consistently and significantly reduce the amount of active and/or excipient(s) and cleaning agent(s) to a concentration within calculated acceptance limits

3.2 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.

3.3 Acceptable Carryover Quantity (ACQ)

The maximum quantity of guiding substance that can be carried over into subsequent manufacture.

3.4 API Starting Material

A raw material, intermediate, or an API that is used in the production of an API and that is incorporated as a significant structural fragment into the structure of the API. An API starting material can be an article of commerce, a material purchased from one or more suppliers under contract or commercial agreement, or produced in-house. They are normally of defined chemical properties and structure.

3.5 Cleaning Process Establishment

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

3.6 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.

3.7 Dedicated Equipment/Plant

For the purpose of cleaning, equipment/plant shall be considered dedicated when it is used for the production of one API or intermediate and the potential for cross contamination does not exist.

3.8 Equipment Train

All the process equipment, including mobile equipment, flexible hoses, fixed and mobile pipe-work etc, used for a specific product, excluding utilities (i.e. all equipment in direct or with risk of contact with the process during production).

6. Procedure for Medicinal Products Equipments

The cleaning evaluation determines the major contaminant(s) to be sampled and tested, along with the sampling locations for each equipment item. Table I below provides guidance for sampling locations for each equipment type. This table does not substitute for a thorough consideration of the design of equipment to identify those locations deemed most difficult to clean, nor does it mandate the inspection or sampling of suggested locations that would require vessel entry or require undue safety concerns based upon the design, size, or intended use of equipment.

If swabbing is used as the sampling method, product-contact surfaces should be swabbed in locations from which there is a likelihood of contamination or carryover to a subsequent product and from the most difficult to clean areas. If a rinsate method is used, a measured volume of solvent used for the final rinse should thoroughly wet all product contact surfaces, and should be circulated, where applicable, through all product contact lines before it is visually inspected or tested in the laboratory for residues. Rinsate
recovery studies can be based on worst case product groupings, and/or by grouping of worst case materials of construction.

Table II is an example on how to justify and document the rationale for sampling site selection and table III is an example of how to tabulate the sampling points and sampling methods. Consideration of locations to sample can be documented as part of the cleaning evaluation documentation (e.g. site SOP) conducted for the development of a sampling plan of the equipment system. For more guidance consult with the guidance on conducting a system design review for sample location selection and documentation.

Examples:

