

It's time to rethink your CRO.™



Implementation of an Electronic Laboratory Notebook in a CRO Environment

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Key goals:

- Paperless, completely electronic data- no conventional forms or lab notebooks
- Catching errors in real time
- Quality audits by exception
- Sample preparation by robotics
- LIMS providing instrument control and data acquisition
- Automated document generation



- Our early perceptions about ELN's:
 - Marketed to share research data across departments
 - Not well organized for regulated bioanalytical CRO environment (but probably could be customized)
 - Some products were GMP-focused (and successful)
 - Evaluation began in April 2009



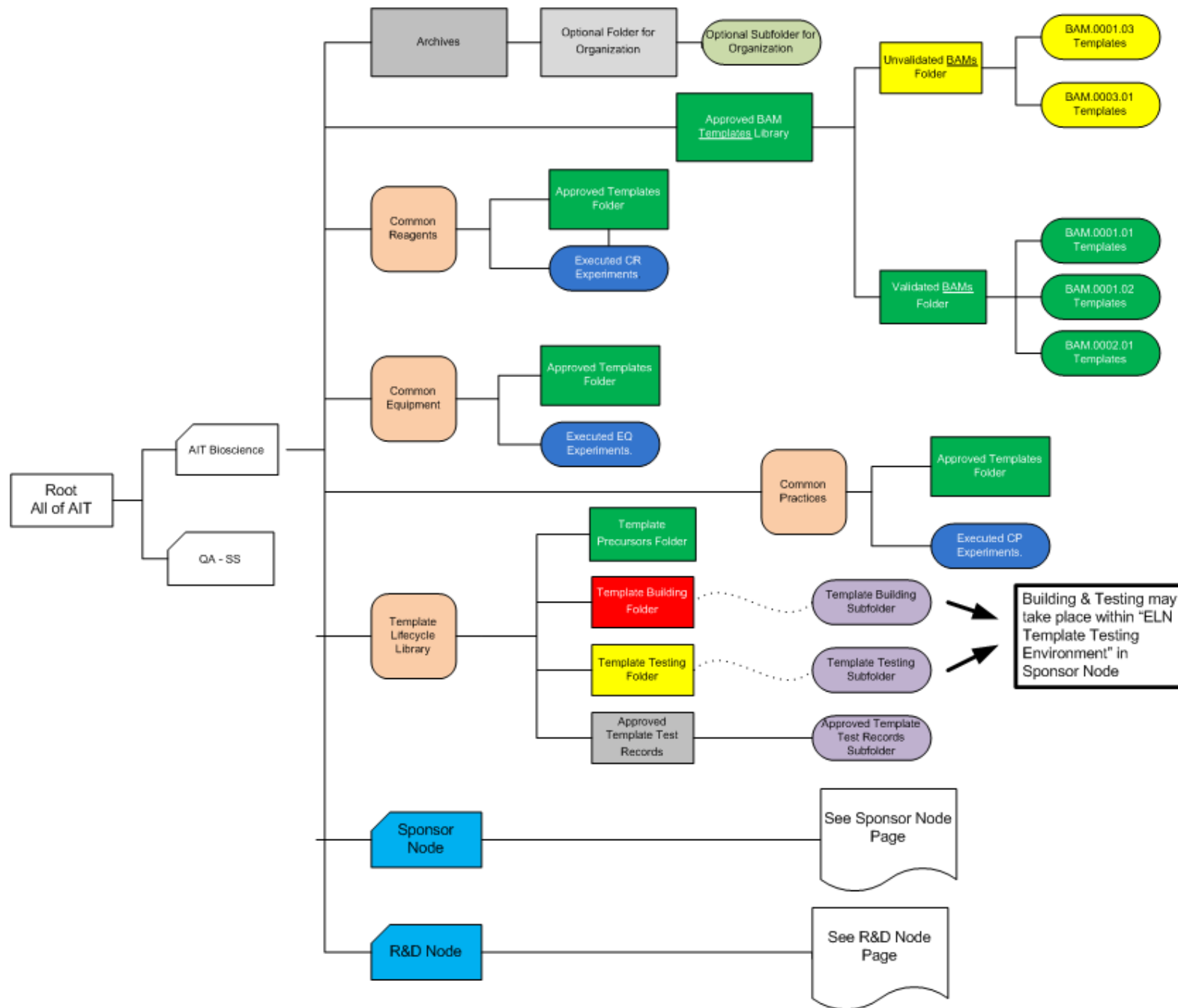
- 2 products evaluated starting June 2009
- Internal development prototype- August-Nov
- IDBS evaluation- Nov-Dec
- Purchase commitment- Dec
- Interviews on user requirements- Jan 2010
- QA vendor audit- Feb
- Final user requirements- March
- Templates, hierarchy, procedures: *IQ/OQ/PQ underway*

