Software Validation

Resources

- GAMP Guide for Validation of Automated Systems (ISPE)
- Munk C et al: ISBT – Guidelines for validation and maintaining the validation state of automated systems in blood banking *Vox Sanguinis* (2003) 85 (Suppl. 1), S1–S14

Assumptions

- Existence of Quality System
- Experience of non-computer validation

Objective

- The objective of validation is to produce documented evidence that provides a high level of assurance that all parts related to the use of an automated system will work correctly and consistently.

Validation….

…is more than just testing.

…demonstrates control.

…ensures compliance.

…generates knowledge.

…establishes future requirements.

…requires a structured approach.

Benefits of Validation

- improve the use of technology;
- improve the business benefits;
- improve the relationship between stakeholders (users, suppliers, authorities, etc.);
- improve operational efficiency;
- reduce the risk of failure;
- improve compliance with regulations.

Regulatory Framework

- Chapter 21 Part 11 Of the Code of Federal Regulations (For Systems with Electronic Records or Signatures) § 11.10 Controls for closed systems.
  - **Validation of systems to ensure accuracy, reliability, consistent intended performance, and the ability to discern invalid or altered records**.

Regulatory Framework

- Chapter 21 Part 211 of the Code of Federal Regulations § 211.68 Automatic, mechanical, and electronic equipment. (Computer Validation in Particular)
  - Appropriate controls shall be exercised over computer or related systems to assure that changes in master production and control records or other records are instituted only by authorized personnel.
  - Input to and output from the computer or related system of formulas or other records or data shall be checked for accuracy. The degree and frequency of input/output verification shall be based on the complexity and reliability of the computer or related system.

Regulatory Framework

- **EU Directive 2003/94/EC (Good Manufacturing Practice)**
  - **Article 8**
    - Premises and equipment to be used for manufacturing operations, which are critical to the quality of the products, shall be subjected to appropriate qualification and validation.
  - **Article 9**
    - When electronic, photographic or other data processing systems are used instead of written documents, **the manufacturer shall first validate the systems** by showing that the data will be appropriately stored during the anticipated period of storage.

Regulatory Framework

- Rules and Guidance for Pharmaceutical Manufacturers and Distributors 2002
  - Annex 11 - Computerised Systems
    - Before a system using a computer is brought into use, it should be thoroughly tested and confirmed as being capable of achieving the desired results. If a manual system is being replaced, the two should be run in parallel for a time, as a part of this testing and validation.

