gamma version would have much higher levels.
- Both 50 mL Conical Tubes and the 20 mL Syringes were significantly above the TOC levels recommended by USP Cleanliness limit and would not be recommended for cleaning validation.

To place an order or receive technical assistance

Order/Customer Service: [SigmaAldrich.com/order](https://www.sigmaaldrich.com/order)
Technical Service: [SigmaAldrich.com/techservice](https://www.sigmaaldrich.com/techservice)

[SigmaAldrich.com](https://www.sigmaaldrich.com)

We have built a unique collection of life science brands with unrivalled experience in supporting your scientific advancements.

Millipore® **Sigma-Aldrich®** **Supelco®** **Milli-Q®** **SAFC®** **BioReliance®**

MilliporeSigma
400 Summit Drive
Burlington, MA 01803

