

SOP-114: Cleaning Validation of Shared Equipment

Granulation suite B • Fluid-bed dryer FBD-02 and high-shear mixer HSM-05

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1 Purpose

This procedure describes how shared product-contact equipment in granulation suite B is cleaned between products and how the cleaning is shown to work. A clean that has not been verified against the limits in Table 2 is not a clean: the next batch may not start.

2 Scope

Applies to every product changeover on FBD-02 and HSM-05, including changeovers between strengths of the same product. It does not cover routine end-of-shift cleaning of the same batch, which follows SOP-109.

3 Responsibilities

Role	Responsible for
Production operator	Performs the clean (§4) and records each step.
Line supervisor	Checks the visual inspection and signs the log.
QC analyst	Takes and tests the swab and rinse samples.
QA validation	Reviews results and releases the equipment.

4 Cleaning procedure

Wear the PPE listed in SOP-101. Isolate the equipment electrically (lock-out tag LO-17) before opening any access panel.

4.1 Preparation

1. Record the previous product, batch number and the time the batch ended. The clean must start within **24 hours** (dirty-hold time).
2. Remove filter bags and gaskets; send them to the parts washer.
3. Dry-brush visible powder from the bowl, spray nozzle and expansion chamber.

4.2 Three-rinse procedure

1. **Rinse 1, potable water**, 60 °C, 5 minutes, to remove loose residue.
2. **Detergent wash**, 1% alkaline detergent CD-40 at 70 °C, recirculated for 15 minutes.
3. **Rinse 2, purified water**, 60 °C, 10 minutes, until the drain runs clear.
4. **Rinse 3, water for injection (WFI)**, ambient, 5 minutes. Collect the *final-rinse sample* from the drain valve during the last minute.
5. Dry with filtered air at 50 °C for 30 minutes.

Never skip Rinse 2. Detergent left on the surface raises the final-rinse conductivity and fails the clean; the whole sequence then has to be repeated from Rinse 1.

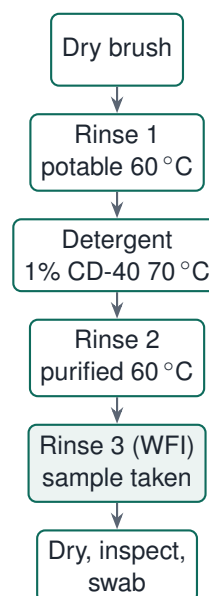


Figure 1: Rinse sequence for FBD-02 and HSM-05.

5 Sampling

Swab four sites on each unit (Table 1) over **100 cm²** each, using the template in the swab kit. Take the final-rinse sample in a TOC vial. Label every sample with the site code.

Site	Location	Why
F1	FBD bowl, lower wall	hardest to drain
F2	Spray nozzle tip	product build-up
M1	HSM impeller underside	shadowed from spray
M2	HSM discharge chute	powder trap

Table 1: Worst-case swab sites.

6 Acceptance limits

Test	Sample	Limit
Visual	All surfaces	No visible residue
TOC	Final rinse	≤ 500 ppb
Conductivity	Final rinse	$\leq 1.3 \mu\text{S/cm}$ at 25°C
Product residue	Swab, per site	$\leq 3000 \mu\text{g}$ per 100 cm^2
Microbial	Swab, per site	≤ 25 CFU per 25 cm^2

Table 2: Acceptance limits after Rinse 3.

7 How the residue limit is set

The residue limit comes from the maximum allowable carryover (MACO) of the previous product into the next one:

$$\text{MACO} = \frac{\text{STD}_{\text{prev}} \times \text{MBS}_{\text{next}}}{\text{SF} \times \text{TDD}_{\text{next}}}$$

where STD is the smallest therapeutic dose of the previous product, MBS the minimum batch size of the next, TDD its largest daily dose and SF a safety factor of 1000.

Worked example: Clorvastatin 50 mg followed by Metrafen 800 mg

$\text{STD}_{\text{prev}} = 50 \text{ mg}$, $\text{MBS}_{\text{next}} = 120 \text{ kg} = 1.2 \times 10^8 \text{ mg}$, $\text{TDD}_{\text{next}} = 800 \text{ mg}$.

$$\text{MACO} = \frac{50 \times 1.2 \times 10^8}{1000 \times 800} = 7500 \text{ mg}.$$

The shared product-contact surface of both units is $25 \text{ m}^2 = 250\,000 \text{ cm}^2$, so the limit is $7500/250\,000 = 0.03 \text{ mg/cm}^2 = 30 \mu\text{g/cm}^2$, that is **3000 μg per 100 cm^2 swab** (Table 2).

8 Deviations

If any result exceeds its limit, stop, tag the equipment *NOT CLEAN*, raise a deviation in the QMS within one working day, and repeat the clean from Rinse 1. Two consecutive failures on the same site trigger a cleaning-process review by QA validation.

9 Records

Keep the cleaning log, sample labels and QC results with the batch record of the *next* product. Retention: product expiry plus one year.

In one line: brush, rinse three times with a detergent wash after the first, sample the last rinse and four swab sites, and release only when every result meets Table 2.