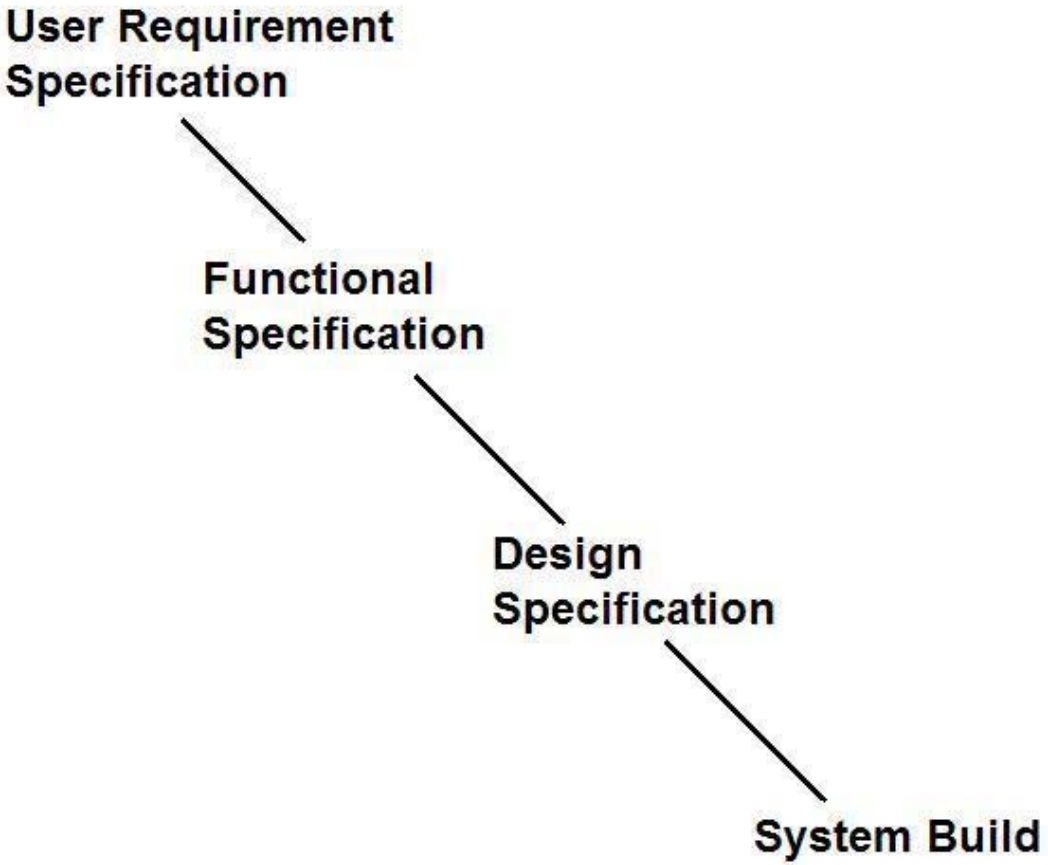
Regulatory Framework

- Rules and Guidance for Pharmaceutical Manufacturers and Distributors 2002
  - **Annex 18 - GMP for Active Pharmaceutical Ingredients** (API's Only)
    - GMP related computerized systems should be validated. The depth and scope of validation depends on the diversity, complexity and criticality of the computerized application.

