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# Cleaning Validation during New Product Introduction in Shared Pharmaceutical Equipment: Development and Application of a Worst-Case Scenario Decision Framework

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## Abstract

**Background:** Multi-product pharmaceutical manufacturing facilities must ensure that the introduction of a new product does not compromise an existing cleaning validation programme. However, regulatory guidance documents provide no systematic, step-by-step framework for this new product introduction (NPI) stage assessment.

**Objectives:** To develop a structured six-parameter worst-case scenario (WCS) assessment framework for NPI-stage cleaning validation decisions and to validate the cleaning procedure for Sitagliptin as the identified worst-case compound across three consecutive production batches**.**

**Methods:** A comparative six-parameter risk assessment was conducted between Sitagliptin 25/50/100 mg film-coated tablets and the site's existing WCS product. Maximum allowable carryover (MAC) was calculated using three methods (dose-based, 10 ppm, and PDE/HBEL-based). Swab and rinse sampling was performed across a ten-equipment chain with a total product-contact surface area of 146,009.41 $cm^2$. Three consecutive validation batches were executed after the manufacture of Sitagliptin 100 mg tablets.

**Results:** Sitagliptin was identified as the site WCS product based on a more stringent per-swab acceptance limit of 1.59 ppm versus 11.2 ppm for the reference product, directly attributable to its larger equipment chain surface area, not potency or solubility. All three validation batches passed all acceptance criteria. Total API carryover was 15.22 mg, 17.24 mg, and 16.16 mg respectively (limit: NMT 150 mg), representing an ~88.5% safety margin.

**Conclusion:** Equipment chain surface area — rather than potency alone — can be the decisive WCS parameter during NPI. The proposed six-parameter framework provides a structured, reproducible, and regulatorily compliant approach applicable to any multi-product OSD facility

## 1. INTRODUCTION

Within multi-product pharmaceutical manufacturing facilities, shared equipment for the sequential production of multiple drug products is a common occurrence. Although this practice is operationally and economically critical, it creates a significant risk of cross-contamination the unintended transfer of a previously produced active pharmaceutical ingredient (API) into a subsequently produced product. Such cross-contamination can lead to sub-therapeutic dosing, toxicity, or hypersensitivity reactions in vulnerable patient populations, particularly for highly potent or allergenic compounds. Cleaning validation (CV) is the accepted regulatory process whereby pharmaceutical manufacturers provide documented proof of their capacity to reduce residues of APIs, excipients, cleaning agents, and microbial contaminants to levels deemed safe for subsequent manufacture.[1,2] Regulatory bodies including the FDA, EMA, ICH, PIC/S, and WHO have mandated cleaning validation as an integral component of cGMP compliance for shared manufacturing equipment.[3,4]

### 1.1 From Empirical Thresholds to Science-Based Exposure Limits

The scientific basis for cleaning validation acceptance limits has evolved considerably over the past three decades. The pioneering work of Fourman and Mullen (1993)[5] established three widely adopted empirical criteria: no more than 10 ppm of a substance carried over to the next product; no more than 0.1% of the minimum therapeutic dose in the maximum daily dose of the next product; and no visible residue on equipment surfaces after cleaning. While practically useful, these criteria were recognised over time as insufficiently risk-based for highly potent or pharmacologically active compounds. In 2014, the EMA published its guideline on health-based exposure limits (HBEL) for shared manufacturing facilities,[6] introducing the Permitted Daily Exposure (PDE) — a scientifically derived, compound-specific threshold considered without appreciable health risk. This, combined with revised PIC/S PI 006-3 recommendations,[4] shifted practice toward individualised toxicological evaluation. In current best practice, MAC is calculated using all applicable methods — dose-based, 10 ppm, and PDE/HBEL-based — and the most stringent value is selected as the controlling acceptance limit.

