PAT700 TOC ANALYZER EXCURSION MODE

Introduction

Regulatory authorities emphasize the importance of continuously monitoring pharmaceutical water systems, with Total Organic Carbon (TOC) measurement being a key indicator of quality. US and European Pharmacopeias define the requirements for TOC analysis and acceptance criteria through USP <643>, Ph. Eur. 2.2.44, Ph. Eur. 0008, and Ph. Eur. 0169 for Purified Water and Water for Injection (WFI). FDA guidance on sterile drug manufacturing, along with EU GMP Annex 1, further mandate proactive monitoring and timely investigation of any deviations to safeguard product quality.

Excursions, even if transient or below action limits, often serve as early indicators of system degradation, and may signal:

- Microbial growth
- Biofilm formation
- Residue accumulation from cleaning processes
- Mechanical failures (e.g., filter or sensor issues)

Therefore, a risk-based approach to monitoring and responding to TOC data is critical for maintaining the validated state and ensuring compliance with Good Manufacturing Practices (GMP).

Common Causes of TOC Excursions

In pharmaceutical water systems, a TOC excursion happens when measured Total Organic Carbon levels stray from established control limits. These excursions are classified into two levels: alert and action.

- An alert level excursion signals a potential drift from normal system performance and prompts closer observation or trending, but doesn't require immediate corrective action.
- An action level excursion warrants formal investigation, as it indicates a potential failure to meet water quality standards set by the US and European Pharmacopeias.

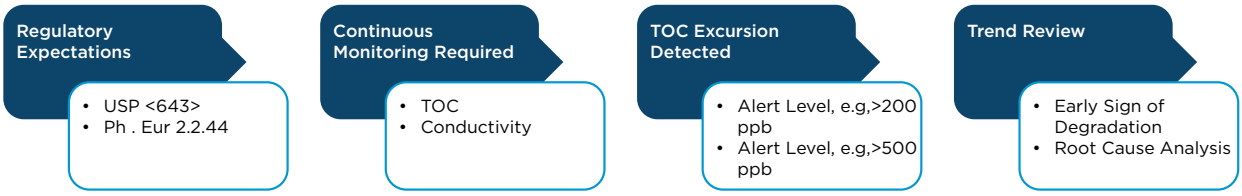
It's worth noting that not all excursions are actual system failures. False positives can occur due to instrument drift, sampling errors, or temporary system fluctuations, while confirmed out-of-specification (OOS) events are verified deviations that reflect real quality risks. Distinguishing between the two is crucial to avoid unnecessary downtime while ensuring product safety and compliance with regulations.

Total Organic Carbon (TOC) excursions in pharmaceutical water systems can arise from various mechanical, microbial, and operational factors. Microbial contamination, particularly biofilm formation in low-flow areas or those with inadequate sanitization, is one of the most common causes, leading to the release of carbon-rich metabolic byproducts.

Filter failures, especially in activated carbon or ultrafiltration units, may allow organic matter to pass through if the filters are saturated, degraded, or not adequately maintained.

Additionally, residual cleaning agents left behind after maintenance or sanitization processes can cause temporary TOC spikes if not thoroughly rinsed out.

Finally, issues with the TOC analyzer, such as sensor fouling, calibration drift, or electronic faults, can lead to inaccurate readings that can be misinterpreted as genuine excursions. Understanding these root causes is essential for conducting effective investigations, implementing timely corrective actions, and maintaining long-term control of pharmaceutical water quality.



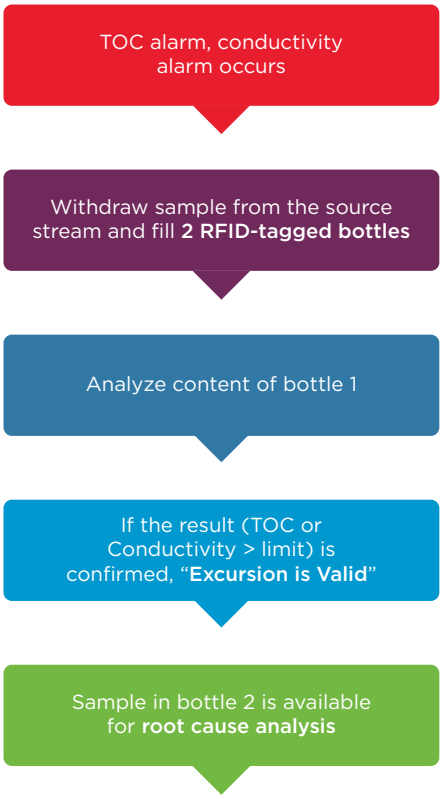
Diagnostic Flow Chart

How does the PAT700 TOC Analyzer help with Root Cause Analysis?

