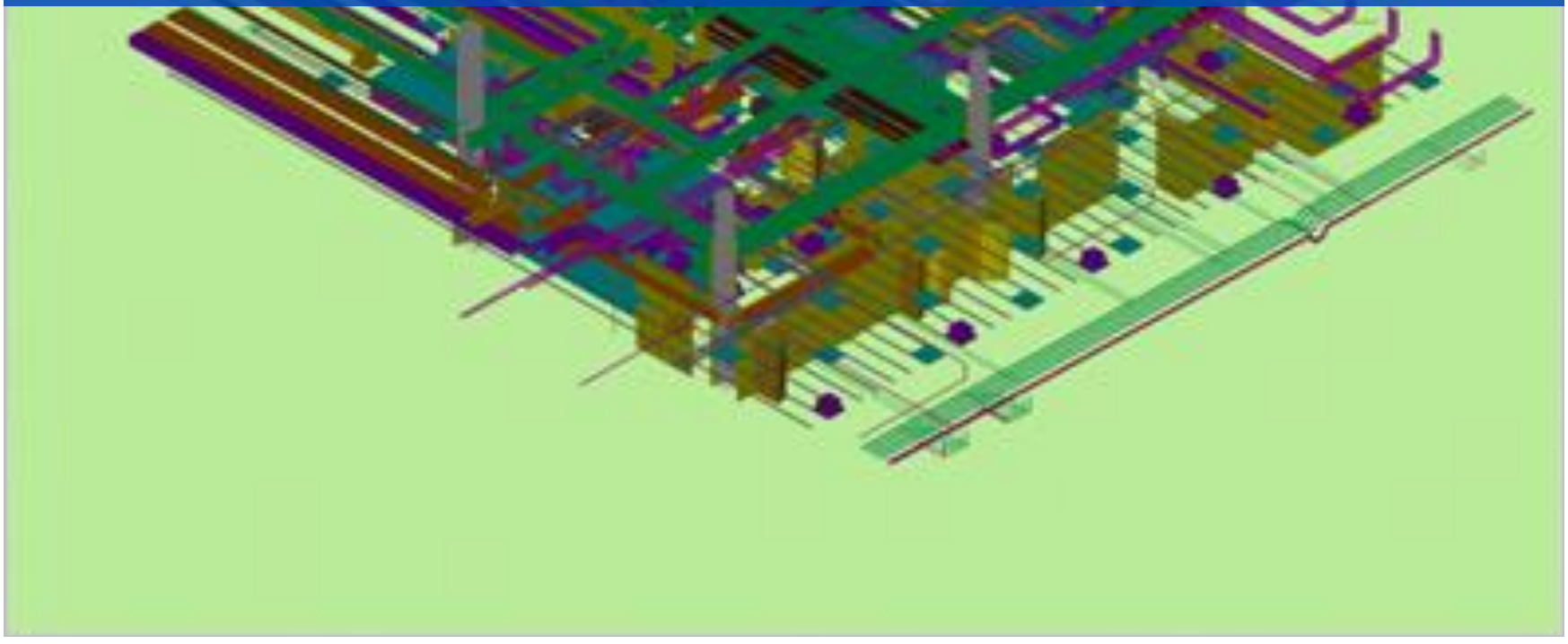
Deerns

...brings concepts to life

The Dry Pharmaceutical Productions



Outline

- Market
- Deerns Objectives
- Opportunities
- Strategy
- Obstacles
- Tactics

Contents

1. Supplies
   a. Supplies
   b. Qualification/Validation Supplies
2. The Pharmaceutical Production Process
   a. Risk Analysis, Ishikawa and FMEA
3. Qualification and Validation
   a. Items to qualifiy?
   b. Parallelism of Engineering and Qualification
   c. The Validation Master Plan
   d. List of Rooms and Equipment Data Sheet
   e. The Qualification Phases DQ, IQ, OQ
   f. Cleaning Validation
   g. GAMP Qualification / Validation
4. References
5. Curricula Vitae

Our Services

5 D Design and Integration of

- Regulatory environment of FDA, EU, WHO, PICscheme incl. complete validation services and support
- Process environment and process flow of API, pharmaceutical and biotech manufacturing
- 3 D design of process, facilities and utilities
- Project management and supervision
- Certification and Facility management consulting

Our Services in the field of validation

- Validation Master Plan
- Master Qualification Plan
- User Requirement Specification and Functional Specification
- Risk Analysis / Qualification Need Analysis
- GMP-Review and FDA Pre-Approval
- Test Plans for DQ, IQ, OQ, PQ
- Protocols for DQ, IQ, OQ, PQ
- Execution of DQ, IQ, OQ, PQ
- Qualification and Test Reports
- Validation

Design Qualification (DQ) | Installation Qualification (IQ) | Operational Qualification (OQ) | Performance Qualification (PQ)

Our Services in the field of validation

In addition to the general qualification / validation we are supplying the auditing of your suppliers, generation of SOPs and policies for example for the strategy of validation of computerized systems.

We are training your personnel either in-house or at our locations.