### 1.2 Worst-Case Scenario Selection: Current Approaches

One of the fundamental principles of cleaning validation strategy in multi-product facilities is the worst-case scenario (WCS) approach, where the most difficult-to-clean or most pharmacologically active compound is selected as the reference for validation. The logic is sound and well-proven: a cleaning procedure validated for the most challenging compound is considered effective for all other products on the same equipment chain.[7]

Typical WCS selection criteria described in literature include standard therapeutic dose (potency), water solubility, toxicological profile (PDE), batch size, and physical characteristics.[8,9] Moura et al. (2025)[10] proposed a structured cleaning validation protocol for QC laboratory equipment, selecting Oxcarbazepine based on its very low water solubility and cleaning history. While such studies have advanced WCS science, these published frameworks share a common limitation: they do not address the

challenge of introducing a new compound into a site with an already-validated cleaning programme.

**1.3 The NPI Gap and the Role of Equipment Surface Area**

In the context of a new product being introduced into an already multi-product manufacturing facility, a key question arises: Does the new compound change the existing WCS assignment at the facility, such that a new cleaning validation study is required? This current guidance, including EMA Annex 15, PIC/S PI 006-3, and FDA's guidance on cleaning validation, recognizes the need for CV during NPI but does not offer a step-by-step approach for the WCS risk assessment required for the decision. [2,3,4] The lack of systematic NPI-specific guidance on this question represents a knowledge gap that QA professionals face in multi-product facilities on a regular basis but are seldom able to find discussed in the literature.

Equally underexplored is the relationship between equipment chain surface area geometry and the acceptance limit stringency as a determinant of WCS candidacy. The acceptance limit, calculated by allocating the MAC to the total product-contact surface area, is more stringent with increasing surface area, independent of the potency, solubility, or toxicological properties of the compound. This aspect, to the best of the authors' knowledge, has not been previously emphasized as a determinant of WCS in the existing literature on cleaning validation.

**1.4 Objectives**

The present study was undertaken with two primary objectives. First, to develop and validate a structured six-parameter NPI-stage WCS assessment framework applicable to multi-product OSD manufacturing facilities. Second, to apply this framework using Sitagliptin 25/50/100 mg film-coated tablets as the model new product and to document cleaning validation outcomes — MAC derivation, per-swab limit determination, and three-batch validation results — in accordance with EMA Annex 15 and PIC/S PI 006-3 requirements.

## 2. METHODS

**2.1 Study Design and Facility Description**

This study employed a retrospective observational design, involving systematic analysis of cleaning validation protocol execution data generated during the NPI of Sitagliptin 25/50/100 mg film-coated tablets at a cGMP-compliant multi-product OSD manufacturing facility in Chennai, India. The facility operates in compliance with WHO-GMP guidelines and Schedule M of the Drugs and Cosmetics Act, 1940, and manufactures more than 30 pharmaceutical formulations on shared equipment chains. All cleaning validation activities were conducted between June and October 2024.

**2.2 Product Profile — Sitagliptin**

Sitagliptin phosphate monohydrate is a selective dipeptidyl peptidase-4 (DPP-4) inhibitor used in the management of type 2 diabetes mellitus, available as film-coated tablets in 25 mg, 50 mg, and 100 mg strengths. The lowest marketed strength (25 mg) was designated as the standard therapeutic dose (STD) for MAC calculation. Sitagliptin has a molecular weight of 407.32 g/mol and is freely soluble in water at approximately 58 mg/mL at room temperature.[11] A common granulation approach was employed, with a single 84 kg batch divided at compression into three tablet strengths; validation was conducted following manufacture of the 100 mg strength, representing the highest API mass per tablet.