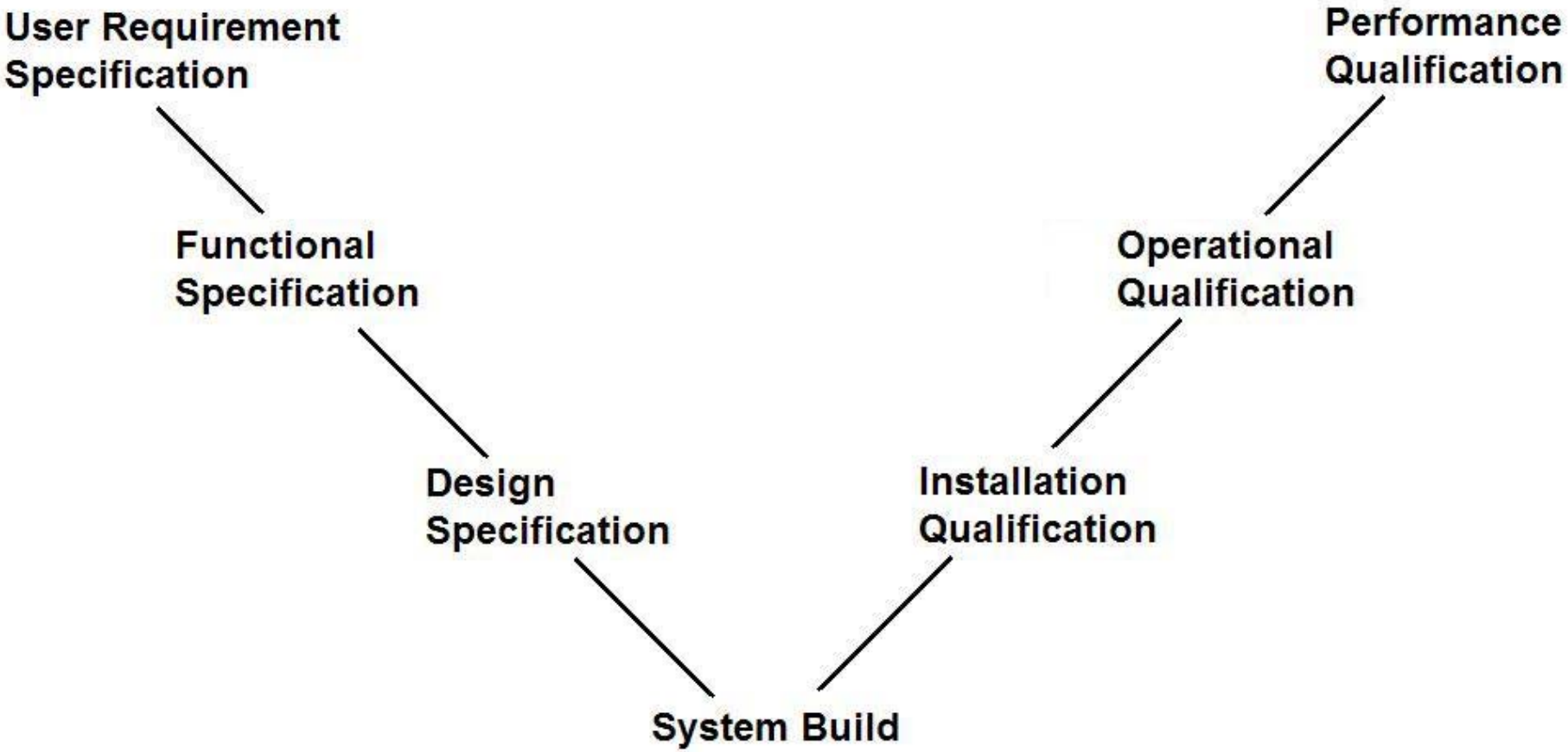
Validation Approach

- Based on methodologies used to manage software development
- Links in to the software development path
- Needs to take account of the complete operating environment