Audits

System Audits
Product Audits
c-GMP Audits
Auditing

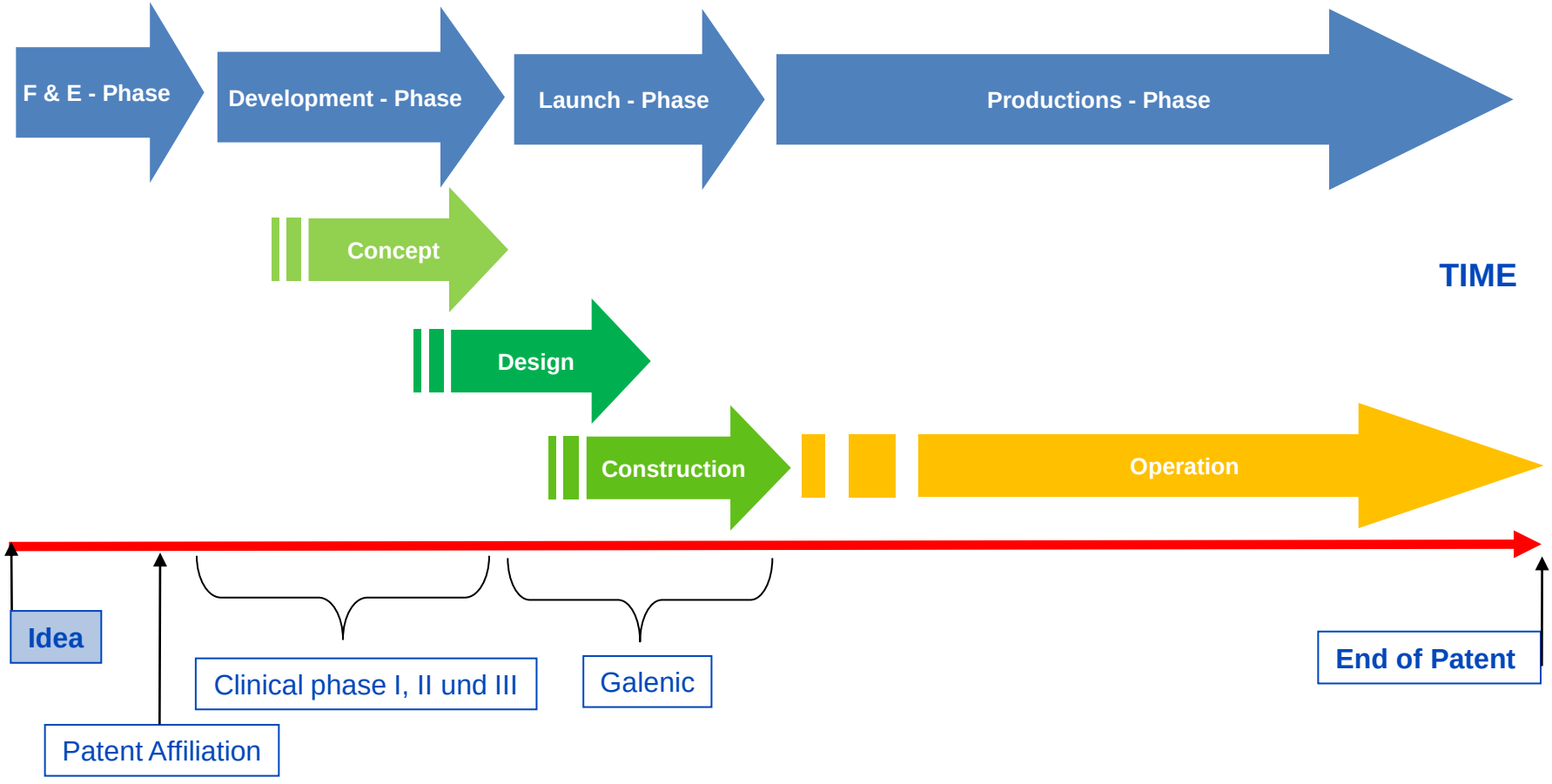
Qualification | Validation prospective und retrospective

We are administrating your projects from the very beginning

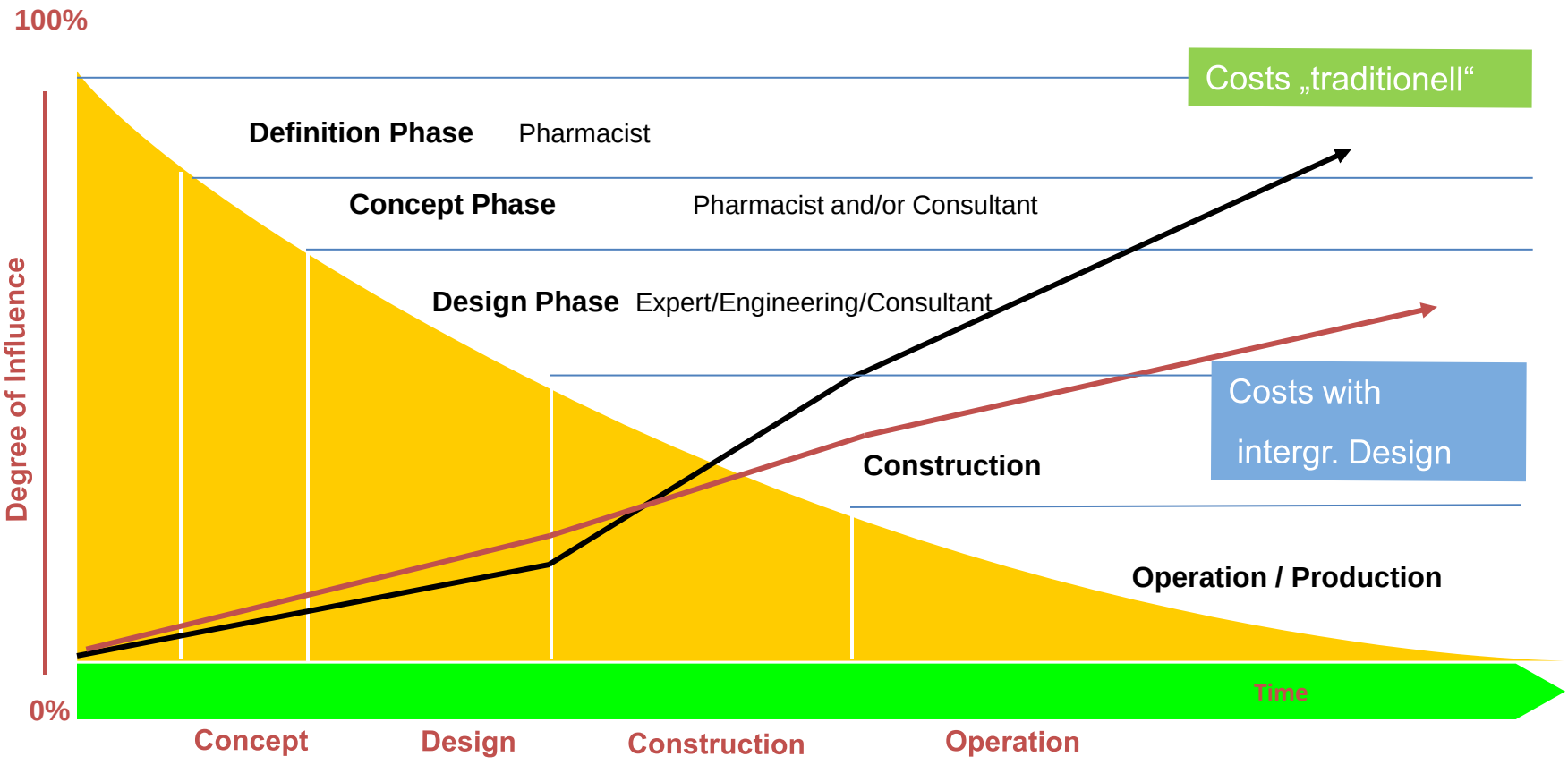
- Qualification of production systems, equipment and machinery
- Validation of Computerized Systems