**2.3 Six-Parameter WCS Assessment Framework**

A structured six-parameter risk assessment framework was developed to evaluate whether Sitagliptin altered the site's existing WCS designation. Sitagliptin was compared against the site's validated Reference WCS Product across six pre-defined parameters. The decision rule: if Sitagliptin demonstrated equal or greater stringency on one or more parameters — particularly per-swab acceptance limit or visual threshold compliance — a full prospective cleaning validation study was mandated. The framework and comparative outcomes are presented in Table 1

**Table 1. Six-Parameter WCS Comparative Risk Assessment: Sitagliptin vs. Reference WCS Product**

| # | Parameter | Sitagliptin | Reference WCS Product | WCS? |
|---|---|---|---|---|
| 1 | Formulation type / route | Film-coated tablet, oral | Film-coated tablet, oral | — |
| 2 | Standard therapeutic dose (STD) | 25 mg | 2.5 mg | Ref. |
| 3 | Water solubility | Soluble (~58 mg/mL) | Very slightly soluble | Ref. |
| 4 | Most stringent MAC | 150 mg (10 ppm criterion) | 75 mg (dose criterion) | Ref. |
| 5 | Per-swab acceptance limit | **1.59 ppm** (SA: 146,009 cm²) | 11.2 ppm (SA: 98,154 cm²) | ★ **SITA** |
| 6 | Visual threshold compliance | Non-compliant | Compliant | ★ **SITA** |
| | Decision: | *Full CV mandated — driven by Parameters 5 and 6* | | |

*SA: Surface Area (cm²); WCS: Worst-Case Scenario; SITA: Sitagliptin designated as WCS; CV: Cleaning Validation.*

As shown in Table 1, despite Sitagliptin's higher STD and greater water solubility, its larger equipment chain surface area generated a markedly more stringent per-swab acceptance limit (1.59 ppm vs. 11.2 ppm), overriding the classical potency/solubility-first selection logic

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**Maximum Allowable Carryover Calculation**

MAC for Sitagliptin was calculated using all three internationally recognised methods per EMA HBEL guidance [6] and PIC/S PI 006-3: [4]

**Method 1** — Dose-based: MAC = (STD × MBS) / (SF × LDD) = 750 mg.

**Method 2** — 10 ppm criterion: MAC = 10 × MBS (mg) / 1,000,000 = 150 mg.

Most stringent — selected as controlling limit.

**Method 3** — PDE/HBEL-based: MAC = PDE (mg/day) × MBS / LDD = 600,000 mg.

The per-swab acceptance limit was initially calculated as 1.64 ppm and revised to 1.59 ppm following a mid-study protocol amendment (Section 2.6.3). The revised limit was applied to all three validation batches.

**Table 2. MAC Calculation Results for Sitagliptin**

| Calculation Method | Formula Basis | Calculated MAC | Selected? |
|---|---|---|---|
| Dose-based | STD, MBS, SF, LDD | 750 mg | No |
| 10 ppm criterion | 10 × MBS / $10^6$ | 150 mg | **YES ✓** |
| PDE/HBEL-based | PDE × MBS / LDD | 600,000 mg | No |
| Per-swab limit (revised) | Post-amendment | NMT 1.59 ppm | Applied |

*MAC: Maximum Allowable Carryover; STD: Standard Therapeutic Dose; MBS: Minimum Batch Size; SF: Safety Factor; LDD: Largest Daily Dose; PDE: Permitted Daily Exposure; NMT: Not More Than.*

**2.5 Equipment Chain and Sampling Plan**

The cleaning validation encompassed ten product-contact equipment units (E1–E10), covering all manufacturing stages from granulation to blister packaging, with a total surface area of 146,009.41 cm² (Table 3). Swab sampling was performed using pre-wetted polyester swabs with methanol: water (50:50, v/v) at 10 mL per swab, targeting worst-case (hardest-to-clean) surfaces. Microbiological sampling preceded API swab sampling at each equipment unit.

**Table 3. Equipment Chain, Surface Area Classification, and Sampling Method**

| Code | Equipment (Generic Name) | Cleaning SOP Type | Sampling Method |
|---|---|---|---|
| E1 | Vibro sifter | Type B cleaning SOP | Swab and rinse |
| E2 | Scoop | Type B cleaning SOP | Swab and rinse |
| E3 | IPC bin (300 L) | Type B cleaning SOP | Swab and rinse |
| E4 | Unit dose sampling rod | Type B cleaning SOP | Swab and rinse |
| E5 | Compression machine | Type B cleaning SOP | Swab and rinse |
| E6 | Metal detector and deduster | Type B cleaning SOP | Swab and rinse |
| E7 | Auto coater | Type B cleaning SOP | Swab and rinse |
| E8 | Visual inspection machine | Type B cleaning SOP | Swab and rinse |
| E9 | Blister packing machine | Type B cleaning SOP | Swab and rinse |
| E10 | De-blister machine | Type B cleaning SOP | Swab and rinse |
| | Total equipment surface area | **146,009.41 cm²** | |

**2.6 Analytical and Microbiological Methods**

**2.6.1 HPLC Method for API Residue Quantification**

Sitagliptin residues were quantified using a validated reverse-phase high-performance liquid chromatography (HPLC) method. The method was validated for specificity, linearity, accuracy, precision, limit of detection (LOD), and limit of quantification (LOQ) prior to cleaning validation execution, confirming its suitability for residue analysis at the required acceptance levels. Chromatographic analysis was performed on a Waters e2695 separation module equipped with a 2489 UV/Vis detector, operated using Empower 3.6.1 software. Separation was achieved on a Zorbax Eclipse XDB-CN column (150 × 4.6 mm, 5 µm). The mobile phase consisted of pH 2.0 phosphate buffer (potassium dihydrogen phosphate anhydrous, adjusted to pH 2.0 with orthophosphoric acid, filtered through 0.45 µm nylon membrane filter) and acetonitrile in the ratio 85:15 (% v/v). The flow rate was 1.2 mL/min, detection wavelength was 205 nm, injection volume was 20 µL, column temperature was 30°C, and the total run time was 15 minutes.The diluent and swabbing solvent used was methanol:water (50:50, v/v). Swab samples were prepared by placing pre-wetted swabs in 10 mL of diluent, sonicating for 2 minutes, and vortexing for 5 minutes. The retention time for Sitagliptin phosphate monohydrate was approximately 5 minutes. System suitability was confirmed when the %RSD of the peak area response across six replicate injections of the standard solution was not more than 5.0. Standard solution was prepared at approximately 10.0 ppm from Sitagliptin phosphate monohydrate working standard.The LOD and LOQ of the validated method were 0.2 ppm and 0.5 ppm respectively — both substantially below the per-swab acceptance limit of 1.59 ppm — confirming adequate analytical sensitivity for residue detection at the required acceptance level. Percentage recovery of Sitagliptin from stainless steel surfaces exceeded 80%; no recovery correction factor was therefore applied to analytical results.

**2.6.2 Cleaning Agent and Microbiological Analysis**

Cleaning agent residue acceptance criterion: NMT 5.0 ppm per swab or 10 mL rinse. Bioburden assessment was performed per harmonised

pharmacopoeial methods (Ph. Eur. 2.6.12/2.6.13; USP <61>/<62>) for TAMC, TYMC, and specified pathogens (*E. coli, Salmonella* spp., *S. aureus, P. aeruginosa*). Acceptance criteria: TAMC NMT 50 CFU per swab or 10 mL rinse; TYMC nil; all specified pathogens absent.

**2.6.3 Mid-Study Protocol Amendment**

A formal protocol amendment was implemented under change control during the active study, revising the per-swab acceptance limit from 1.64 ppm to 1.59 ppm following the addition of an equipment unit to the chain. A visual threshold study at 1.59 ppm confirmed the scientific validity of the revised criterion before validation batch execution commenced.

**2.7 Validation Execution — Three Consecutive Batches**

Prospective cleaning validation was performed across three consecutive commercial-scale batches of Sitagliptin 100 mg (Batches R1, R2, R3) per EMA Annex 15[2] and PIC/S PI 006-3.[4] Cleaning was performed by trained personnel using Type B cleaning SOPs after each batch. Acceptance criteria are presented in Table 4.

