Manufacturing Optimisation Inside the Pharmaceutical Supply Chain.

Business System Compliance

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Cork, April 3/4 2003
Agenda

- Business System Compliance Overview
- Data migration - verification or validation?
- Validation life cycle
- Specification
- GMP criticality - cost and benefit
- Audit trails and Part 11
- Qualification instances (environments)
- IQ/OQ for Datastream
- Data migration
- PQ
- Cutover
Main Types of Business Systems

- Supply Chain (MRP/ERP/MES)
- LIMS
- Document Management Systems (eDMS)
- Maintenance(/Calibration) Management Systems (MMS)
Compliance Issues with all Business Systems
Compliance Issues with all Business Systems

- Complex and enterprise wide
  - Many business processes
  - Many SOPs
  - Many users to be trained
  - Many interfaces to other systems – manual or electronic

- GxP Criticality
  - Mix of GxP and non-GxP critical functionality

- System
  - Usually highly configurable but local modification needed
  - Merge supplier’s systems with client’s systems

- Data
  - Migration from legacy systems
  - Range of data – master, static and dynamic

- Cut-over (go live)
  - Must be quick (and compliant)
  - Nearly impossible to go back
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Data Migration – Verification or Validation?

• In this context – Verification = Data Sampling
• There is no question that much of the data is critical e.g. master data, lot statuses.
• Hence the question should be: Can we validate by verification only?
• The answer depends on the complexity of the migration code
• However in principle:
  – A straight copy allows verification
  – Significant data omission or change requires validation
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Validation Life Cycle
Front end

Vendor Audit

User Requirement Specification

Functional Specification

Scenarios
Process & Data analysis w/s

Workflow extensions
Complex scripts
Reports
Interfaces

Risk (GMP) and Part 11 Assessment

Core
Customisations

Configuration Specification

Design Specification

Build
Source Code Review

Test

Core s/w IQ

Datastream s/w
& base config,
Oracle s/w

Basic Config.
Specification

Hardware & Op system
Change control

ABB
Validation Life Cycle
Front end

1. Transfer to validation environment
2. SAT=FAT (GMP=IQ/OQ, non-GMP)
3. Config IQ
4. Limited training, controlled manuals and system support SOPS's
5. Migration IQ/OQ
6. Migration spec, write & test
7. Config OQ
8. Migration for UAT
9. Migration for UAT

Cutover Migration

SAP change control

Formal training & approved manuals and system support SOP's

Cutover Qualification

Validation Report

Numbers relate to data copies
Specifications

Reviewed all specifications:

- Consistency
- Quality
- Completeness
- Traceability
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GxP Assessment General

- A detailed GxP assessment avoids qualification for non-GxP functions. Standard testing can be employed for these.
- It facilitates identification of electronic records for Part 11
- Input = functional and configuration spec(s)
- Output = split into GxP critical and non-GxP critical:
  - Configuration (reduces work in IQ)
  - Functions (reduces work in OQ and PQ)
  - Data (reduces work in migration qualification and cutover)
- Example -

<table>
<thead>
<tr>
<th>FS</th>
<th>Criticality</th>
<th>Reason</th>
<th>Design Response + Reference</th>
<th>Qualification Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.1.1</td>
<td>GxP</td>
<td>e.g. Related to lot status</td>
<td>e.g. DS 1.1 (drawing 1.5)</td>
<td>e.g. OQ 9.1</td>
</tr>
<tr>
<td>1.1.2</td>
<td>Non-GxP</td>
<td>e.g. Solely financial</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>1.1.3</td>
<td>Out of scope</td>
<td>Manual process covered by SOP xx-xx-xx</td>
<td>N/A</td>
<td>PQ 9.2</td>
</tr>
</tbody>
</table>
GxP Assessment General

Function or Component

Does the function or component affect product quality?

Yes

Does the aspect affecting product quality have a backup?

Yes

Is the backup mechanism failsafe and / or alarmed?

