

The power of non-specificity in cleaning validation

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Background

There is a simple concept that has stood out and that is the power of non-specificity in cleaning validation.

TOC is a technique that measures total organic carbons; therefore, it is comprehensive for organic compounds and precisely because it is not specific only for one type of drug, excipients, degradation products and detergents; it is much more reliable to guarantee that there is no type of contamination and, in addition, detects the presence of bacteria as well.¹⁻⁷ Many have criticized the TOC technique as an application for cleaning validation in the Pharmaceutical Industry because it is a non-specific technique. In accordance with USP <643>, identification of the source of contamination is not required as long as TOC levels do not exceed established limits.



Since the publication of the inspection guide on cleaning validation in 1993 at the FDA, several studies have been published to demonstrate the suitability of TOC in measuring contaminating residues.¹⁻⁷ The use of TOC can be justified for direct tests of surface samples, as well as for tests of indirect samples (rinse water). In either case, since the TOC does not identify or distinguish between different compounds containing oxidizable carbon, any carbon detected must be assigned to the target compound(s) for comparison with the established threshold.¹⁻⁷ There is a specific non-dispersive infrared detector TOC for method development with applications in cleaning validation with a detection limit of 0.4ppb.¹⁻⁷

This equipment is capable of analyzing both water-soluble drugs and insoluble drugs, which are usually the most critical cases.¹⁻⁷

It has 3 analysis modes

- (1) Rinse sampling – TOC measurement method
- (2) Swab sampling – aqueous extraction – TOC measurement method
- (3) Swab sampling – direct combustion carbon measurement method

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Summary

TOC is a technique with lower cost and allows a method development in a simpler way in a shorter period of time, especially when compared to the HPLC and LC/MS/MS techniques that are specific, but have a higher cost. Through a rationale with properly established residue limits, TOC is perfectly suited for use in cleaning validation applications.

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Conflicts of interest

Authors declared no conflicts of interest.

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