- Agitation
- The extent of manual intervention required to produce expected results

Product Grouping
For the purpose of cleaning validation a group of related products to be identified and a single product selected as 'worst-case' or representative of the product family The rationale for the grouping must be documented. Types and examples of product grouping include:

Figure 1: <u>Types and examples of product grouping</u>

Cleaning for the same chemical entity. Cleaning for drug product formulations with same API(s).	Crude and Pure for the same API. Validation runs for either step may be equivalent. Formulations within a drug product family, such as different strengths or similar base formulations.
Cleaning with the same cleaning instructions	Products A, B and C are cleaned using the same procedure. If B is the worst case and its' cleaning procedure is successfully validated, then A and C would also be considered validated.
Products cleaned manually using the same procedure	Several products using essentially identical equipment (e.g., reactors, centrifuges, blenders, granulators, mills, tablet presses) and cleaned using the same procedure. This procedure typically includes dismantling to clean, and visual inspection

Once products are appropriately grouped, the worst-case product or products can be selected from among the group for the purpose of executing the cleaning validation protocol. A number of scenarios are possible:

- Within a group, two or more products may be determined to provide an equivalent 'worst-case' challenge to the cleaning procedure. Once the rationale for equivalency has been documented and approved by the Quality Authority, the equivalent products are used to demonstrate the effectiveness of the cleaning procedure during validation.
- Example: Product A and Product C are established as equivalent worst-case challenge products for the cleaning procedure used for products A, B, C, D and E.

During validation, any lot combination of Products A and C are used to fulfill the 3 validation cleanup requirement (e.g. 3 of A **or** C, 2 of A and 1 of C **or** 1 of A and 2 of C).

- Within a group, two or more products are determined to be 'worst-case' challenges, but are not equivalent. Each worst-case product should be subjected to the 3 validation cleanup requirement.

- The same cleaning procedure is used for two or more groups of products. Each worst-case product within each group should be subjected to the 3 validation

group for purposes of validation. These groupings and representative sampling sites should be documented and justified. The documentation should be approved by the Site Quality Team and Site Production Team. If equipment grouping is used, cleaning validation should be performed using three (3) executions of the same cleaning procedure using any combination of equipment within a group. Document and justify if the number of cleaning executions to be used for validation is different than 3 (three).

Figure 1: <u>Types and examples of equipment grouping</u>

Types and examples of equipment grouping include:

Identical Equipment (Grouped by type and similar or identical utilities and accessories)	Reactors (vessels with heating, cooling and a condenser); Receivers (tanks with no heating, with or without agitation) cleaned by an individual procedure. Blenders or Mixers (same configurations/accessories with respect to cleaning). Tablet Presses (same cleaning procedures/accessories/ parameters)
Grouped by gross function	Where one individual cleaning procedure is used for all product cleanups (e.g., Centrifuges and dryers, or Fitzmills and Comils, Granulators). This applies where there is mostly manual disassembly.
Grouping Minor Equipment	For example, scoops, shovels, filter plates, filter housings, spatulas. Relatively small equipment that is manually cleaned and has no moving parts can usually be cleaned by the same procedure.

- Equipment design (e.g., Heating/cooling, Mixing, gross function) and geometry (e.g., shape and size)

- The ability of an individual procedure to produce expected results, i.e., uses the same cleaning instructions.
  - A change in the sequence of cleaning cycles constitutes a different cleaning recipe and should not be considered equivalent for the purpose of validation.
- CIP design including spray device pattern, pump size, and supply line diameter.

- Process piping routing and aggregate surface area is sufficiently similar. Pipe routing and size should be considered and appropriate test cases identified. If a scientific rationale can be justified with approval by site Quality, that a set of piping is sufficiently similar, a worst test case selection is appropriate for the purpose of validating the set. Otherwise, multiple piping configurations should be represented