Training Course
Computerized System Validation in the Pharmaceutical Industry
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Change Control

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Agenda

Change Control

Definitions

Guidelines

Configuration management

Responsibilities

Planned/unplanned changes

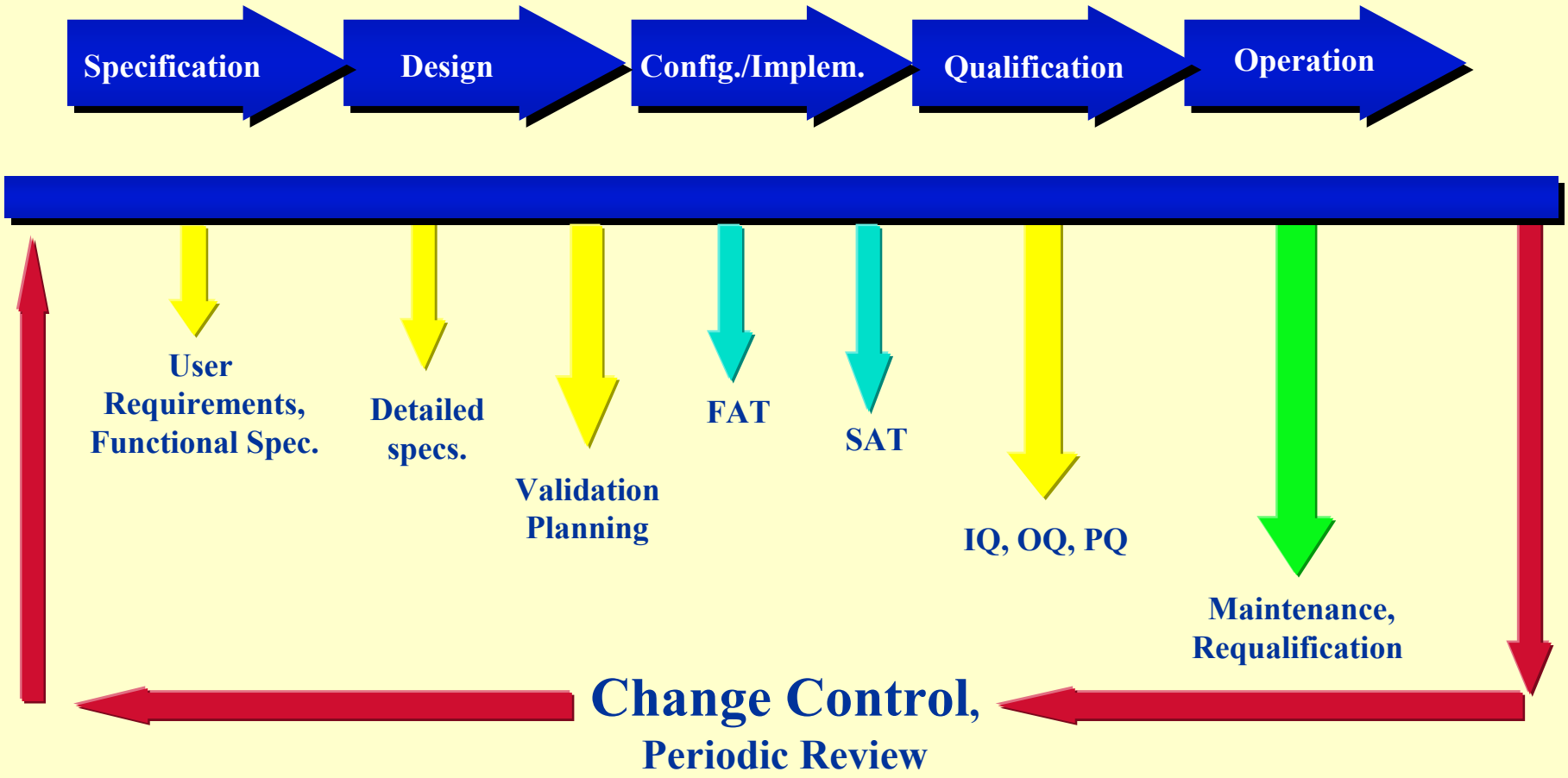
Classification

Sources of changes

Example/Annex:

Template "Change request form ABC Pharma"

System Development Life Cycle
(Generic Approach)



Change Management Attributes

- Responsibility of system owner together with the end-user
- No universal procedure
- More than one procedure may be appropriate
  - Organization
  - Infrastructure
  - Component being changed
  - Position in life cycle
- Change request typically initiated by user

Reasons for Planned System Changes

- Hardware
- Software
  - Release update
  - Bug fixes
- IT Infrastructure
  - Network
  - Server
  - PCs
- Personnel
- Supplier

Change Management Regulations/Guidelines

"…..**change control measures** can apply to equipment, standard operating procedures, manufacturing instructions, environmental conditions, or any other aspects of the process system that has an effect on ist state of control, and therefore on the state of validation."

Proposed Rules, 21 CFR parts 210 and 211, May 3, 1996

Configuration Management Definition ANSI/IEEE

"A formal engineering discipline that provides methods and tools to identify and control software, hardware and related documentation throughout its development and use."

Standards

IEEE 828: Software configuration management plans

IEEE 1042: Software configuration management

Change Management Regulations/Guidelines

- **USA**

  CFR GMP sections 210 and 211

  PDA Technical Report No. 18

- **Europe**

  EU GMP Guide, Annex 11

  GAMP Guide

Requirements of the FDA

Most recent statement of the FDA (CDRH) in:

General Principles of Software Validation

- Published in the Federal Register on 11 January 2002 (Docket No. 97D-0282)
- "Provides guidance to medical device manufacturers and FDA staff"
- Only applicable for Medical Devices, but considerable influence on other sections

CDRH: Center for Devices and Radiological Health

General Requirement

- All configuration items shall be clearly defined every time
- All configuration items are subject to change control after their release for use
- All changes have to be documented in a formal way

PIC/S Guidance PI 011-1 "Good Practices for Computerized Systems in Regulated GxP Environments", Draft January 2002

- Changes are mentioned in chapters
  - 17. Change Management
  - 18. Change Control and Error Report System
  - 20. Data Changes - Audit Trail/Critical Data Entry

GAMP 4

Changes are mentioned in

- Configuration Management
  - Guideline “Project Change Control”, Annex M8
- Change Control during system operation
  - Guideline “Operational Change Control”, Annex O4
- Periodic Review
  - Guideline “Periodic Review”, Annex O1

GAMP: Good Automated Manufacturing Practice

The Change Control Phases

- Change request (User)
- Evaluation, decision (System Owner)
- Evaluation of realization (IT/Service Provider)
- Definition of validation activities, priorization, risk assessment (System Owner, IT, QA)
- Implementation (IT/Service Provider)
- Change review (QA)
- Release of computerized system (System Owner)

Changes - Roles & Responsibilities

System Owner

- Approval and release for realization
- Release of system after completion

QA

- Review/Approval of CC request
- Risk evaluation
- Review of entire documentation
- Review/Release of systems after completion

Business

- CC request
- Preparation of risk assessment
- Testing
- Generation of documentation

Classification of Changes

Example:

- Major Change
  - A change to a validated computerized system that, in the opinion of change-control reviewers, necessitates substantial efforts to implement the change and return the system to a validated status.
- Minor Change
  - A change to a validated computerized system that, in the opinion of change-control reviewers, requires a relatively small effort to implement the change and return the process to a validated status.