- Qualification of M&E and pharmaceutical water systems
- Process and Product validation
- Cleaning validation

Life Cycle of a Pharmaceutical Product



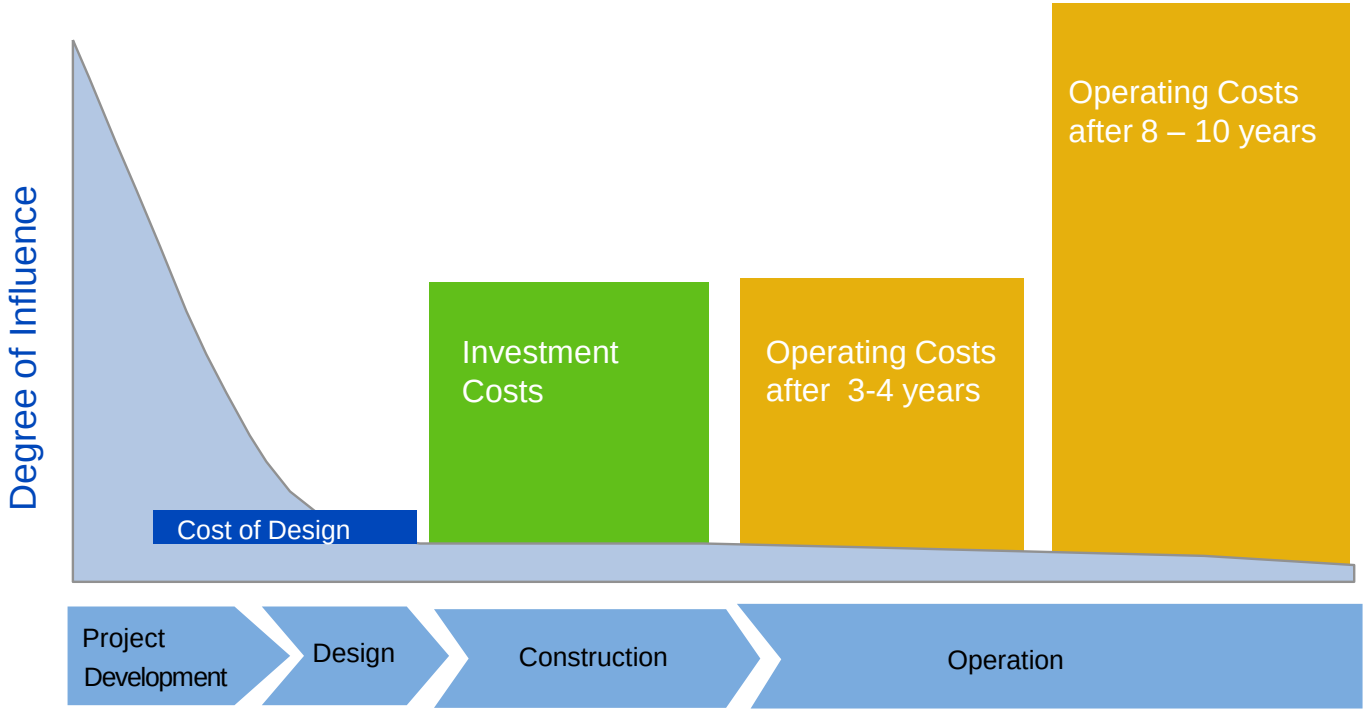
Life Cycle of a Project



With CAQ, integrated design and installed facility management and asset management more than 15 % of costs can be cut off.

Development of Costs

Already after 3 to 4 years the operating costs equal the investments !



Guides and Regulatories

- World Health Organization (WHO) Good Manufacturing Practice (GMP)
- Pharmaceutical International Convention (PIC) GMP
- Food&Drug Administration (FDA) GMP/ Code of Federal Regulation 21 (CFR)
- EU GMP
- GHTF/SG1/SG2/SG3/SG4 (Harmonization Guide)
- United States Pharmacopeia (USP)
- Good Automation Manufacturing Practice (GAMP)
- Deutsches Arzneibuch (DAB)
- VDI 2083 Blatt 1-12
- Technical Comittee (TC) ISO TC 209, WG 1-8
- ISO 14644, 1-3
- ISO 14639, 1-3

Processes

Pharmaceutical Processes

- Bulk Chemicals
- Bulk Biotechnology
- Solid Dosage Forms
- Semi Solid Dosage
- Parenterals, Ophthalmica and Freeze Drying
- Aerosols and Sprays

Risk Analysis Criteria for Production Processes:

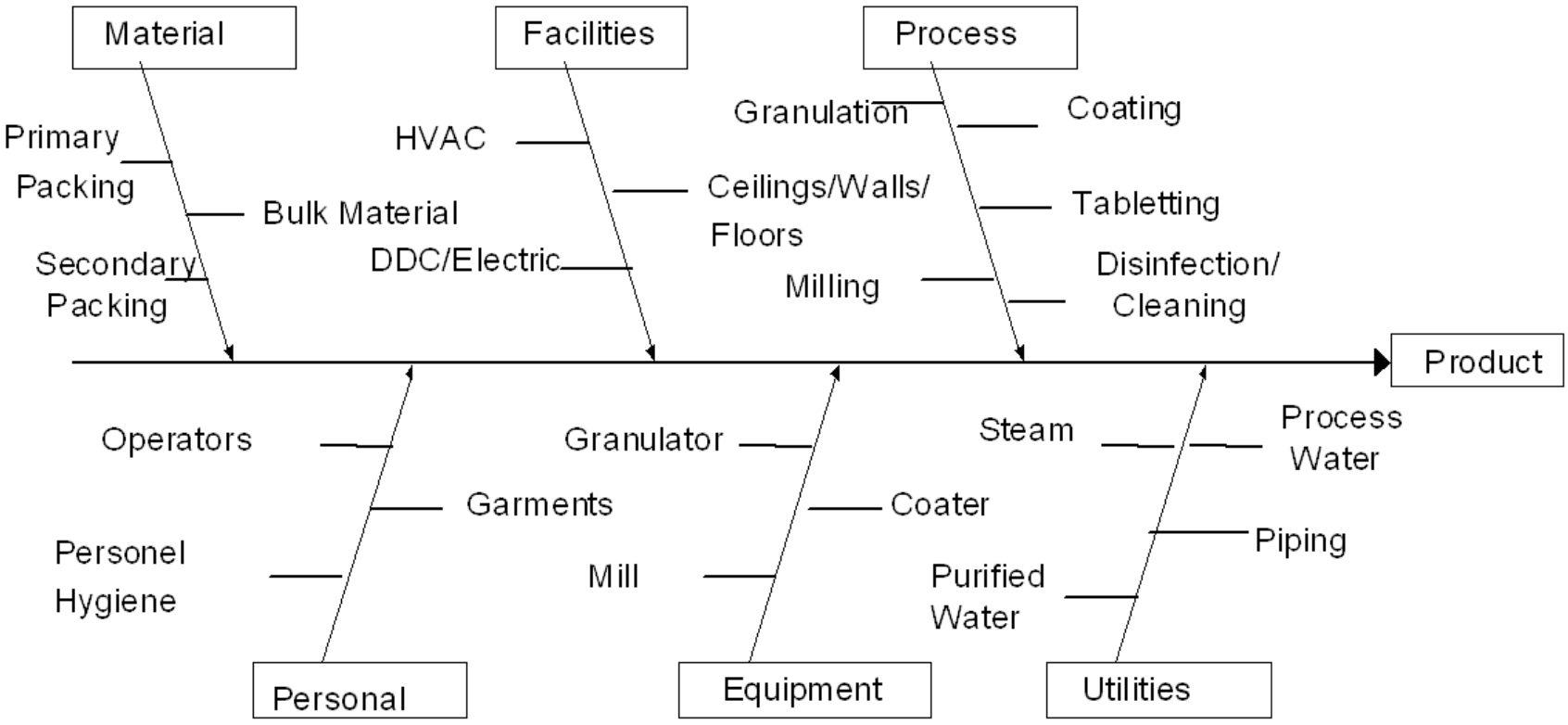
- Normal Products
- High Potent Materials
- Radioactive Materials
- Steroid Products
- DNS/RNS Critical Materials
- Cancerogenic Products

Production Chain for Solid Dosage Forms

For the qualification and validation the whole production chain from delivery to distribution has to be regarded. For a solid dosage form production the chain looks like

- delivery
- incoming inspection / quality control
- warehouse of raw / bulk material
- transport and logistics / material and personal flow
- dispensation
- granulation
- mixing and milling
- tabletting
- coating
- capsulation
- primary packaging / blistering
- secondary packaging
- inprocess control / quality control of finished products
- distribution packaging
- quarantine
- warehouse of finished goods
- distribution

Ishikawa Diagram of a Solid Dosage Form Production



Qualification of Building and M&E Services

(due to Risk Analysis)

- Clean Environment (Ceiling, Floors, Partitions, Isolators, Zone Concepts)
- HVAC: Heating, Ventilating, Air Conditioning
- Purified Water (DI Water, Purified Water, Water for Injection [WFI])
- Pure Steam & Process Steam
- Drinking Water
- Process Water and Neutralization | Desinfection
- Exhaust, Vacuum, Pressurized Air & Process Air
- Sanitary Installations
- Fire Protection (Sprinklers, etc.)
- Electrical Systems and Cabling
- Control and Monitoring
- Lighting, Automation, Transport, CIM
- Gas Supply
- CIP/SIP (Clean in Place, Steam in Place)
- Furniture incl. Sluices, Change Rooms and Lab Equipment

Qualification of Supplementary Equipment and Measuring Devices

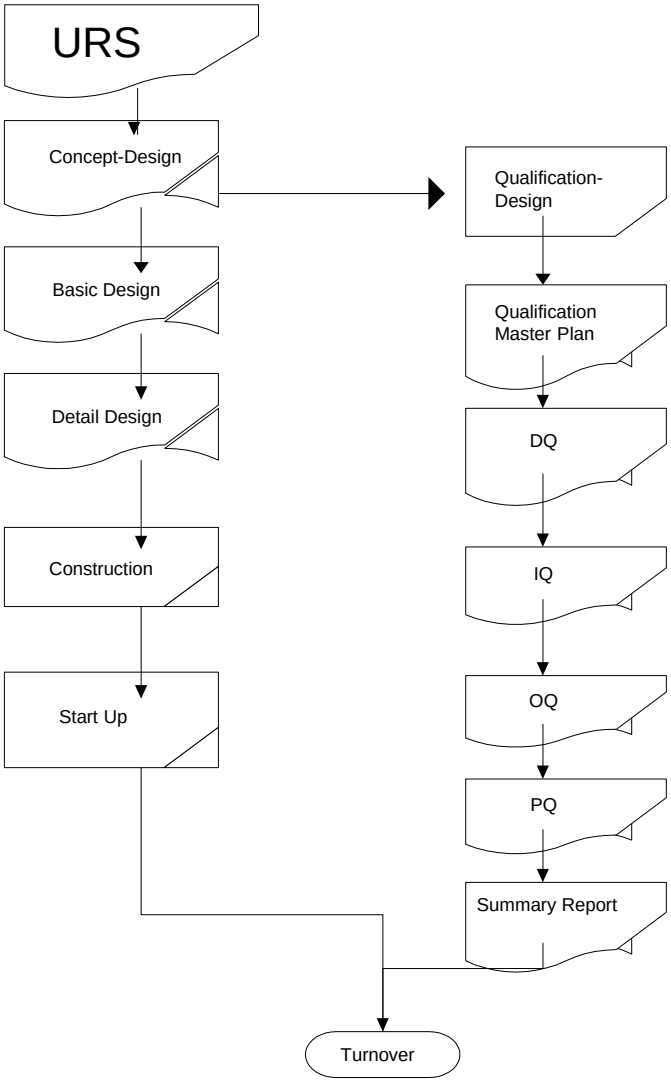
Supplementary Equipment has to be also qualified, for example