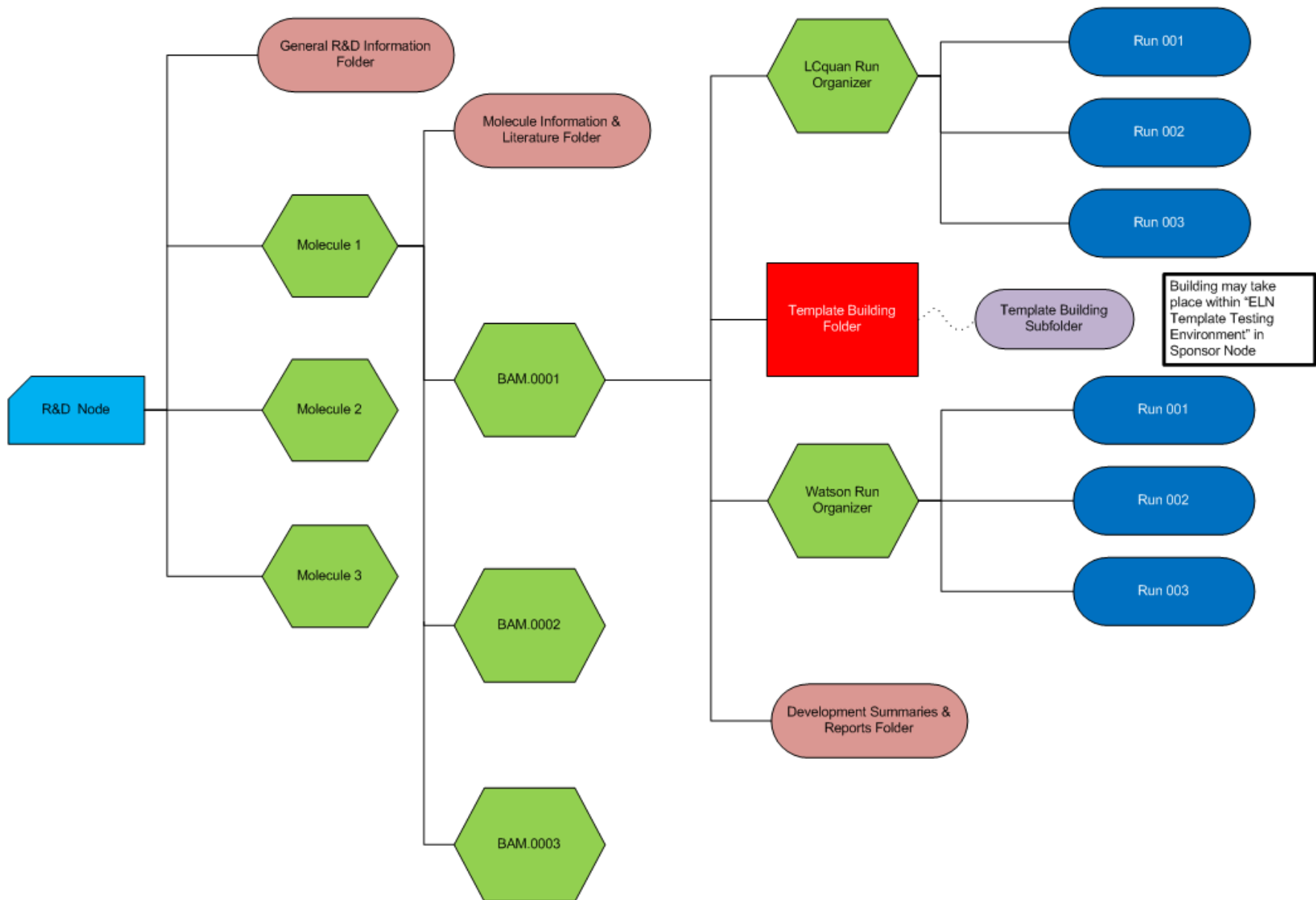


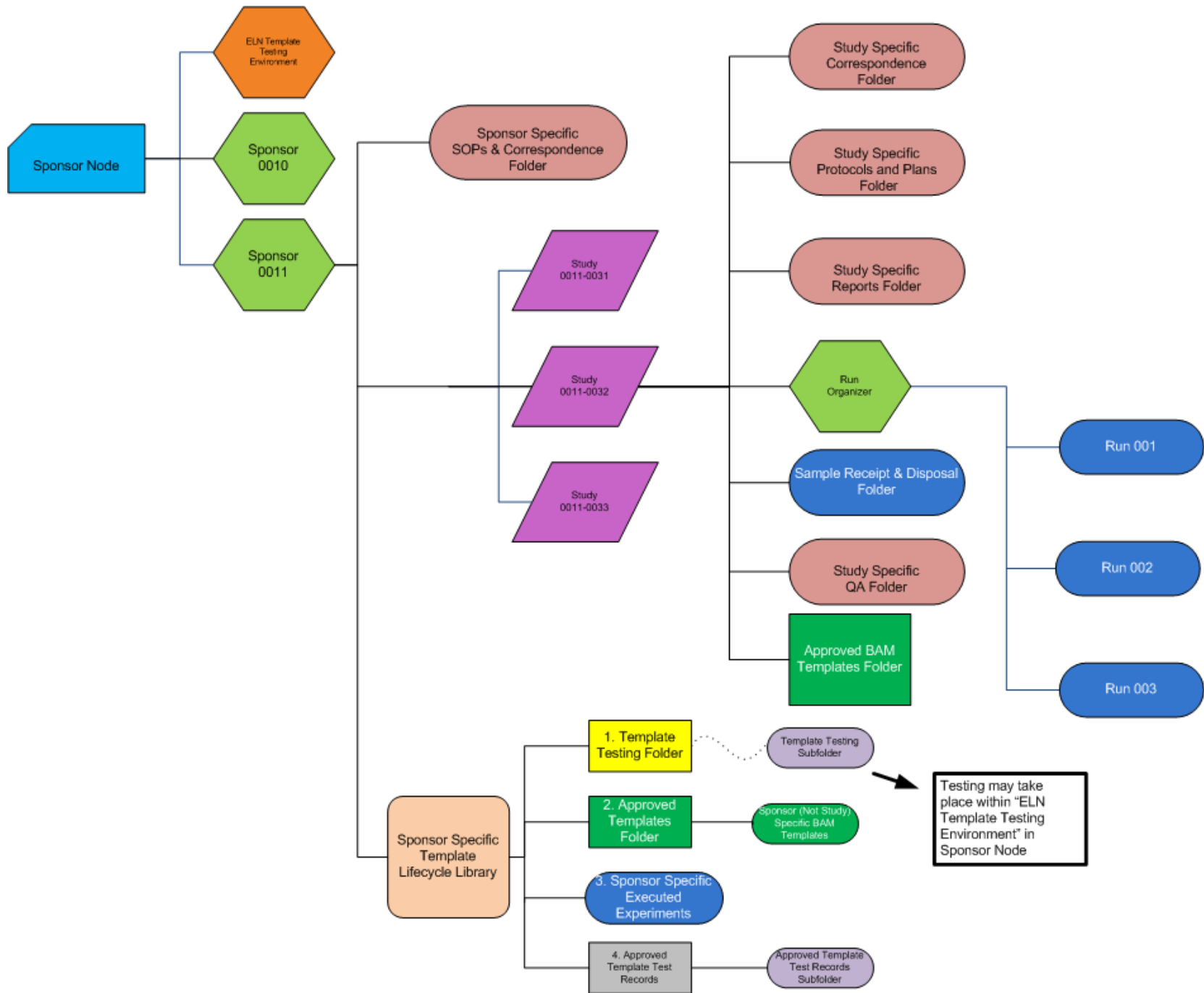
- **Unstructured** like a paper lab notebook, but also **searchable**, like a web search
- **Structured method management system** with controlled forms
- **Hierarchical organization** similar to Windows Explorer and prior legacy systems
- **Validated templates** for repetitive tasks
 - Business, scientific rules enforced
 - Error prevention during the lab activity
 - Audit by exception