Change Management
Sources of Change

- **Software**
  - **Software failures: bugs/defects**
  - **Enhancements**
  - **New version(s) of operating system**
  - **New version(s) of layered software**
  - **New version(s) of application(s)**
  - **Program temporary fixes: patches**

Change Management
Sources of Change

- **Hardware**
  - **Computer**
    - **Failures: disk, memory, power supply, etc.**
    - **Controlled processes: sensors, etc.**
    - **Firmware**
  - **Updated Hardware**
    - **New components, boards**
  - **Additional Hardware**
    - **New peripherals**
    - **Expanded use**

Change Management
Sources of Change

- **Network**
  - **Hardware, software, security**
  - **Other uses**
- **People**
  - **New people, new procedures, errors**
- **Vendors**
  - **New software, hardware, etc.**

Unplanned System Changes

Characteristics

- Short or no advance warning period
- Require
  - immediate evaluation
  - immediate solution for the problem
  - temporary quarantaine of the system
- Problem: Documentation must be generated retrospectively

Change Management
Repetitive Change

- Time-driven but periodic
- Part of preventative maintenance
  - Replacement of parts
  - Re-calibration
- Require verification

Traceability of Changes

Ensure traceability by

- assigning clear attributes, e.g.
  - system name, version No.
  - requester
  - reason for change (benefit of change)
  - running number of change request
  - optional: cost
  - status of realization
  - approval of change and release of system with signatures
- documentation on CC form
- if CC form is an electronic document, then 21CFR Part 11 is fully applicable

Traceability

Traceability of requirements must be ensured by e.g.

- Traceability Matrix
- Database
- Tools (e.g. Telelogic “DOORS”)
- Implementation and documentation in the software (code) itself

On-going evaluation

Once a process is validated, it must be maintained in the validated state by a number of procedures that assure that the process remains in the state-of-control.

There should be written procedures for:

- Security of data generated (including back-up)
- Access control (including password change)
- Emergency recovery
- **Change Control**
- Personnel Training

Change Management

- Change Control/Change Management implies the control of change and not the computer-related system
- Configuration Management
  - Automatic capture and storage of component relationship for computer-related system
  - Build history of component relationship

Change Management Attributes

- **Change management**
  - **Characteristics**
    - **Implementation**
    - **Recording of change**
    - **Periodic evaluation Sign-off**

Change Management Documentation

- **Document**
  - **How? Who? Review? Approvals?**
  - **Possible documents affected:**
    - **SOPs**
    - **Problem report/incident log**
    - **Change request including course of action**
    - **Qualification activities**
    - **Change report**

Changes in Complex Systems (Example: SAP)

Change	Frequency	Effort
Release change	rare	very high
Bug fixes, support packs	frequent	medium - high
New functionalities	frequent	low - medium
New authorizations	frequent	very low
New core data	very frequent	very low
New hardware	rare	low - medium

All changes have to be tested on the integration system which is operated in parallel (synonym: validation- or QA-system).

Changes during System Development

Prior to operation

- often in the IQ/OQ Phase

What has to be done?

➔ new system specification necessary

➔ update of documentation

Freezing of System Design

When does the Change Control Process start during system development?

Design Freeze

Agreement among all involved parties that no further changes to a design document, system, or system software will be made without the use of change control procedures. The purpose of a design freeze is to prevent coding, testing, or qualification of an evolving system or its software and to ensure that the qualification program is directly tied to the as-build-system.

System Log Books

- Capture execution of day to day activities concerning operation of the system
- Act as a historical reference of changes considered "minor" and not requiring comprehensive change control documentation
- Can capture small "glitches" not documented elsewhere

Baseline
Definition of the FDA (1995)

"A specification or product that has been formally reviewed and agreed upon, that serves as the basis for further development, and that can be changed only through formal change control procedures."

The Baseline Concept

- The Baseline is freezing the current status of the system
- All Configuration elements are working together
- Baselines should be generated
  - with new releases
  - at important milestones/Changes
- The Change Management starts with the (new) Baseline

Change Management
Cost of Change

Should be part of the Change Control SOP and request formate and include evaluation of

- Indirect costs
- Savings of the change
- Return on investment
- Alternatives existing (instead of change)