Standard Operating Procedure

TITLE: General Cleaning and Housekeeping for Production Facilities and Equipment

SOP: QA-125 Revision 008- 11/28/21

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1. PURPOSE

   1.1 To provide a system for the complete and timely cleaning, and prevention of infestation in Production areas to prevent cross-contamination or introduction of impurities into products.

   1.2 To ensure that cleaning of the production equipment is accomplished in accordance with written and approved production SOP's, and in accordance with cGMP. To describe a criteria for labeling major equipment to show level 2 cleaning status, in-process product name, and equipment code/name.

2. SCOPE

   2.1 Applies to all areas of the facility that are involved in the production of final products.

   2.2 Applies to all equipment that is used to contain, hold, or has been in contact, in any way, with raw materials intermediates or final products.

   2.3 Specifically applies to Pest Control activities for the facilities.

3. RESPONSIBILITY

   3.1 Production Department is responsible for plant areas and equipment cleaning and proper documentation of cleaning work as required by Nanophase quality system.

   3.2 QA/QC Department is responsible for verification of cleaning (when required by the procedures) and validation of cleaning methods

   3.3 QA/EHS is responsible for managing pest control program for the facilities.

   3.4 Maintenance Supervisor (or facility Manager) is responsible for reviewing monthly pest control reports and corrections based on inspections findings.

4. ASSOCIATED MATERIALS

   4.1 QA-120A Equipment Cleaning Form-QA-120XX

   4.2 Pest Control Report Log

   4.3 Process specific Cleaning SOPs

   4.4 Equipment Status Form (QA-132A)

   4.5 21 CFR Part 211.105

   4.6 NTC-025 Equipment Cleaning Policy

4.7 MFG-01-054A Approved Chemical Cleaning List

4.8 QA-125X Arae cleaning verification checklist form.

5. PROCEDURE

5.1 **Facility Cleaning**

5.1.1 Each individual department area is responsible for the removal of all trash and debris that results from the ordinary course of operation during normal work hours.

5.1.2 All trash is disposed of in a proper manner that is in keeping with the local ordinances for trash containers and trash removal. No dumping of rejected or outdated products or special waste into the trash containers is permitted. Special and Nonspecial waste is disposed in accordance with the local, state, and federal regulations.

5.1.3 To prevent contamination of the facility, all janitorial equipment is kept cleaned and maintained in good working order.

5.1.4 Manufacturing floors are cleaned on a daily basis with non-toxic cleaning agents. Regular housekeeping is maintained. Area cleaning are recorded on QA-125X, where "X" is replaced with specific area cleaning form number. See an example of F/A area cleaning form QA-125A below.

QA-125A Rev 001, 11/22/2021

Fill Room Cleaning **CREW/TURNO** _____ **DATE/FETCHA:** _____

Room # Habitación #	Take out the Trash Sacar la basura	Sweep the Work Area Barrer la area de trabajo	Mop the Work Area Trapear la area de trabajo	Clean Windows, Walls & Curtains Limpiar ventanas, paredes y cortinas	Clean Tables and/or Conveyors Limpiar mesas y/o bandas de la máquina	Clean Equipment in use (Scale, filler, laser, etc.) Limpiar equipo que está usando	Refill PPE Mantener PPE	Wrap completed pallets in plastic Envuelva los pallets terminados en plástico	Turn off equipment not in use. (Laser, Ink Printer, Conveyor, etc.) Apague el equipo que no esté en uso	Supervisor Review Revisión del supervisor
1										
2										
3										
4										
5										
6										
7										
Aisles / Caminos del pasillo										

Note: Write the shift/date at the top of the page and initial for each item performed. Write N/A for items not completed. Mopping is required when cleaning the room between products or if the room will not be used on the following shift.

Nota: Escriba el turno / fecha en la primera línea y ponga sus iniciales para cada elemento realizado. Escriba N / A para los elementos no completado Se requiere trapear al limpiar el cuarto entre productos o si el cuarto no se utilizará en el siguiente turno.

QC Walkthough Check
Initials/Date

5.1.5 Additionally, Manufacturing facilities are thoroughly cleaned during planned shutdowns.

5.2 **Pest Control**

5.2.1 An experienced firm specializing in the prevention of infestation by rodents, birds, insects, and other vermin is contracted to provide regularly scheduled services for the facilities.

5.2.2 Rodenticides, insecticides, and fungicides are not used unless they are registered, and used in accordance with the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA). In addition, they are designed and used to prevent the contamination of equipment, components, containers, closures, labels, packaging, and final product.

5.2.3 A facility map is kept to show the location of all traps and bait equipment. The location of traps and bait equipments with in the facility is marked above the equipment. Bait stations are used outside the facility, traps are used inside.

5.2.4 A Pest Control Log book is kept for each site. Report includes; the date, area treated, product used, pest activity summary, observations, and the identities of pest control technician along with reviewer (NTC), Maintenance Supervisor reviews each report and schedule repairs (if necessary, based on inspection findings). Proof of Supervisor review is indicated by his/her initials on actual report.

5.3 **Equipment Cleaning Scheme**

5.3.1 Equipment used in manufacturing, blending, screening, and packaging are routinely cleaned during and after the production cycle. Level of cleanliness and frequency is based upon the nature of operation and contamination control.

5.3.2 Cleaning inspections are documented in QA-120 forms, process specific cleaning forms, or forms specific to cleaning included in batch records.

5.3.3 Cleaning levels and procedures specific to each vital manufacturing are defined in various manufacturing work instructions. Cleaning methods for Bulk Pharmaceutical Chemicals (BPC) are validated. The basis for cleaning levels is determined by "*NTC-025 Equipment Cleaning Policy*".

5.3.4 When production equipment is used for many different products; a written, approved, and validated cleaning procedure (required for BPC products) is used to assure that cross contamination has been minimized to a safest possible levels.

5.3.5 The Production Manager or Supervisor, depending on the type of contaminant present, determines the appropriate approved method and sequence of approved cleaning agents for each individual product.

5.3.6 Cleaning for BPC is documented in equipment specific Cleaning Log. Appropriate cleaning forms are attached to related batch record.

5.3.7 Production and processing equipment used in drug component manufacturing (BPC) are labeled with a status form. Status forms (QA-132A) are filled out and posted at processing or production equipment including the equipment identification as follows;

- Equipment Name-if when only one of a particular type of equipment exists in a manufacturing facility (e.g., Jaygo Blender, Sweco Sifter, etc)
- Equipment Code Number- Unique to a processing equipment (e.g., RS-12, ARS-1, etc)
- QA-132A also indicates identity of in-process product, previous product, and level 2 cleaning status.

5.4 **Equipment Cleaning-Frequency and Type**

5.4.1 **Dedicated equipment** is inspected every 3 years to determine if a Level 2 cleaning is required due to excessive build-up of product, signs of contamination or after maintenance work has taken place on any product contact surface. If it is determined that no level 2 cleaning is required, all documentation is updated at the reactor stations for the next term of 3 years.

5.4.2 Most processes employ Level 0 cleaning, which is a removal of excess byproducts from the equipment to maintain optimal process performance. Level 1 cleaning is normally performed at the end of each lot or batch for accountability purposes. Level 2 cleaning is completed after use and before the change in materials is introduced by using validated cleaning methods for BPCs.

5.4.3 Blenders, Sifters, and dispersion equipment are cleaned based on their use. During a large campaign, they are inspected every 6 months and Level 2 cleaned every 3 years (for BPC manufacturing). However, Level 1 cleaning is performed between the lots/batches for accountability (mass balance) purposes.

5.4.4 Level 1 and 2 cleaning verifications are performed by documenting cleaning in appropriate cleaning sheets and/or completing the Equipment Cleaning Log. The Equipment Status sheet (QA-132A) is used to display Level 2 cleanings for BPCs.

5.4.5 All Level 2 cleanings are inspected by QA, if the inspection reveals evidence of contamination, then the particular vessel, equipment, or utensil is not used until it has been re-cleaned and inspected by Quality Assurance.

5.4.6 **ZN-8690 Blue Poly Drums**
ZN-8690 formulation is prepared in blue poly drums, which are FDA approved for food contact. These drums are reusable after each use. However, the drums are cleaned (LEVEL 1) after each batch under directions as outlined in ZN-8990 MBR for production and blending. Labels QA-132B through QA-132D are used as appropriate according to each stage of drum use.

6. APPROVALS

Originator	Date
Department Head	Date
Quality Assurance	Date

7. CHANGE HISTORY

Revision#	Date	Reason for change
000	3/22/96	Original
001	12/18/96	Removed forms from SOP. Removed Housekeeping Log (QA-125A), and 5.2, added a ref. to MFG-05-500
002	3/31/03	Removed Ref to obsolete SOP MFG-05-500. Changed logo.
003	8/15/08	Combined procedures QA-110, 120, and 132 into QA-125. Added reference to NTC-025, removed form QA-125B.
004	6/24/11	Added section 3.4, revised section 5.2.4.
005	8/15/12	Added section 4.8 and 5.4.6 to add cleanliness status labels and use criteria for ZN-8690 blue poly drums. Added form QA-120M-P
006	11/4/13	Added form QA-120Q
007	5/28/15	Added form QA-120R (G2).
008	11/22/21	Added association to area cleaning form, see section 5.1.4.

Signature Manifest

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All dates and times are in Central Time Zone.

QA-125 General Cleaning and Housekeeping for Production Facility and Equipment

Originator

Name/Signature	Title	Date	Meaning/Reason
System Administrator (SYSADMIN)		24 Feb 2025, 10:32:52 AM	Approved

Department Head

Name/Signature	Title	Date	Meaning/Reason
Nadir Ali (MALI)	Director, EH&S and Quality	10 Mar 2025, 10:13:23 PM	Approved

QA

Name/Signature	Title	Date	Meaning/Reason
Nadir Ali (MALI)	Director, EH&S and Quality	10 Mar 2025, 10:13:59 PM	Approved