- *Entities* in IDBS E-Workbook:
 - Templates
 - Master templates
 - Customized templates
 - Experiments (based on templates or free-form)
 - Groups, folders (to organize content, apply rules)
 - Sponsors
 - Molecules
 - Studies









Navigator

<Choose Filter>

- Root
 - Administrators
 - AIT Bioscience
 - Approved BAM Templates Library
 - Common Equipment
 - Common Practices
 - Common Reagents
 - ELN Archives
 - R&D Node
 - General R&D Information Folder
 - GLP-1
 - Sponsor Node
 - Template Lifecycle Library
 - 1. Template Precursors Folder
 - 2. Template Building Folder
 - 3. Template Testing Folder
 - 4. Approved Template Test Records Folder

Task Flow

Task Folders	Use Filter	Filter Column	Filter Value
All	<input type="checkbox"/>	Entity N...	=

Entity Name	Task Name	Priority	Status	Due Date	Requestor
REFSTD...	Data review...	Normal	Compl...	Jul 9, 2010	Ron Shoup
4123	Data review...	Normal	Compl...	Jul 10, 2...	Ron Shoup
4123	Data review...	Normal	Compl...	Jul 11, 2...	Ron Shoup

Home Page

User: Ron Shoup (shoupr)

[New Experiment](#)
[New Template](#)
[New Report](#)

Recent Items

- matq /Root/Shoupgroup1/0010 CLIENT/0010-5566 STUDY/Data/matq
- 1345 /Root/Shoupgroup1/0010 CLIENT/0010-5566 STUDY/Data/1345
- Template Precursor - Test Pl... /Root/AIT Bioscience dev/MyProject/Template Precursor - Test ...
- Test Plan Execution Experiment /Root/AIT Bioscience dev/MyProject/Test Plan Execution Experi...
- REFSTD - Sim - X8888-000366 /Root/AIT Bioscience/Template Lifecycle Library/2. Template Buil...
- Reference Standard Registra... /Root/AIT Bioscience/Template Lifecycle Library/2. Template Buil...
- cszc /Root/Shoupgroup1/0010 CLIENT/0010-5566 STUDY/Data/cszc
- BEQ.0010 06-Jul-2010:02 (1 ... /Root/Shoupgroup1/0010 CLIENT/0010-5566 STUDY/Data/BEQ....
- BEQ.0010 06-Jul-2010:03 (1 ... /Root/Shoupgroup1/0010 CLIENT/0010-5566 STUDY/Data/BEQ....
- Equipment Receipt v0.3 /Root/Phase 2 Template Testing/_Master Templates/Equipment ...

Recent Searches

Sent Tasks

Task Name	Sent To	Priority	Due Date	Status
Data review 1 (REFSTD - dopamine HCl - ...		Normal	Jul 9, 2010	Completed
Data review 1 (4123)		Normal	Jul 10, 2010	Completed
Data review 1 (4123)		Normal	Jul 11, 2010	Completed

To do Tasks

Task Name	Received From	Priority	Due Date	Status
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Pending Tasks



- LEB Test Bioscience Group
 - BAM Method Lifecycle Folder
 - Client Study Data Node
 - Common Lab Processes
 - Common Reagents Lifecycle Folder
 - Equipment Lifecycle Folder
 - 01 Eq Template Development
 - 02 Eq Template Validation
 - 03 Eq Template Approved for Use
 - 04 Eq Template Retired
 - Executed Equipment Experiments
 - Primary Template Folder
 - R&D Node
 - 01 General R&D Information & Tools
 - 01 Official List of BAMs
 - K' Calculator
 - Caffeic Acid & CAPE
 - Ethyl Glucuronide
 - Fentanyl
 - Glucose
 - Leucovorin
 - Losartan
 - BAM.0013
 - BAM.0013 Templates Being Built
 - BAM.0013 Instrumental Analysis Template
 - BAM.0013 Sample Preparation Template
 - LCquan Data Organizer
 - Tuning & Gradient Development
 - Method Evaluation Test Plan Summary
 - Study Information Summary
 - Templates Being Built
 - Watson Data Organizer
 - Molecule Information & Literature
 - Correspondence
 - Related Literature
 - Standards & R&D Samples Information
 - Structures & MW

