All cleaning practices requiring validation should first be evaluated and the results of the evaluation documented and approved. Every aspect of the cleaning practice should be reviewed including all materials and methods involved.

Cleaning instruction-records or SOPs with attached checklists, should include all relevant cleaning parameters and confirmation that significant steps have been completed.

Scope and Applicability

This guideline is applicable to all plants and equipment used to manufacture medicinal products and APIs and/or their intermediates (excluding biotechnology processing) within Operations and R & D.

Note: R&D do not carry out formal cleaning validation during development(owing to the limited number of batches and changing processes/equipment), but cleaning verification must be carried out.

Definitions

Cleaning Validation

Cleaning validation is a validation program to verify that the processes and procedures used to clean product residue from process equipment and components, will consistently and significantly reduce the amount of active and/or excipient(s) and cleaning agent(s) to a concentration within calculated acceptance limits

Drug Substance (DS) or Active Pharmaceutical Ingredient (API)

Any substance or mixture of substances intended to be used in the manufacture of a drug (medicinal) product that when used in the production of a drug becomes an active ingredient of the drug product. Such substances are intended to furnish pharmacological activity or other direct effect in the diagnosis, cure, mitigation, treatment or prevention of disease or to affect the structure and function of the body. Note: Also known as Bulk drug or Drug Substance.

Cleaning Process Establishment

Cleaning carried out to establish an effective cleaning method for API or intermediate prior to formal cleaning validation.

Cleaning Verification

Specific evidence (which may include analytical data) that demonstrates contaminants (process or cleaning process related) are below a predetermined level that may affect the safety and quality of the next product.

Free From Gross Contamination

A state of cleanliness in which the equipment train may not be visibly clean but is free from any large quantities of material hold up. The amount of solid/liquid remaining in the equipment is not quantified but is assessed by visual inspection (e.g. through a sight glass on a reactor). Typically equipment is cleaned free from gross contamination through a single rinse and residual material is estimated at less than 5%. For pressure filters free from gross contamination normally requires the heel to

Based on toxicity / minimum therapeutic dose

Cleaning Instruction-Records
Equipment Cleaning Instruction-Records should be written in a detailed stepwise format for manual cleaning methods and in a defined sequential operation for automated cleaning systems.

Completion of each significant cleaning cycle should be recorded either manually (initial, date, and time) or using a validated computerized system.

Such instruction-records should include or reference, at least, the following parameters, where applicable:

- Cleaning and sanitizing agents, including concentration, amount to be used and contact time;
- Quality of water or other solvents used;
- Requirements for equipment disassembly and re-assembly;
- Temperature and pressure parameters;
- Flow rates or times of known volumes for wash solutions and rinses;
- Identification of defined recycle and transfer piping pathways for cleaning;
- Start and end times of each critical cleaning cycle or step;
- Volume or weight of rinse;
- Number of rinses;
- Frequency of cleaning (e.g., Campaign length or after each batch);;
- Tools and/or utensils employed;
- Agitation, recirculation, and/or reflux;
- Draining and drying;
- Identification and inspection of dead-legs;
- Method for indicating equipment cleaning status;
- Method for protecting clean equipment from contamination;
- Maximum time intervals for between use and cleaning; and
- Verification of critical cleaning steps and supporting data (e.g., UV, pH, visual inspection).

Cleaning Solutions that are prepared and stored should be prepared following written instructions-records and labelled to indicate, at least, the following information:

- Signature or initials of person preparing the solution;
- Concentration of solution at time of preparation;