Yes

The function or component is NOT GxP CRITICAL

No

No

The function or component is NOT GxP CRITICAL

The function or component is GxP CRITICAL

No

The backup mechanism is NOT GxP CRITICAL

Yes

The backup mechanism is GxP CRITICAL
Datastream GxP Assessment

- Purchasing – Mostly non-GMP
- Inventory – Some GMP
- Maintenance – Mostly GMP
- Calibration – Almost all GMP
- Interface to financial system – Mostly non-GMP
- Led to Audit Trail specification ensuring Part 11 compliance
- Time to produce ~15 man days
- Time saved in qualification ~100 man days
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Production (or Master) database is IQ’ed and then kept clean ready for production (i.e. no historical data from qualification)
<table>
<thead>
<tr>
<th>Transfer</th>
<th>When</th>
<th>Why</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Prototype to master clean database (could be production)</td>
<td>Ready for qualification</td>
<td>Clean copy for qualification and production</td>
</tr>
<tr>
<td>2 Master to qualification database</td>
<td>After IQ</td>
<td>For OQ</td>
</tr>
<tr>
<td>3 Master to migration qualification database</td>
<td>After IQ</td>
<td>For migration OQ</td>
</tr>
<tr>
<td>4 Master to training database</td>
<td>After IQ</td>
<td>For training</td>
</tr>
<tr>
<td>5 Existing production to copy production</td>
<td>Anytime before migration OQ</td>
<td>For migration OQ</td>
</tr>
<tr>
<td>6 Existing production copy to migration qualification</td>
<td>After master to migration transfer</td>
<td>For migration OQ</td>
</tr>
<tr>
<td>7 Master to PQ</td>
<td>After OQ</td>
<td>For PQ1</td>
</tr>
<tr>
<td>8 Existing production copy to PQ</td>
<td>After Master to PQ</td>
<td>For PQ1</td>
</tr>
<tr>
<td>9 Existing production to New production</td>
<td>After PQ1</td>
<td>This is Cutover</td>
</tr>
</tbody>
</table>
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IQ/OQ for Datastream

• **IQ**
  - Hardware
  - Operating system
  - Supporting software version numbers
  - Main software version numbers in correct environment
  - GxP critical configuration flags

• **OQ**
  - GxP critical sub-function tests
  - Interface tests (NB- Interfaces transferring data from non-GxP systems should be qualified to ensure GxP data is not overwritten).
  - Need to set up test data – master data and static data
Data Migration

- Formal mapping document(s) are required from the existing to the new system
- Only qualify GxP data (as defined by the GxP assessment)
- OK to apply different approaches for different data
  - Manual input - 100% verification at cutover
  - Unmodified migrated data - Sample at cutover
    - $\sqrt{n} + 1$ records
    - Check all fields on first and last records
    - Check first three fields on rest of records
  - Modified data - migration qualification
- Any intermediate files containing GxP data are electronic records and need to be secure
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PQ

• Based heavily on SOPs or formal training manuals
  – Simplifies protocol
  – Qualifies SOPs and/or training manuals

• SOPs/Training manuals must be frozen or approved

• Can also split to have PQ2 after cutover confirming the system works out in the field
Cutover

• A lot happens at cutover so we use Cutover Qualification to ensure GxP critical parts

• Main elements:
  – Production environment
  – Migration of data
    • Greatly simplified if migration has been qualified
  – Security settings, training and procedures
Cork, April 3 2003

Summary

URS and VP may be reversed

Validation Plan (VP)

Business Processes & User Requirements Specification (URS)

Supplier Audit/Part 11 assessment

Functional Design Specification (FDS)

SOPs

Training records

Performance Qualification (PQ2)

Change control

Validation Report (VR)

Migration Specification, Build and Qualification

Cutover Qualification (CQ)

Performance Qualification (PQ1)

Operational Qualification (OQ)

Update Part 11 assessment

Installation Qualification (IQ)

Software Integration Testing

GxP/Risk Assessment

GxP assessment defines critical functions, data and configuration and later can include traceability to qualification protocols

Hardware & Software Design and Configuration Specification

Good Programming Practice & Software Source Code Review

Traceability within the specifications and the GxP Assessment

Only qualify critical configuration, functionality and data
• Business Process Definition
• Compliance and Validation
• Part 11
• Project Management
• Business Readiness
• Implementation
• Support