Method development
organized by molecule

Files for:

published papers
sources and PO's
method development attempts
stability data summaries
method extraction procedures
instrument conditions
notes and precautions

Title: Structures & MW

Version Type: DRAFT

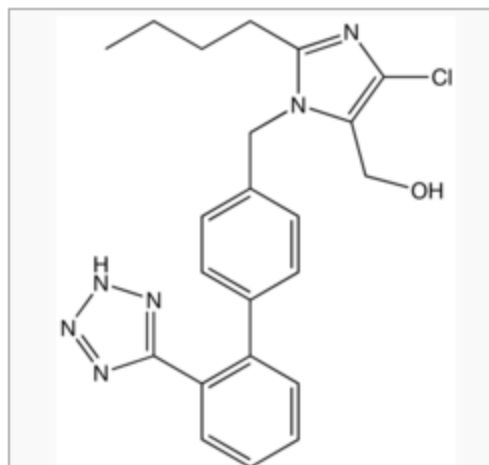
Version Number: 2



(v0) Structure & Info: Losartan.pdf



Losartan



Systematic (IUPAC) name

(2-butyl-4-chloro-1-[[2'-(1H-tetrazol-5-yl)
biphenyl-4-yl]methyl]-1H-imidazol-5-yl)methanol

Identifiers

CAS number	114798-26-4
ATC code	C09CA01
PubChem	3961
IUPHAR ligand ID	590
DrugBank	APRD00052

Chemical data

Formula	$C_{27}H_{23}ClN_6O$
Mol. mass	422.91

(v1) Structure & Info: Losartan Carboxylic Acid.jpg



Title: MS-MS Tuning & UPLC Gradient

Version Type: DRAFT

Version Number: 2



(v0) FINAL: TSQ #1 BAM.0013 MS-MS Parameters.pdf



Scan Editor Syringe Pump Divert Valve Method Summary

Calibration Correction Method

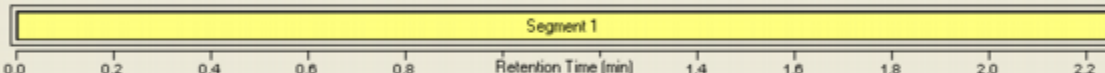
Run Settings

MS Acquire Time (min): 2.25

Segments: 1

Current Segment: 1

To display a chromatogram here, use Quantum/Open Raw File...



Segment 1 Settings

Segment Time (min): 2.25

Tune Method: C:\calbur\methods\BAM.0013\TSQ1_BAM0013_001.TSQTune

Scan Events: 1

Chrom Filter Peak Width (s): 3.0

Collision Gas Pressure (mTorr): 1.5

Current Scan Event: 1

Scan Event 1

Scan Event 1

Scan Type: SRM

Polarity:

Positive Negative

Data Type:

Centroid Profile

Decustering Voltage:

QCV (V): 10

Same value for all SRMs

Scan Width (m/z): 0.010

Scan Time (s): 0.050

Coll. Energy (V): 10

Peak Width

Q1 (FWHM): 0.70

Q3 (FWHM): 0.70

Use Tuned S-Lens Value

	Parent Mass	Product Mass	Collision E	S-Lens
1	423.145	207.086	21	86
2	432.145	207.086	21	89
3	437.137	235.049	17	89
4	446.137	235.049	17	89
*	446.137	235.049	17	89

Micro Scans: 1

Copy ScanEvent

Paste ScanEvent

Help

Tune

(v1) FINAL: TSQ #1 BAM.0013 UPLC Gradient.jpg



(v1) FINAL: TSQ #1 BAM.0013 UPLC Parameters.jpg



(v1) Chrom Peaks: Losartan LLOQ system check.jpg



Version-controlled Templates for Regulatory Studies

IDBS E-WorkBook Suite - Workbook Editor

File Record Item View Tools Window Help

Home Page Shipment Receipt v0.1

Title: **Shipment Receipt v0.1** Version Type: **VERSION**
Version Number: **4**

(v3) Spreadsheet: Shipment Receipt

Shipping Information

Shipment ID	Entry
AIT Study Number	
Shipping Site Name	
Shipping Site Address	
Shipping Site Coordinator	
Shipping Site Phone	
Shipping Site Email	
Date of Receipt	
Airbill/Courier #	
# Shipping Boxes	
Condition of Shipping Boxes	
Stored Prior to Accessioning?	

