affect product quality adhere to the approved specification and are correctly installed.

3.6 Operational Qualification

Documented verification that all functional aspects of a facility or system which affect product quality, perform as intended throughout all anticipated operating ranges.

3.7 Performance Qualification

Performance Qualification provides documented verification that all aspects of a Facility or System, which can affect product quality perform effectively and reproducibly based on the approved process method and specifications.

3.8 Process Validation

Establishing documented evidence, which provides a high degree of assurance that a specific process will consistently produce a product meeting its pre-determined specifications and quality characteristics.

3.9 Cleaning Validation

Establishing documented evidence that a specified cleaning procedure will provide a high degree of assurance that it can be used to consistently clean a piece of equipment or a facility to a predetermined acceptable level of cleanliness.

3.10 Direct Impact System / Component

This is a system / component that is expected to have a direct impact on product quality. These systems / components are subject to qualification.
In some instances, Direct Impact Systems / Components will depend on Indirect Impact Systems / Components for effective operation and therefore, any interfaces need to be carefully assessed.

3.11 Indirect Impact System / Component

This is a system / component that is not expected to have a direct impact on product quality, but typically will support a Direct Impact System / Component. These systems / components are not subject to qualification, but are subject to Good Engineering Practice (GEP).

3.12 No Impact System / Component

This is a system / component that will not have any impact, either directly or indirectly, on product quality. These systems / components are not subject to qualification, but are subject to Good Engineering Practice.

3.13 Good Engineering Practice

Established engineering methods and standards that are applied throughout the project lifecycle to deliver appropriate, cost-effective solutions [ref. 5.2.1].

are used they should be identified.

5.7 Commissioning Strategy

The strategy for commissioning of Facilities and Systems, as an element of GEP, should be considered at an early stage in the project. For each stage of the commissioning process this should identify the following:

- Activity (see Appendices 1 and 2).
- Scope of the activity.
- Interface with formal qualification activities
- Persons responsible, e.g. testers, witnesses, approvers.
- Process by which the activity is to be undertaken, including any documentation requirements.
- Records to be produced, how they should be registered and archived.

The strategy should avoid duplication of testing, wherever this is justifiable. All rationale/justification should be documented.

Some qualification activities, described later at 5.9 and 5.10, may be undertaken at the System supplier's factory, provided that the location and environment have no effect on the installation or operation and that they are conducted in accordance with cGMPs. In this instance, site testing of these elements should be sufficient to demonstrate that the transfer to site has not affected the installation or operation.

5.8 Design Qualification (DQ)

The purpose of DQ is to assure that the design of a proposed new or modified facility; system or equipment meets cGMP requirements and is suitable for its intended purpose. In addition to the equipment operation, particular attention also should be made to the design for routine cleaning of the equipment.

Compliance with both cGMP and suitability of use should be documented. DQ integrates the URS and FS and relevant design documents e.g. design specifications, in assuring that what has been designed will meet both regulatory and internal requirements. The underlying theme of assuring design compliance prior to the construction or manufacture of the facility, system or equipment is inherently logical and avoids costly errors in judgment.

The documentation of the DQ aspects of the qualification scheme shall be prescribed in the VP. The actual specification documents to be reviewed and the responsibilities for both the technical and cGMP compliance review of

the design shall be clearly mandated. QA shall perform the cGMP review. All review activities shall be documented.

The DQ Program / Protocol and Report shall be prepared, commented on and approved by the persons identified in the Validation Plan.

The results of the OQ should comprise the original completed OQ Program / Protocol with its check sheets, etc., marked up with the results observed, comparisons with the pre-determined acceptance criteria, references to any documents (e.g. commissioning records, justification reports) retained elsewhere, signed and dated by the persons involved, together with any relevant attachments, such as additional raw data and deviation reports.

The OQ should be satisfactorily completed before the start of PQ. There could be some items that may not be complete and these require a technical judgment before delaying the start of PQ. The rationale for commencing PQ prior to satisfactory completion of OQ should be formally documented and approved. This is valid even if combined OQ / PQ programs / protocols are to be executed.

The completed OQ results should be presented as a report or a number of completed OQ results combined into a summary report.

The OQ Report shall be prepared, commented on and approved by the persons identified in the VP.

5.11 Performance Qualification (PQ)

5.11.1 Performance Qualification Program / Protocol

PQ follows IQ/OQ. Although described below as a separate activity, it is acceptable to include PQ testing as part of the OQ exercise. The PQ is the final qualification activity prior to performing Process Validation (PV). PQ assesses that the equipment and ancillary systems, as connected together can perform effectively and reproducibly. The PQ is performed using production materials, qualified substitutes or simulated product and subject to processing conditions encompassing upper and lower operating limits or ‘worst case’ conditions. PQ bridges OQ, with its emphasis on demonstrating equipment function, and PV with its emphasis on process capability and consistency. PQ takes OQ one step further due to the requirement to include production materials, qualified substitutes or simulated product.

A properly executed OQ and PQ means that PV can be conducted using routine process conditions. There are no specific requirements for the number of runs to be performed in PQ. One of the goals of PQ is to demonstrate consistency. Multiple runs or trials, especially for the critical elements of PQ, should be included.

The PQ Program / Protocol shall verify that all aspects of a Facility or System which can affect product quality perform effectively and reproducibly based on the approved process method and specifications. The activities comprising PQ will have been identified in the VP.

The PQ Program / Protocol should be kept specific to product quality related items only.

6.3 Appendix 1: Examples of factors which can determine impact on product quality

A positive answer to any of the questions below will signify a conclusion of direct impact for that system / component. It should be noted that this list of questions is not exhaustive.

. Does the system/component have direct contact with the product (e.g. air quality)?

. Does the system/component provide an ingredient or component to the process (e.g. raw material, USP water)?

. Does the system/component produce data, which is used to accept or reject product (e.g. electronic batch record system, critical process parameter chart recorder)?

. Does the system/component produce control or manipulate the process in such a way as to affect product quality without independent verification?

a) Does the normal operation or control of the system/component have a direct effect on product quality?

b) Does failure or alarm of the system/component have a direct effect on product quality or efficacy?

. Does the system/component have a direct impact on product purity, safety, efficacy, identity or the measurement or monitoring of these attributes?

. Is the system/component used in cleaning or sterilizing (e.g. clean steam)?

. Is the system/component the official archive or record of cGMP related data (e.g. production, training, change control)?

. Is the system/component used for product complaints, returned goods, product release or recall, or product history?

. Does the system/component control stock information, stock tracing, stock status, location or shelf life?

0. Does the system/component impact or affect reconciliation, partial use of components or split lots?

1. Does the system/component send GMP data to any other validated computer system?

12. Does the system/component impact or affect coding of raw materials, formulated or packaging components (e.g. label identification)?

13. Is the system/component used in analytical tests associated with a product specification, analytical method or compendia?

14. Can the system/component have a direct impact on product quality in any other way?