**Table 4. Acceptance Criteria for All Three Cleaning Validation Batches**

| Parameter | Acceptance Criterion | Regulatory Basis |
|---|---|---|
| Visual inspection | No visible residue on surfaces | EMA Annex 15; PIC/S PI 006-3 |
| Total API carryover | NMT 150 mg | 10 ppm criterion (most stringent) |
| API per swab | NMT 1.59 ppm | Derived from MAC / surface area |
| Cleaning agent | NMT 5.0 ppm per swab or 10 mL | Industry standard |
| TAMC | NMT 50 CFU per swab or 10 mL | Ph. Eur. 2.6.12 / USP <61> |
| TYMC | Nil (0 CFU) | Ph. Eur. 2.6.12 / USP <61> |
| Specified pathogens | Absent (E. coli, Salmonella, S. aureus, P. aeruginosa) | Ph. Eur. 2.6.13 / USP <62> |

NMT: Not More Than; TAMC: Total Aerobic Microbial Count; TYMC: Total Yeast and Mould Count; CFU: Colony Forming Units.

## 3. RESULTS

Results of the NPI-stage WCS assessment, MAC calculations, mid-study protocol amendment, and three-batch cleaning validation are presented below, in the order conducted.

**3.1 WCS Assessment Outcome**

Of the six parameters evaluated, Sitagliptin demonstrated greater stringency on two: per-swab acceptance limit (Parameter 5) and visual threshold compliance (Parameter 6). The per-swab acceptance limit for Sitagliptin was 1.59 ppm versus 11.2 ppm for the Reference WCS Product — a sevenfold difference arising entirely from the larger equipment chain surface area (146,009.41 cm² vs. 98,154.26 cm²). This occurred despite Sitagliptin's higher STD (25 mg vs. 2.5 mg) and superior water solubility, properties that would have precluded WCS designation under a classical potency- or solubility-first framework. The visual threshold study independently confirmed non-compliance at 1.59 ppm, corroborating the need for full prospective cleaning validation. Based on Parameters 5 and 6, Sitagliptin was designated the site WCS compound and a three-batch prospective cleaning validation study was mandated.

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**3.2 MAC Calculation Results**

As presented in Table 2, the 10ppm criterion yielded the most stringent MAC value (150 mg) and was selected as the controlling acceptance limit. Dose-based (750 mg) and PDE/HBEL-based (600,000 mg) methods were substantially less stringent. The initial per-swab limit of 1.64 ppm was revised to 1.59 ppm following the mid-study amendment described in Section 3.3.

**3.3 Mid-Study Protocol Amendment**

During the active study, an equipment unit was added to the validated chain, necessitating a formal protocol amendment under change control. The total surface area increased accordingly and the per-swab acceptance limit was recalculated and revised from 1.64 ppm to 1.59 ppm. A visual threshold study at 1.59 ppm confirmed the scientific validity of the revised criterion. All three validation batches were executed under the revised limit of NMT 1.59 ppm. No further amendments were required.

**3.4 Cleaning Validation Results** — Three Consecutive Batches

The cleaning validation results for all three batches are presented in Table 5. All batches met all pre-defined acceptance criteria

**Table 5. Cleaning Validation Results — Batches R1, R2, and R3**

| Parameter | Criterion | Batch R1 | Batch R2 | Batch R3 |
|---|---|---|---|---|
| Visual inspection | No visible residue | **Pass ✓** | **Pass ✓** | **Pass ✓** |
| Total API carryover (mg) | NMT 150 mg | 15.22 | 17.24 | 16.16 |
| API carryover vs. limit | — | **Pass ✓** | **Pass ✓** | **Pass ✓** |
| API per swab (ppm) | NMT 1.59 ppm | Within limit | Within limit | Within limit |

| Parameter | Criterion | Batch R1 | Batch R2 | Batch R3 |
|---|---|---|---|---|
| Cleaning agent (ppm) | NMT 5.0 ppm | BQL | BQL | BQL |
| TAMC (CFU) | NMT 50 CFU | Within limit | Within limit | Within limit |
| TYMC (CFU) | Nil | 0 CFU | 0 CFU | 0 CFU |
| Pathogens | Absent | Absent | Absent | Absent |
| Overall status | Validated | **VALIDATED** ✓ | **VALIDATED** ✓ | **VALIDATED** ✓ |

BQL: Below Quantification Limit; TAMC: Total Aerobic Microbial Count; TYMC: Total Yeast and Mould Count; CFU: Colony Forming Units; NMT: Not More Than.