The software development path

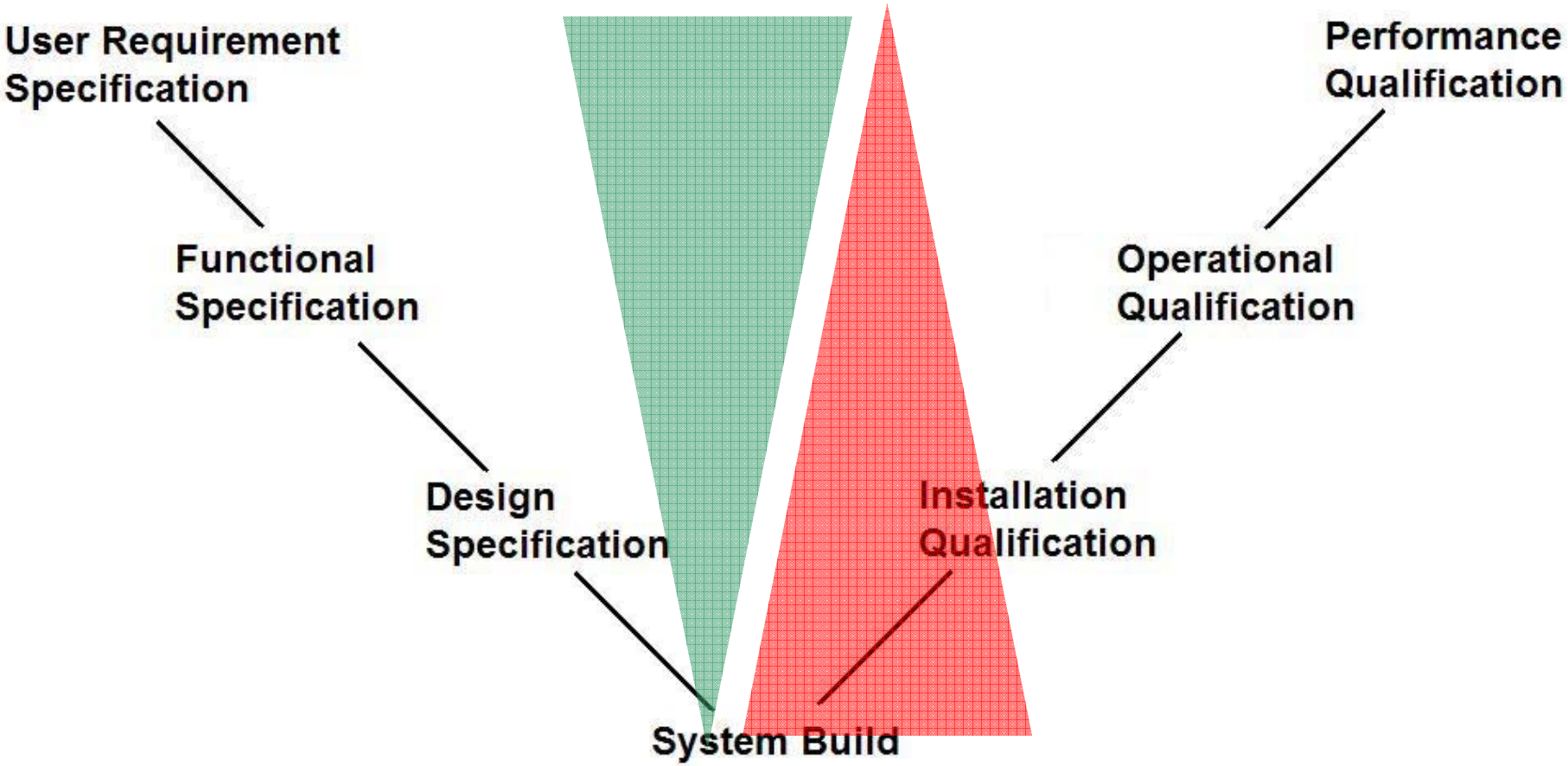


The validation process



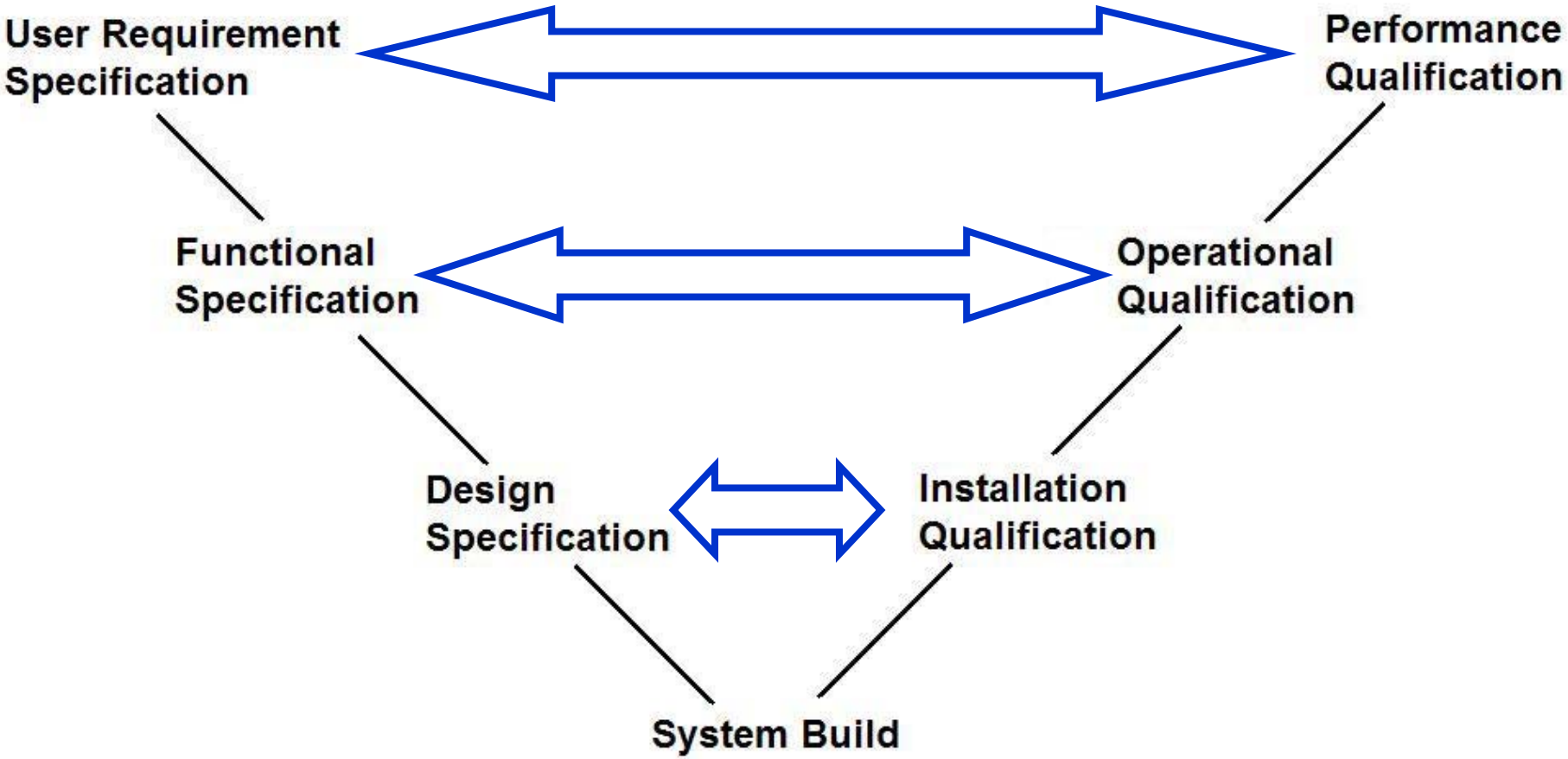
ISBT 128
More than Identification

The validation process

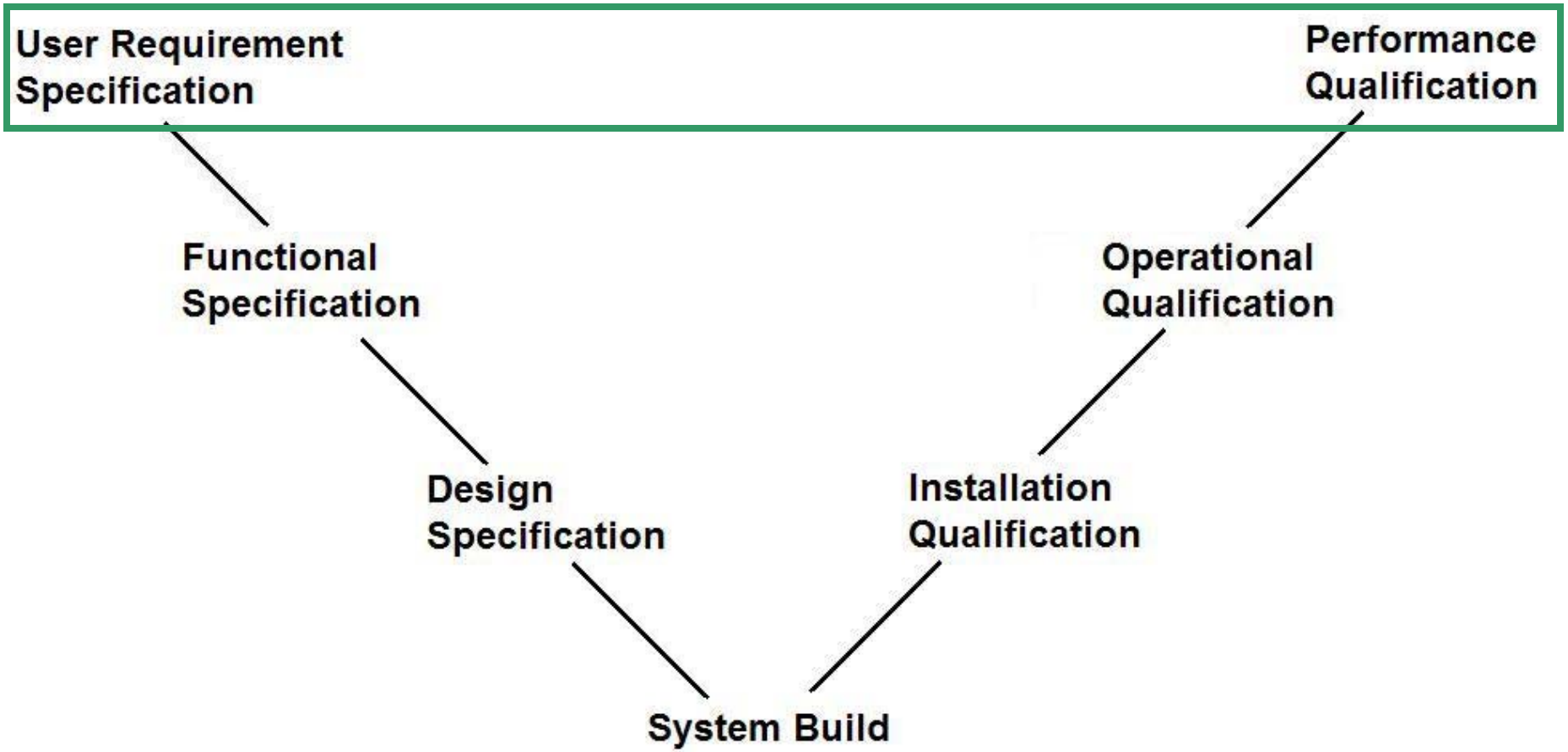


ISBT 128
More than Identification

The validation process



The validation process



User Requirements Specification

- Each requirement statement should be uniquely referenced and be no longer than 250 words;
- Requirement statements should not be duplicated or contradicted;
- The URS should express requirements and not design solutions;
- Each requirement should be testable;
- Both user and supplier must understand the URS; ambiguity and jargon should be avoided;
- Wherever possible, the URS should distinguish between mandatory/regulatory requirements and desirable features.

Supplier Qualification

- The nature of the qualification will depend on:
  - the user's policies for supplier qualification;
  - the nature of the automated system;
  - the risk assessment.
- Assessment type
  - questionnaire/survey
  - on-site audit
- To ensure that the supplier:
  - uses a recognized development methodology
  - provides adequate support and maintenance

System Evaluation

- Evaluating the system against standards including GxP;
- Evaluating the system against established requirements;
- Evaluating the needs of system and environment configuration;
- Evaluating the requirements for installation;
- Evaluating the training requirements;

Risk Assessment

- identifies critical control points
- determines the degree of testing required
