Guidance Number 014

Figure1: Guidance on item to be considered as part of the cleaning evaluation is given in the following table.

Guidance on items to be considered as part of the cleaning evaluation is given in the following table.

Item No.	Items to be considered in the Cleaning Evaluation	Include consideration/justification for:
1.	Material to be cleaned	• Process Intermediates • APIs • Raw Materials (including processing aids, catalysts) • In-process Materials and Drug Products • Cleaning and sanitizing agents • Solvents • Bacterial Endotoxins, when applicable • Microorganisms, when applicable

Item No.	Items to be considered in the Cleaning Evaluation	Include consideration/justification for:
2.	Equipment to be cleaned	• List of major equipment including size and surface finish materials expected to be exposed to product in each piece of equipment ○ Surface finish materials may be separated into major (e.g. glass lining of a reactor) and minor (e.g. PTFE gaskets and valve faces).
3.	What residues will be tested for	Consider, as applicable: • API Process intermediates • Potential degradation products, by-products or conversion products from manufacturing process • Stability of material(s) being cleaned under the proposed cleaning conditions • Microbiological (when applicable considering the nature of the Drug product formulation) • APIs • Raw materials • Toxic solvents • Detergents

Item No.	Items to be considered in the Cleaning Evaluation	Include consideration/justification for:
4.	Cleaning agents	• Solvents • Detergents • Others (e.g., acid)
	Rationale for selection of cleaning agents	• Based on the chemical nature of the major materials identified and expected to be present in the residue • Safety and toxicity considerations, including suitability for use in pharmaceutical application • This selection may be based on reference data, prior process experience, or solubility testing. • Availability in bulk, ease of disposal, compatibility with laboratory sample prep methods, and cost • Solubility of the processing materials in the cleaning agents. A standard procedure may be used to test the solubility of the processing materials in the cleaning agents and should include consideration of solubility rates and rinse contact time. • Solubility of the cleaning agent in the rinse vehicle • Compatibility of the materials of construction with the cleaning agents.
5.	Outline of suggested cleaning methodology • Critical cleaning parameters and ranges • Extent of equipment disassembly • Extent of manual cleaning required	Cleaning critical parameters • Cleaning agent Concentration • Quantities (% vessel volume) • Temperature • Distillation/reflux/flow rates • Cleaning times (recirculation, stir, etc.) • Cleaning method (e.g., spray balls, flooding, power hosing, manual)

Item No.	Items to be considered in the Cleaning Evaluation	Include consideration/justification for:
6.	Design Review	• P & ID, Dimensional Drawing, or Walk-down review, if applicable • Identify dead legs, or other locations requiring manual intervention. • Make recommendations for cleanable equipment or process piping improvements. • Document the alternative solutions if design recommendations are not carried out for any reason. • Select disassembly points for inspection, swabbing, and possibly manual cleaning. • Select appropriate tools and cleaning reagents with consideration for compatibility with materials of construction. • Review the CIP system if applicable including an examination of spray device coverage.
7.	Residual acceptance criteria	• One acceptance limit for all pieces of equipment, or equipment-specific limits. • Worst case limit or limit based upon individual product combinations or worst case A/B combinations. • Microbial or endotoxin limits, where applicable.

Item No.	Items to be considered in the Cleaning Evaluation	Include consideration/justification for:
8.	Determination of appropriate Cleaning Interval	• Identify trends in the product stability profile and determine impact of cleaning, if any. • Identify trends in the product impurity profile and determine impact of cleaning, if any. • Evaluate data from the initial campaign of new products, to determine the appropriate cleaning interval for subsequent campaigns. • Look for trends in deviation reporting for established cleaning procedures that provide evidence that campaign length was a contributing factor to the failure(s) if any. • Consider factors such as polymerization or product caking that could interfere with cleaning after an extended campaign • Evaluate between lot rinsing, and the amount of residue typically remaining. • Cleaning for dedicated equipment and campaign length (for both dedicated and non dedicated equipment) should evaluate the potential for Microbial buildup.
9.	Which analytical and sampling method(s) will be used Where sampled (applicable locations)	• Rinsate and/or Swabbing • Sampling methods • For rinse samples, ensure all product contact surfaces are rinsed • Consider product accumulation sites when evaluating swabbing location