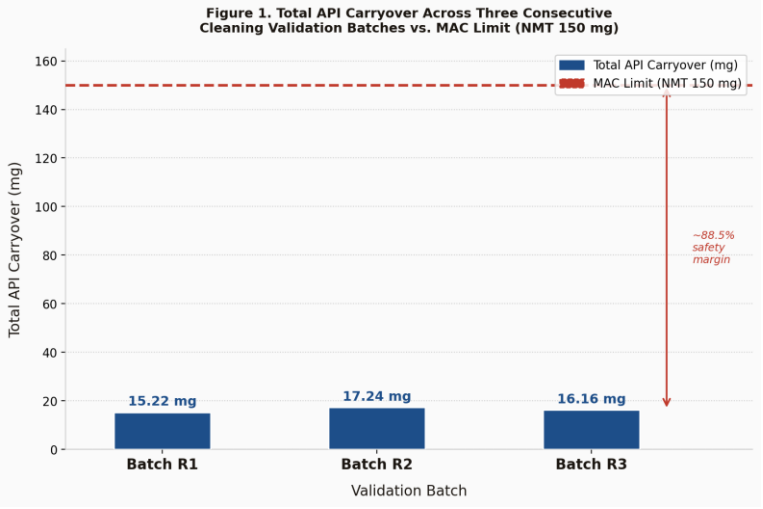


Figure 1. Total API Carryover Across Three Consecutive Cleaning Validation Batches vs. MAC Limit (NMT 150 mg)

Total API carryover values of 15.22 mg, 17.24 mg, and 16.16 mg were recorded for Batches R1, R2, and R3 respectively — all well within the 150 mg MAC limit. The maximum observed carryover (17.24 mg, Batch R2) represents 11.5% of the limit, yielding an ~88.5% safety margin (Figure 1). Per-swab concentrations were within NMT 1.59 ppm at all sampling points across all ten equipment units for all three batches. Cleaning agent residues were BQL in all samples. TAMC was within 50 CFU/swab, TYMC was zero, and all specified pathogens were absent across all three batches.

## 4. DISCUSSION

The present study describes the development and prospective validation of a structured six-parameter WCS assessment framework for NPI in a multi-product OSD manufacturing facility, with Sitagliptin as the model compound. The results demonstrate that the framework successfully identifies WCS candidacy beyond classical potency- and solubility-driven paradigms, and that the resultant cleaning validation confirmed robust and consistent cleaning performance across three consecutive batches.

### 4.1 Equipment Surface Area as the Primary WCS Driver — A Novel Finding

The most significant finding of this study is the identification of equipment chain surface area geometry — rather than API potency or solubility — as the decisive WCS parameter for Sitagliptin. Under classical selection frameworks, Sitagliptin would not qualify as a worst-case candidate: its STD (25 mg) is tenfold higher than the Reference WCS Product (2.5 mg), and its water solubility (~58 mg/mL) is substantially greater. However, the more restrictive per-swab limit was driven solely by the larger Sitagliptin equipment chain surface area (146,009.41 cm² vs. 98,154.26 cm²), yielding 1.59 ppm versus 11.2 ppm.This has a clear mechanistic basis: the per-swab limit equals the MAC divided by the total product-contact surface area. Despite both products sharing the same 10 ppm MAC criterion (150 mg), the larger Sitagliptin chain reduced the per-swab limit to 1.59 ppm — a demanding value requiring full prospective validation. This finding challenges the framework proposed by Moura et al. (2025),[10] who selected Oxcarbazepine based on solubility in a QC laboratory context. While solubility and cleaning difficulty remain valid criteria, equipment surface area geometry must be incorporated as an explicit, mandatory parameter in any NPI-stage WCS framework, particularly where equipment chains vary substantially between products.

