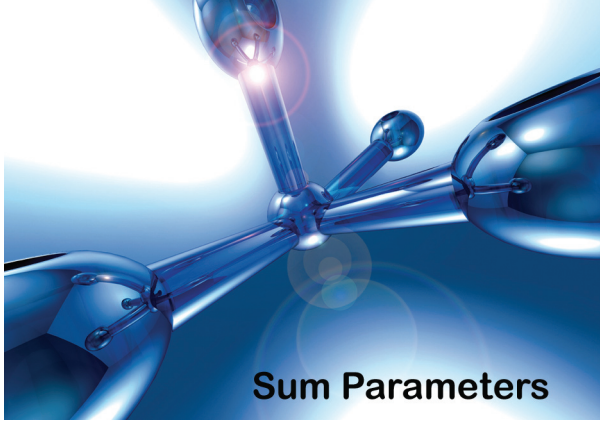
Application Note

TOC determination in Cleaning Validation



"Cleanliness" is of special significance in the production of any kind of drug, since highest purity and careful handling of substances and active substances are essentials in the pharmaceutical industry. The basic requisite is the effective removal of residual product due to production plant. A clean plant reduces contamination of medication. When using batch process, cleaning afterwards is particularly important due to the production of several drugs in the same production plant. In this case a contamination by the previous product must be prevented. Cleaning validation ensures the efficiency of the cleaning process.

Cleaning process
The selection of the cleaning process is the deciding factor in effective cleaning of the plant. Two processes are normally used.

CIP (Clean in place)
The cleaning is done automatically and without dismounting the plant. In this case the plant has to have a CIP-design (Rinsing system with recycling possibility, no dead volumes) which usually requires a high investment.
On the other hand it is possible to optimise time, temperature, cleaning agent and solvents, resulting in a very effective cleaning. The automatic rinsing enables a standardised and validated procedure.

COP (cleaning out of place)
For COP, the complete plant needs to be dismounted and all components cleaned individually.

This procedure requires more time and staff dedication. Due to the individual cleaning the standardisation and validation is more difficult. But the advantages here are low investment and the opportunity to inspect all components visually.

Sampling and analytics
Depending on the cleaning process, several facilities can be used for sampling to check the cleaning efficiency. The easiest and fastest way is the analysis of the final rinse solution. Depending on the solvent used, the subsequent analysis can be carried out with HPLC or TOC.

The TOC-Analytic for the Cleaning Validation shows some dedicated advantages:

1. Easy to use
   - The TOC-measurement is independent of the product and very flexible
   - The TOC-method is an easy method with few sample preparation
   - TOC-determination is easy to validate
   - TOC-determination can be combined with other parameters like (TN_b and IC) to get more information (e.g. -TN_b for the biopharmaceutical)
2. Fast analysis
   - Water samples can measured very quickly – a typical measurement time is four minutes
3. Low running costs
   - Few consumables
   - No solvents

TOC-V Series

TOC-V CPH with ASI-V

The modular system of Shimadzu TOC-V series simplifies TOC-Analysis, regardless of how samples of final rinse or swab method are measured. The TOC-V_{CPH} is based on the proven technologies of catalytic combustion (680°C) and NDIR-detection. In this way, it is possible to detect equally low molecular mass acids and invisible particles. Due to its measuring range of up to 25.000 mg/L (detection limit: 4 µg/L), the instrument is not only suitable for the low range but also for analysis of highly contaminated samples, for example during the cleaning validation process.

Simultaneous TN_b (total nitrogen) with the help of the TNM-1 module can differ from product and rinsing agent, especially with biopharmaceutical products.

TOC-Control V

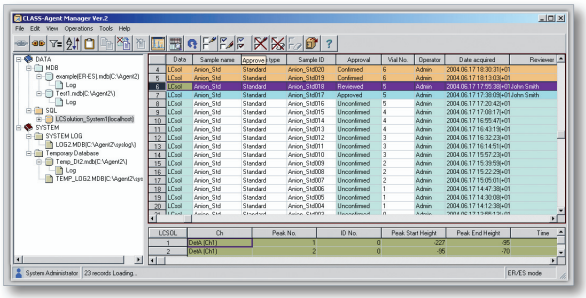
The TOC-Control V software transforms the TOC-V Series into state-of-the-art fully automatic and GLP/GMP compatible quality control system. An integrated module with audit trail, raw data management and user administration supports compliance with FDA 21 CFR Part 11 requirements

Class Agent – Data management

In addition to the current analyses, data archiving of the analytical results is of increasing significance. One of the best known examples of data-archiving requirements is 21 CFR Part 11, regulated by the American FDA, describing the administration of electronic data and the application of electronic signatures. Electronic records and electronic signatures are only considered to be equivalent to a printed analysis report with a handwritten signature when the applied software meets very specific criteria.

Shimadzu offers a complete solution with the comprehensive Class Agent software package. It enables the user to structure, store and secure electronic records in a powerful database. The data can be retrieved from the database in readable format at any time.

The electronic signature consisting of the user name and password is required, for instance, to access analytical results. The complete name, time stamp and type of performed action are documented in the audit trail.



Class Agent Menu

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