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Cleaning verification: exploring the effect of the cleanliness of stainless steel surface on sample recovery

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Highlights

1. Stainless steel surface cleanliness affects API recovery.
2. Improper cleaning is a major contributor to low and variable recoveries.
3. With proper cleaning consistent recoveries are obtained for small molecules and proteins.
4. This study helps minimizing the risk of false negative results and of unintentional product to product carryover that could jeopardize patient safety.

Abstract

The parameters affecting the recovery of pharmaceutical residues from the surface of stainless steel coupons for quantitative cleaning verification method development have been studied, including active pharmaceutical ingredient (API) level, spiking procedure, API/excipient ratio, analyst-to-analyst variability, inter-day variability, and cleaning procedure of the coupons. The lack of a well-defined procedure that consistently cleaned coupon surface was identified as the major contributor to low and variable recoveries. Assessment of acid, base, and peroxide washes, as well as the order of treatment, showed that a base-water-acid-water wash procedure resulted in consistent, accurate spiked recovery (>90%) and reproducible results (S_{rel}≤4%). By applying this cleaning procedure to the previously used coupons that failed the cleaning acceptance criteria, multiple analysts were able to obtain consistent recoveries from day-to-day for different APIs, and API/excipient ratios at various spike levels. We successfully applied our approach for cleaning verification of small molecules (MW <1000 Da) as well as large biomolecules (MW up to 50,000 Da). Method robustness was greatly influenced by the sample preparation procedure especially for analyses using total organic carbon (TOC) determination.

Keywords: Cleaning method development, cleaning verification, coupons, RPLC, TOC

1. Introduction