- Isolators
- Autoclaves
- Sterilizers
- Sterilization Tunnels
- Cleaning Devices
- Weighing Cabins and Weighing Devices

Measuring Devices to be qualified, for example

- HPLC (High Pressure Liquid Chromatographie)
- Temperature Monitoring and Control
- Particle Counters
- Microbial Monitoring Devices

Engineering Qualification



Parallel Process of Qualification/ Validation and Engineering

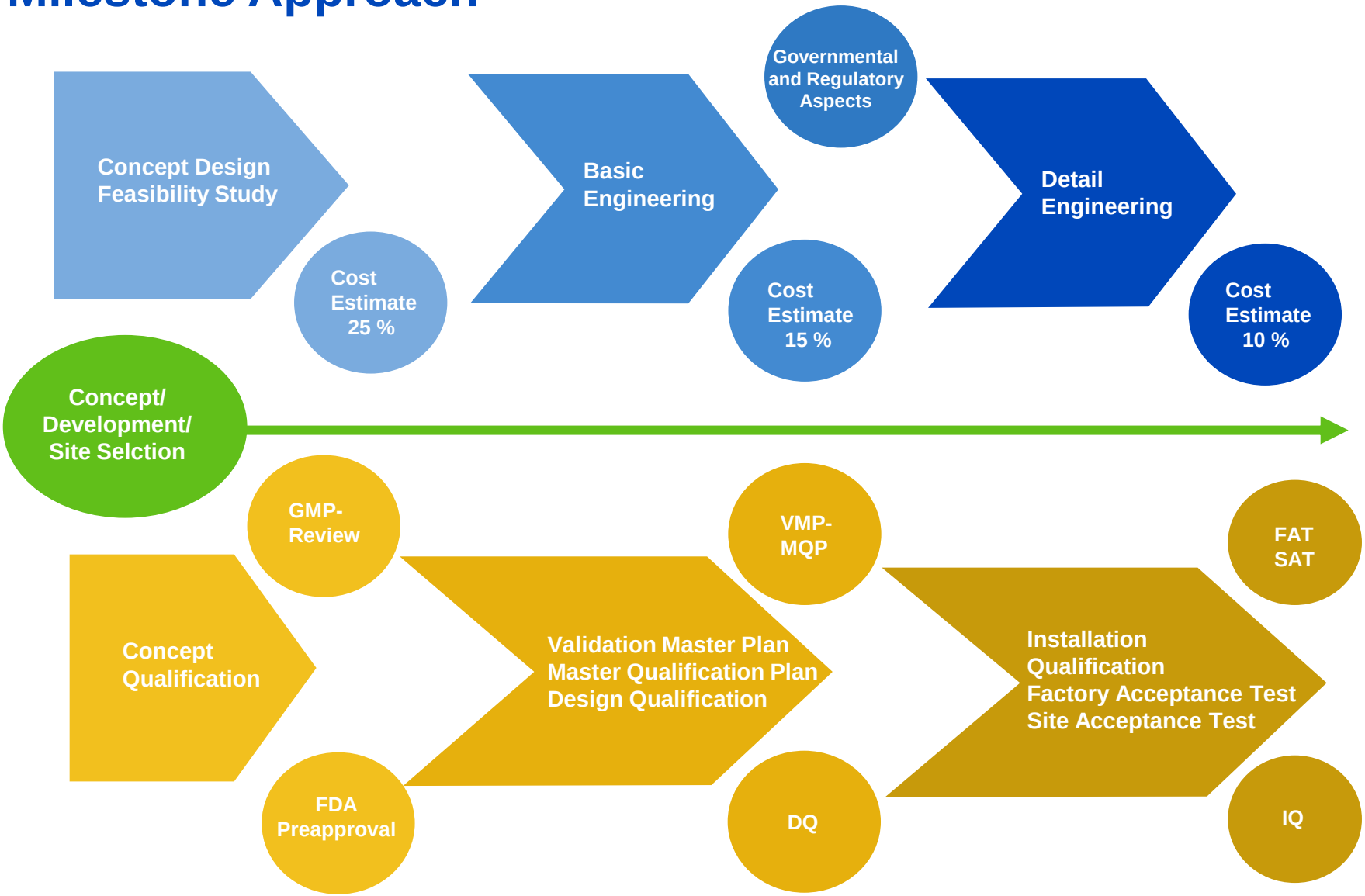
Design Qualification (DQ)

Installation Qualification (IQ)

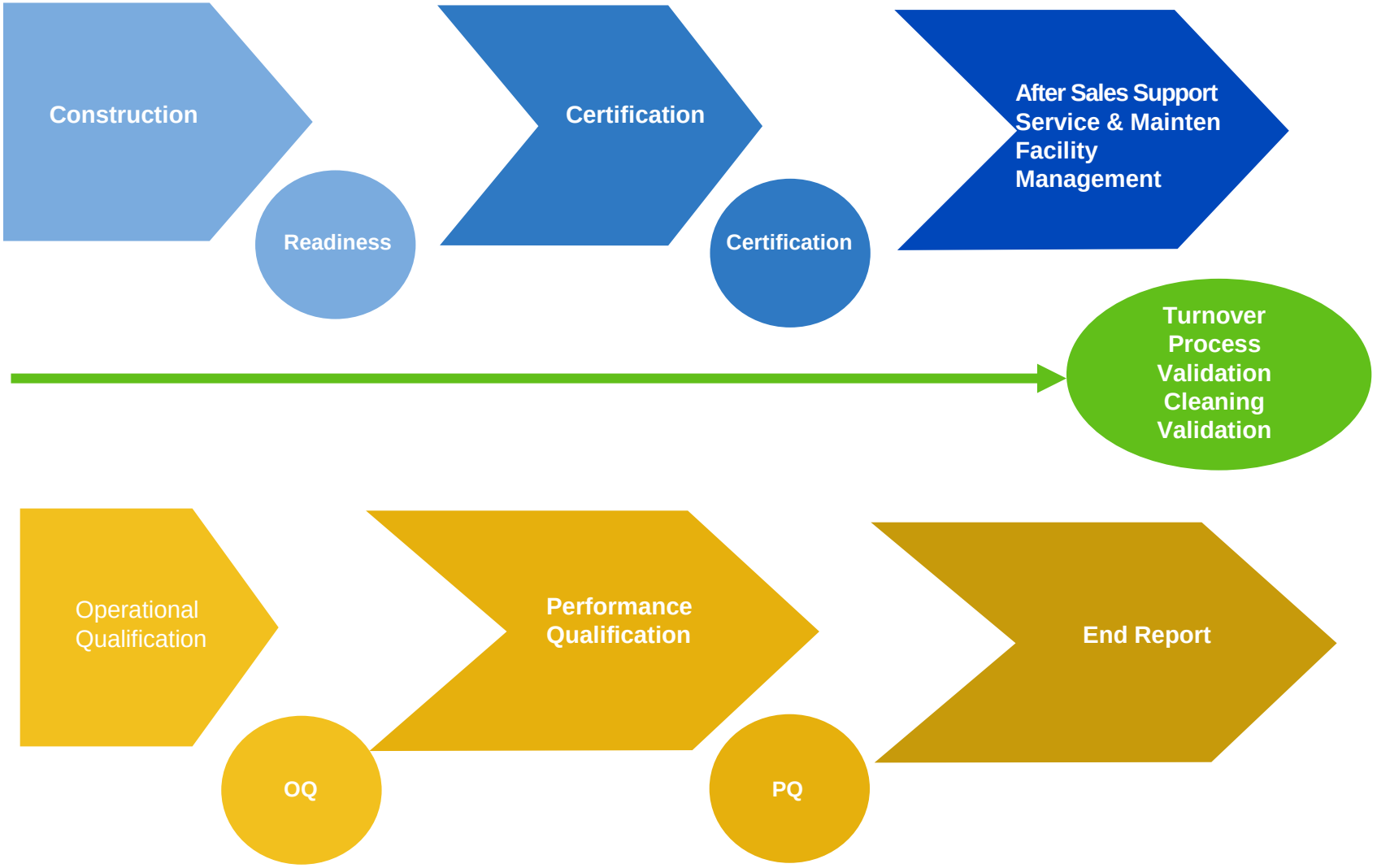
Operational Qualification (OQ)

Performance Qualification (PQ)

Milestone Approach



Milestone Approach



Qualification Validation Process

- Design Qualification (DQ)
- Installation Qualification (IQ)
- Operation Qualification (OQ)
- Performance Qualification (PQ)

Qualification Plan -

Development

Execution

Approval

Computerized

System

Validation

End Report

Process Validation - Cleaning Validation

Services

Qualification and Validation Services

- Validation Master Plans / Master Qualification Plans
  encl. Risk Assesment and Identification of Critical Installations
- Scheduling of Qualification and Validation
- Design Qualification
- GMP Reviews and FDA Preapproval
- Installation Qualification with Factory and Site Acceptance
  Tests of Critical Installations
- Operational Qualification with Challenge Tests and Certification
- Performance Qualification and Final Report
- Qualification of Computerized Systems (GAMP)

General Services

- Policies for Qualification and Validation
- Project-specific Standard Operating Procedures (SOPs)

Following Validation Steps are distinguished

- Qualification and/or Equipment Validation
- Process Validation
- Validation of Computerized Systems
- Cleaning Validation

The qualification is the documented evidence, that the facility, the process or the system is built in accordance with the functional specifications and is functioning properly and constantly due to the designed parameters of the production and the specifications of the process. In general 4 phases are performed (see also Mile Stone Approach):

- Design Qualification (DQ)
- Installation Qualification (IQ)
- Operational Qualification (OQ)

Validation Master Plan

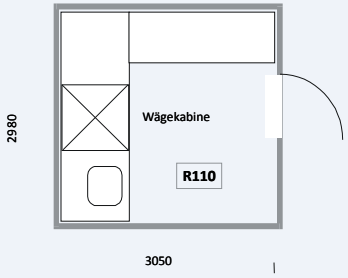
1. Introduction
2. Scope
3. Definitions
4. Regulatory Aspects
5. Organization and Responsibilities
6. Documentation and Distribution
7. Methods of Qualification
   - 7.1 General
   - 7.2 Numbering
   - 7.3 Validation Documents
   - 7.4 Acceptance Criteria
   - 7.5 Test Plans
8. Standard Operating Procedures
   - 8.1 General Procedures
   - 8.2 Specific Procedures
9. Project Description
   - 9.1 General
   - 9.2 Specifications
   - 9.3 Schedule and Overview
10. Equipment Data Sheet
11. Description of Environment
    - 11.1 Room Data Sheets
    - 11.2 Personal and Material Flow
12. 11.3 Building Specifications
    - 11.4 Health, Safety & Fire Protection
    - 11.5 Ex Zones
13. Logistics and Transport
    - 12.1 Infrastructure
    - 12.2 CIM
14. Cleaning and Hygiene
15. Additional Quality Assurance
    - 14.1 Quality Management Handbook
    - 14.2 SOPs
    - 14.3 Service & Maintenance
    - 14.4 Calibration
    - 14.5 Training of Personnel
16. Validation Matrix
17. Validation Schedule
18. Literature
19. Abbreviations and Terms
20. Enclosures
    - 19.1 Room Data Sheets
    - 19.2 Equipment Data Sheets

Equipment Data Sheet

Equipment Data Sheet – Maschinen-Nr. ……

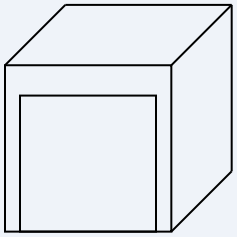
Abteilung XXXXX

Wägeraum 1, lfd. Nr. AB 1.2, Stockwerk 1, Raum-Nr. 110



Beschreibung:
Verwägekapelle

Hersteller:
XXXXXX



Abmaße:

Länge:	2200 mm
Breite:	2200 mm
Höhe:	2400 mm
Fläche:	4,84 m²
Volumen:	11,62 m³

Materialspezifikation:

Verkleidung:	Edelstahl, 316L, gebürstet glatt
Fenster:	Einscheibensicherheitsglas
Rahmen:	Edelstahl, 316, gebürstet glatt
Beleuchtung:	600 lux
Schallleistung:	< 65 dB (A)
Klassifizierung:	verwendbar für L3