- determines the focus of testing effort
- defines risk mitigation plans
- results in ‘better/smarter’ testing

IQ, OQ and PQ

- Installation Qualification
- Operational Qualification
- Performance Qualification

IQ, OQ and PQ

- Installation Qualification
  - IQ shows that the system has been installed correctly.
- Operational Qualification
  - Tests functional elements and insures that the system will meet all defined user requirements under all anticipated conditions of manufacturing, i.e. worst case testing.
- Performance Qualification
  - Demonstrates that the computerized process will consistently produce acceptable product/output under **normal operating conditions**. The demonstration is achieved by using the appropriate methods and tools for process validation.

Installation Qualification (IQ)

- hardware and software installation;
- installation conditions (wiring, utilities, UPS, etc.);
- interface connections;
- calibration, preventative maintenance;
- safety features;
- supplier documentation, prints, drawings and manuals;
- software and hardware documentation;
- spare parts list;
- software backup;
- security aspects;
- environmental conditions (such as temperature, humidity).

Operational Qualification (OQ)

- configuration;
- process control limits monitored by the automated system;
- software operational parameters (link to the functional and design specifications ideally as provided by supplier);
- automated system operational specifications;
- process operating procedures;
- process change control;
- training;
- preventive maintenance and calibration and monitoring;