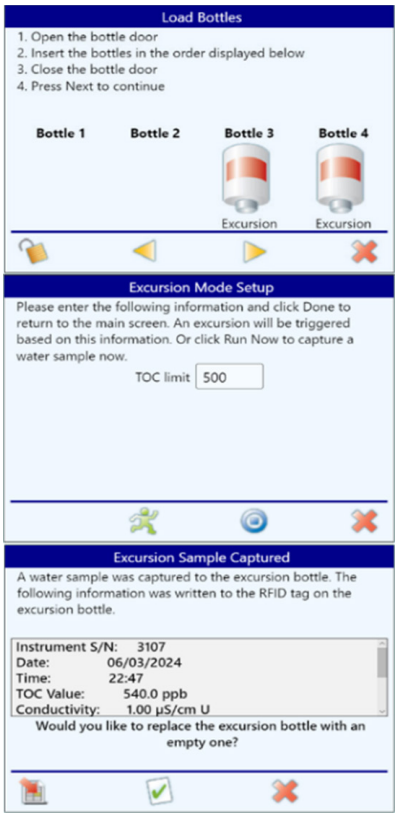
Because it features a built-in Onboard Automated Standards Introduction System (OASIS) that can be equipped with RFID,* the PAT700 analyzer plays a crucial part in root cause analysis. When a TOC or conductivity alarm is triggered, the analyzer can alert users and automatically capture water samples from the stream using RFID-tagged bottles. The RFID tags store critical data at the time of the excursion, such as:

- Instrument serial number
- Date
- Time
- TOC value
- Conductivity

The content of the first bottle is analyzed immediately to confirm the excursion. If the excursion is confirmed, the second bottle can be sent to the laboratory for investigation and root cause analysis.



ANATEL PAT700 TOC Analyzer excursion mode workflow



ANATEL PAT700 TOC Analyzer display setup

Summary

Total Organic Carbon (TOC) analyzers play a crucial role in the continuous monitoring of pharmaceutical water systems, ensuring water quality. Requirements from US and European pharmacopeias, FDA guidance, and EU GMP Annex 1 define strict TOC limits, necessitating an investigation of deviations.

TOC excursions can indicate early signs of system degradation due to microbial contamination, filter failures, and cleaning residues. These excursions are classified into alert and action levels, with the latter requiring formal investigation.

The PAT700 TOC Analyzer supports root cause analysis through its excursion mode, which uses the OASIS system with RFID-tagged bottles to automatically capture water samples in the event of TOC or conductivity alarm. This system enables efficient investigation and root cause analysis by sampling the water at the time the excursion occurs, thereby avoiding a delay between alarm acknowledgment and the collection of a sample from the process.

*Not available in all territories. Consult your Beckman Coulter Life Sciences representative with questions.

References

- The Rules Governing Medicinal Products in the European Union Volume 4 EU Guidelines for Good Manufacturing Practice for Medicinal Products for Human and Veterinary Use - Brussels, 22.8.2022 C (2022) 5938 final
- Guidance for Industry Part 11: Electronic Records; Electronic Signatures — Scope and Application U.S. Department of Health and Human Services, Food and Drug Administration, Center for Drug Evaluation and Research (CDER), Center for Biologics Evaluation and Research (CBER), Center for Devices and Radiological Health (CDRH), Center for Food Safety and Applied Nutrition (CFSAN), Center for Veterinary Medicine (CVM), Office of Regulatory Affairs (ORA), August 2003, Pharmaceutical CGMPs
- Cleaning in the Pharmaceutical Industry & the crucial role of TOC Analyzers, DOCID:2025 GBL EN 107830 v1

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