Equipment Data Sheet – Maschinen-Nr. ……

Abteilung XXXXX

Wägeraum 1, lfd. Nr. AB 1.2, Stockwerk 1, Raum-Nr. 110

Medienanschlüsse:

Elektro-/Nachrichtentechnik:

Elektroversorgung:	400 V, 15 A	
Elektroversorgung:	220 V, 6 A	
Datenanschluß:	Profibus-DP	
Steuerung:	S7-300	
Vibronet:		

Heizung-Kälte-Lüftung:

Zuluft:	1000 m³/h	Qualität: U14 filtriert
Abluft:	1500 m³/h	Qualität: 2 x U14 filtriert
Umluft:	2000 m³/h	Qualität: 2 x U14 filtriert
Zusatzkälte:	20 KW	Qualität: 6 /14 C
Hausvakuum:	300 Nm³/h	Qualität:

Medien:

Druckluft:	20 Nm³/h, DN 15	Qualität: 6.0
Stickstoff:	2 Nm³/h, DN 6	Qualität: 6.0
AP-Wasser:	0,5 m³/h	Qualität: USP, WFI
API-Wasser:	0,2 m³/h	Qualität: PharmEU
Abwasser:	0,7 m³/h	Qualität: belastet, > 40 C

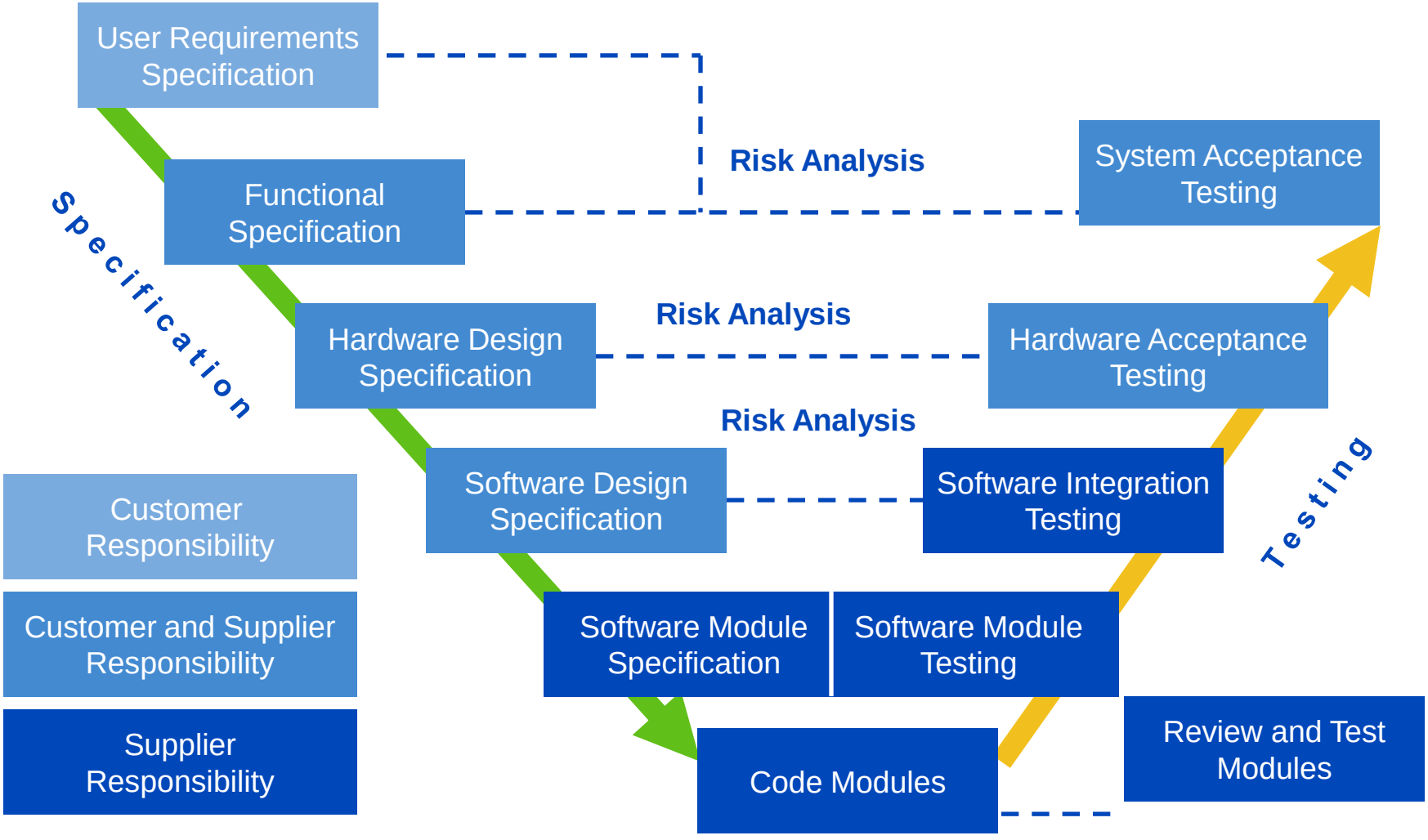
Validation Concept of Computerized Systems

* Functional Specifications can comprise mechanical, electrical and software functional specifications for systems embeddedd in manufacturing equipment.

