

DATA MANAGEMENT TOOLS FOR INDIVIDUALIZED THERAPIES

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TYPES OF TOOLS

A good tool improves the way you work. A great tool improves the way you think. - Jeff Duntemann

A Brief History of Database Applications

Twentieth Century

- Thick-client architecture
- Limited number of users
- Proprietary code
- Home-grown data structures
- Minimal workflows
- Difficult to configure
- Mammoth validation



Twenty-first Century

- Web-based
- Open subscription models
- Based on open source
- Industry standard data structures
- Workflows for all data
- Lots of configuration options
- Risk-based validation



Architecture for a Maintenance Management system



- Equipment / Assets •
- Environments / Locations •
- Materials / Spare parts ٠
- Procedures / Job Plans / SOPs ٠
- Personnel / Teams •
- Work Orders •
- Routing / Approval logic •
- Planning Data ٠



Architecture for a Quality Management system



- Equipment / Assets •
- Environments / Locations •
- Materials / Consumables •
- Procedures / Work instructions •
- Personnel / Teams •
- **Deviations / Investigations** ٠
- Routing / Approval logic •
- Planning Data ٠



Architecture for a Manufacturing Execution system



Connecting

- Equipment / Assets •
- **Environments / Locations** •
- Materials / Consumables •
- Procedures / Production Recipes •
- Personnel / Teams •
- Process Orders •
- Routing / Approval logic •
- Planning Data ٠

Knowledge

Pharmaceutical

Architecture for a Laboratory Information Mgmt system



- Equipment / Assets •
- Environments / Locations •
- Materials / Consumables •
- Procedures / Methods •
- Personnel / Teams •
- Test Orders / Activity Orders •
- Routing / Approval logic ٠
- Planning Data ٠



What does a Data Management tool require?



- Equipment / Assets
- Environments / Locations
- Materials / Consumables
- Procedures / Methods / Instructions
- Personnel / Teams
- Activity Orders
- Routing / Approval logic
- Planning Data



LIMS EBR CASE STUDY

"The table of elements does not contain one of the most powerful elements that make up our world, and that is the element of surprise." — Lemony Snicket

LIMS EBR Case Study

- Project Details
- Implementation •
- Data Migration •
- Validation and Reporting ٠
- Go Live •





LIMS EBR PROJECT DETAILS

Do not let what you cannot do interfere with what you can do

Laboratory Information Management System + ELN



CAPABILITIES

- Maintains lab equipment ٠
- Monitors room environments
- Maintains lab materials and components
- Maintains testing instructions •
- Maintains personnel authorities
- Maintains process workflows •
- Maintains E-signatures •
- Generates EBRs •



Our Project



- Multi-national Biotech Startup ٠
- Personalized cell therapy • (clinical III)
 - Three sites in North America
 - Multiple sites in China ٠
- Hospitals and Processes in ٠ China
- Scientists and Analysts in N. ٠ America





Cloud Advantages



- Manufacturing processes are standardized across all sites (multiple CMOs)
- Using IoT devices, real-time environmental monitoring
- No infrastructure to purchase or maintain, nothing to install
- Ease of data analysis
- Minimization of licensing costs for software
- A single Helpdesk for computer issues
- Instantaneous rollout of software
 improvements across sites



Other Cloud Advantages



- Distributed database
 implementation
- Continuously monitored identity and access management
- Unlimited data storage
- Elastic load balancing



What the CSP (Cloud Service Provider) Manages:



- Runtime •
- Middleware ٠
- Operating systems •
- Virtualization •
- Servers •
- Storage •
- Networking ٠



What the Pharma Company Manages



- Application maintenance •
- Associated data + Database ٠
- 21CFR Part 11 / Annex11 . aspects
 - Audit trails
 - Data Integrity •
 - Application security •
 - E-records and E-• signatures
 - Application validation ٠



Mitigation of Data Integrity Issues



Connecting

Pharmaceutical

- Environmental configuration
 - Multiple Environments
- Encryption configuration
- Auto-creating snapshots
- Cron job to sync snapshots to S3
- Testing under Controlled Circumstances

Cloud Disadvantages



- 1. Clinical data for Chinese citizens may not reside on servers outside of China
- 2. China does not allow VPNs
- 3. The Chinese government has full authority to monitor all network traffic
- 4. The Chinese government blocks SSL data



IMPLEMENTATION

Back up my hard drive? How do I put it in reverse?