- data to prove stability and capability of the process where the automated system is used;
- evaluations for potential failure modes and worst-case conditions (risk analysis and critical control points, failure mode and effect analysis, fault tree analysis).

Performance Qualification (PQ)

- use of actual computerized parameters and procedures established in OQ and used during in operation;
- reconfirm acceptability of the computerized processes as established in OQ;
- reconfirm process repeatability and assure process stability when used in the field with trained operators;
- data conversion and migration to the new platform.

Performance Qualification (PQ)

- Challenges to the process should:
  - simulate conditions that will be encountered during routine operation
  - include the ranges of conditions covered by the standard operating procedures
  - be repeated enough times to assure that the results are meaningful and consistent
- Challenges may need to include forcing the process to operate at its allowed upper and lower limits.

Further Resources

- GAMP – Guide for Validation of Automated Systems. *GAMP Forum, ISPE*
- Munk C et al: ISBT – Guidelines for validation and maintaining the validation state of automated systems in blood banking *Vox Sanguinis* (2003) 85 (Suppl. 1), S1–S14

Further Resources

- General Principles of Software Validation; Final Guidance for Industry and FDA Staff. U.S. FDA
- Good Practices for computerised systems in regulated ‘GxP’ environments. PIC/S – Pharmaceutical Inspection Convention & Pharmaceutical Inspection Co-Operation Scheme.