### 4.2 Three-Method MAC Calculation — Scientific Necessity

Application of all three MAC calculation methods reflects regulatory best practice per EMA HBEL guidance[6] and PIC/S PI 006-3.[4] The 10 ppm criterion's dominance in this case reflects the relatively small subsequent product batch size — a variable frequently overlooked in WCS discussions but capable of being the controlling factor when HBEL-derived limits are permissive. The PDE/HBEL limit (600,000 mg) was, as expected, several orders of magnitude less stringent, consistent with Sitagliptin's well-characterised safety profile. No single MAC method can be assumed universally controlling; the three-method approach is a scientifically necessary safeguard.

### 4.3 Robustness of Cleaning Procedure — Safety Margin Interpretation

Total API carryover values of 15.22–17.24 mg across three batches against a 150 mg MAC limit yielded an ~88.5% safety margin, demonstrating

highly effective and reproducible cleaning performance. The inter-batch pattern — slight increase from R1 to R2, returning toward R1 levels in R3 — is consistent with normal operational variability and does not represent a directional trend toward failure. The range of 2.02 mg across three batches reflects a stable, in-control cleaning process. This safety margin also supports a post-validation routine monitoring programme based on periodic swab verification rather than full re-validation.

**4.4 Mid-Study Amendment — Real-World QA Complexity**

The revision of the per-swab limit from 1.64 ppm to 1.59 ppm during the active study, processed under formal change control, represents a real-world QA challenge virtually absent from published cleaning validation literature. The approach taken — recalculation, visual threshold re-study, change control approval, and application of the revised criterion to all validation batches — represents a methodologically sound and regulatorily compliant response. All three batches passing the more stringent revised limit further underscores the robustness of the cleaning procedure. Cleaning validation frameworks should formally incorporate change control provisions as standard — a feature not described by Moura et al. (2025)[10] or comparable published studies.

**4.5 Limitations and Future Directions**

This study has several acknowledged limitations. First, the WCS outcome is site-specific; facilities with different equipment configurations may yield different results under the same framework. Second, formal statistical analysis (ANOVA, %RSD, confidence intervals) of inter-batch carryover data was not performed and is recommended for future applications. Third, individual per-swab location results were not fully reported owing to data confidentiality constraints. Fourth, long-term post-validation routine monitoring data remain pending. Future work should apply this framework to highly potent APIs and biologics, and across multiple manufacturing sites to establish generalisability.

## 5. CONCLUSION

The present study developed and validated a structured six-parameter worst-case scenario assessment framework for new product introduction in a cGMP-compliant multi-product oral solid dosage manufacturing facility, using Sitagliptin 25/50/100 mg film-coated tablets as the model compound. The framework successfully identified Sitagliptin as the site worst-case product — a designation driven not by potency or solubility, but by the stringency of its per-swab acceptance limit (NMT 1.59 ppm), arising from the larger product-contact surface area of its equipment chain (146,009.41 cm²). This challenges the prevailing potency-first paradigm of WCS selection and underscores the critical role of equipment chain surface area geometry as a determinant of per-swab acceptance limit stringency. Prospective cleaning validation across three consecutive batches confirmed that the cleaning procedure consistently removed Sitagliptin residues below the controlling MAC of 150 mg, with carryover values of 15.22 mg, 17.24 mg, and 16.16 mg, representing an ~88.5% safety margin. All microbiological and cleaning agent criteria were met across all batches. The six-parameter NPI-stage WCS assessment framework described herein is proposed as a structured, reproducible, and regulatorily compliant model for NPI-stage cleaning validation decision-making in any multi-product OSD facility.

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**Conflicts of Interest** - The authors declare that they have no conflicts of interest.

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