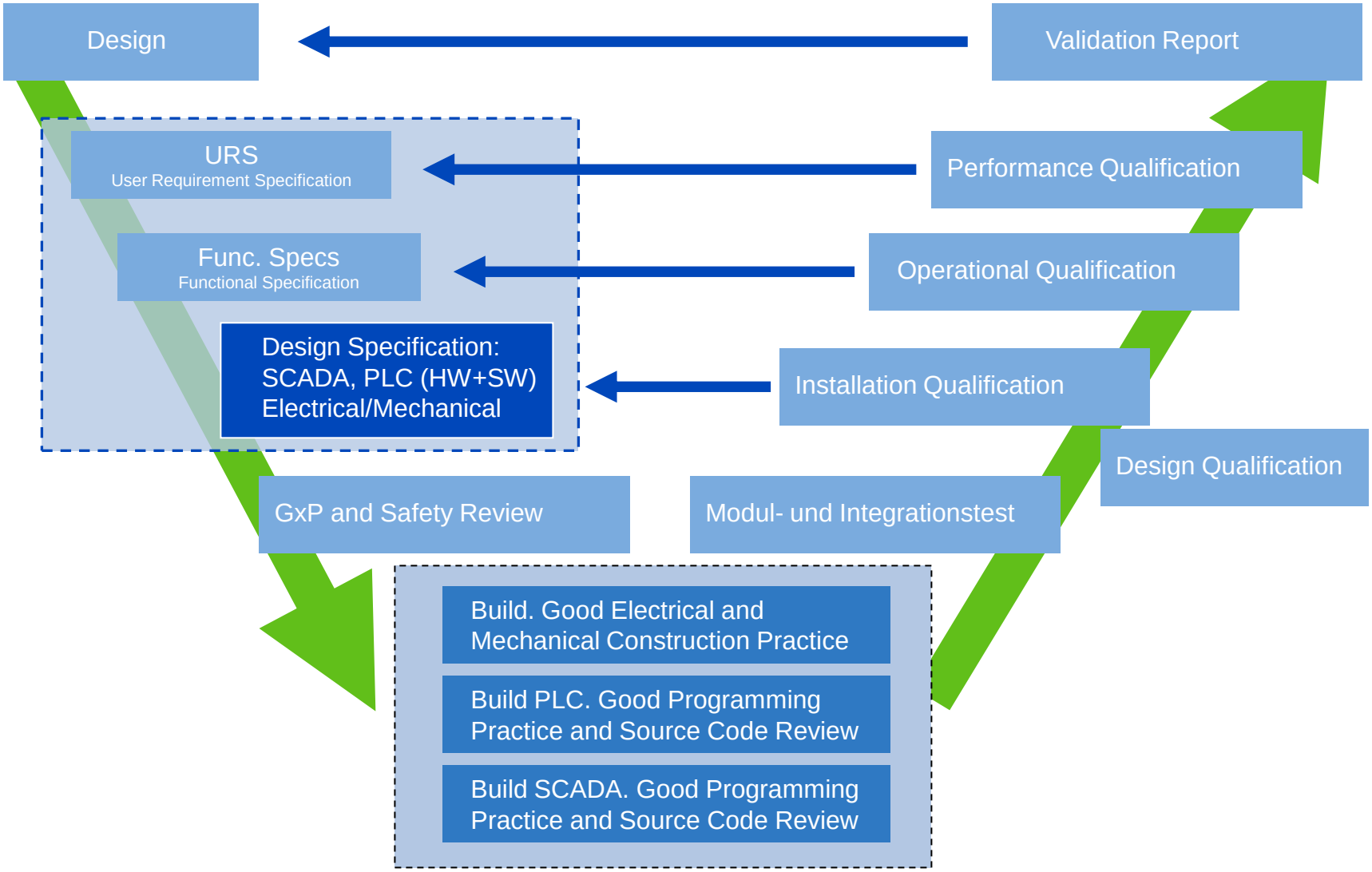
** Systems embedded in manufacturing equipment or linked to control and monitoring instrumentations.

*** Testing carried out by supplier can form part of subsequent IQ&OQ evidence if adequately controlled and witnessed. This can help reduce the amount of testing needed later, particulary in software OQ.

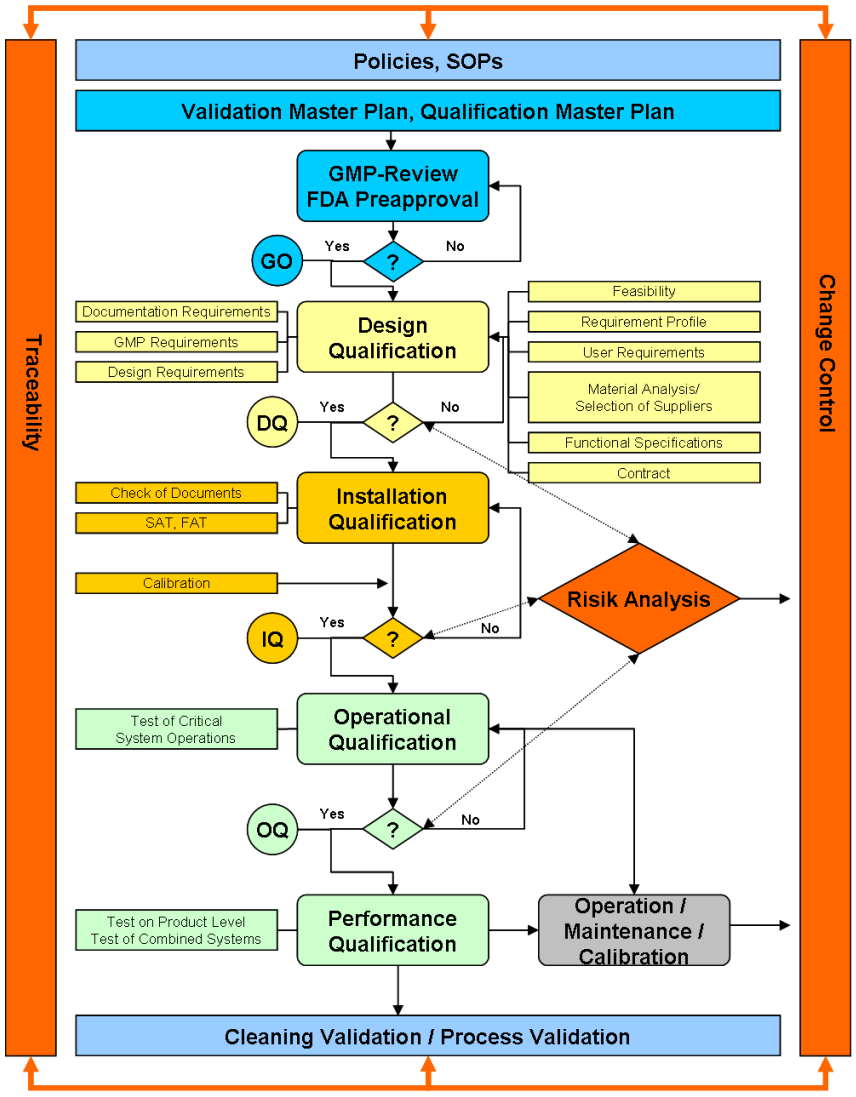
Qualification Services (V-Model GAMP) and Part 11 Conformity



Qualification Approach (extended V-Model GAMP)



Validation Life Cycle



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