Implementation: Lead Team



- Small team of representatives
- Standardized
 - Data formats (naming strategies, hierarchies)
 - Data movements (who can see what)
 - Work flows
 - Security profiles
- Good Project Management
- Thousands of decisions



Implementation: Pilot Site



Connecting

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Knowledge

- Create one instance
- Data Migration Issues:
 - Non-hierarchical data
 - New naming strategies
 - One-offs
 - Missing data
- Data discrepancies:
 - Similar equipment with dissimilar data



DATA MIGRATION

Data is a precious thing and will last longer than the systems themselves

Data Migration



- Crucial aspect of IT projects
- Migration tools must be validated
 - Free comparison tools
 - 100% verification
- Must have data dependency models
 - Parent data must be loaded before child data
 - Support data must be loaded before mainstream data
 - Missing data must be generated



Data Migration Methodology



- 1. Freeze the old system
- 2. Extract existing data
- 3. Re-format, re-create, create new data
- 4. Get QA to approve the data
- 5. Import the new data
- 6. Manage the existing historical data in the old system



Data Migration Magnitudes



- Simple System? 50,000 records to create or migrate
- SQL extracts, Spreadsheets, filters, formulae
- Importation dry-runs
- QA approval of final data, via spreadsheet
- Data Comparison
 - Extracted data after load and compared
 - Validated comparison tools



VALIDATION

Nothing is fool-proof to a sufficiently talented fool

Risk-based CSV



- Low risk elements are not directly • tested
- Standard components of the database • or application interface are considered low risk
- Configured elements are considered ٠ high risk
 - Tested in FAT •
 - Tested to Configuration Specs •
 - Tested under simulated conditions



Test Rigor: Low to High



- Test certificate provided by vendor
- Test document completed by vendor
- Test via visual inspection
- Test via code comparison
- Test under software simulated conditions
- Test under hardware simulated conditions
- Test under actual conditions, dry
- Test under actual conditions, using water
- Test under actual conditions, using analog materials
- Test under actual conditions, using actual materials



Our Project



- ASTM E2500 Approach for GAMP class 4
 - COTS elements tested indirectly (low risk)
 - Configured elements tested directly (high risk)
 - Testing in FAT and SAT leveraged in OQ
- Procedure approach for PQ
 - Extensive operational SOP
 - PQ testing walks thru the SOP
- Leverage validation across sites
 - Functional testing not repeated



Traceability is Non-linear



DO

- Trace user requirements to risk elements
- Trace user requirements to functional requirements
- Trace functional requirements to IQ/OQ/PQ tests
- Put FRS references in each test case
- Make the DQ report into the Traceability Matrix

DON'T

1

- Trace functional requirements to detail design elements
- Trace the detail design elements to the configuration (1)
- Trace commissioning, FAT, or SAT testing (2)

Thoughts on how to validate differently



- 1. Equipment links to Specifications (1:□)
- 2. Specifications can be listed in a work order
- 3. Work orders can specify acceptance criteria for completion
- 4. Work orders are e-signed
- 5. Photos or scanned documents can be attached to the work order
- 6. Work orders can be routed around for additional approvals
- 7. Multiple related work orders can be aggregated
- Can a validation be performed as a series of work orders?



REPORTING

On the other hand, you have different fingers



Book ends

- Validation Project Plan ٠
- Validation Project ٠ Summary Report





Testing Reports

- Background / Overview
- Results Summary
- Deviations / Nonconformances
- Modifications
- Conclusions



GO LIVE

You don't drown by falling in water. You drown by staying there.

Go Live is not the End of the Project!



- Checklist one week before Go Live
- Checklist one day before Go Live
- Checklist day of Go live
- Activities after Go Live
 - Shadow users
 - Immediate helpdesk response
 - Follow up training
 - Issues resolution / Punchlist management



Go Live for Other Sites



- Checklists
 - Data checking
 - Punch lists
 - Training
 - Shadowing
- CSP Benchmark Testing
 - Latency checking
 - Security overrides
 - Usage scalability



Journey of Data Management Tools







AWS Product SLA Information

Service Level Agreements (SLA's) for AWS Enterprise Services

Enterprise Agreements (only available upon request)Standardized customer agreement:https://aws.aSLAs AWS customer support:https://aws.aService terms:https://aws.aAcceptable use policy:https://aws.a

https://aws.amazon.com/agreement/ https://aws.amazon.com/premiumsupport/ https://aws.amazon.com/service-terms/ https://aws.amazon.com/aup/

Service level agreements (SLAs) for AWS products

Amazon S3: Amazon EC2 and EBS: Amazon RDS: Route53: CloudFront: https://aws.amazon.com/s3/sla/ https://aws.amazon.com/ec2/sla/ https://aws.amazon.com/rds/sla/ https://aws.amazon.com/route53/sla/ https://aws.amazon.com/cloudfront/sla/



QUESTIONS?

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