(v1) Placeholder: Shipment Notification

(v1) Placeholder: Air Bill

(v2) Placeholder: Email Confirmation of Delivery

Task Flow

Task Folders	Use Filter	Filter Column	Filter Value
All	<input type="checkbox"/>	Entity N...	=

Entity Name	Task Name	Priority	Status	Due Date	Requestor
BAM.00...	Approvals ...	Normal	In-Pro...	May 28, ...	Brian Engel
testing ...	Ron Shoup	Normal	Compl...	Jun 14, 2...	Ron Shoup



Completing an Experiment Based on Templates

Spreadsheet (ABS-23May2010-36) - READONLY

File Edit View Insert Format Tools Experiment Help

Tahoma 11 B I U A^xA A_x \$ % +.0 +.00

Instructions for Creating a Shipment Receipt Record

1. Enter information into the [Shipping Information](#) table.
2. Close out of the spreadsheet and attach the following to the Eworkbook experiment:
 - a) Shipping notification form
 - b) Airbill
 - c) Email confirmation of delivery
3. Version Save the Experiment
 - a) Version save the experiment by clicking the blue disk icon on the E-WorkBook menu bar. *(Be sure you do this on the E-WorkBook menu bar, with the spreadsheet closed. Do not try and save the record from within the spreadsheet.)*

Shipping Information

	Entry
Shipment ID	ABS-23May2010-36
AIT Study Number	0115-9566
Shipping Site Name	Midstates Phase I CRU
Shipping Site Address	2207 State St, Union City, MI 48824
Shipping Site Coordinator	James Troost
Shipping Site Phone	543-253-1245
Shipping Site Email	jtroost@midstates.com
Date of Receipt	23-May-2010
Airbill/Courier #	ADF234235235
# Shipping Boxes	2
Condition of Shipping Boxes	Intact, no exterior damage, dry ice remaining
Stored Prior to Accessioning?	No



Digital signatures on sections of experiment

Home Page ABS-23May2010-36

Title: ABS-23May2010-36 **Version Type:** VERSION **Version Number:** 3

(v2) Spreadsheet: Shipment Receipt

Digitally signed by Ron Shoup
Reason: Scientific Review
Date: May 23, 2010 8:23:25 AM

(v2) Placeholder: Shipment Notification

File: Shipment Notification

(v1) Placeholder: Air Bill

File: Air Bill

Digitally signed by Ron Shoup
Reason: Attest as Exact Copy
Date: May 23, 2010 8:26:01 AM

(v1) Placeholder: Email Confirmation of Delivery

File: Email Confirmation of Delivery

pick list.

b) Enter an "Expiration Date"

4. Check the Status table "Is Form complete?" & "Passed All Field Checks?" fields to see if the mandatory fields are completed and field validation checks have been passed

a) Red indicates missing data or validation errors. Green indicates all fields are completed.

b) Enter an user entered issues in the comment field

c) Review any issues on the Issue Tracking table and enter comments as appropriate.

d) A valid Stock Solution Prep ID will only be generated if all Mandatory Fields have been completed, all field checks have passed or the user has entered comments to address these issues.

5. Enter a label value into the Label Generator table.

6. Enter the Procedure steps into the Procedure table, as required.

7. Rename the Experiment

a) Copy the Stock Solution prep ID (in the Status Table) by right-clicking over the field and selecting Copy

b) Close the spreadsheet.

c) Open up the Reports Properties menu option

Normal Edit HTML

	Entry	Field Status
Date	5-Oct-2009	
Lot Number		
CoA		
CoA Reference		
Material Name		
Material_Type		
Exhausted Status		
Potency Value		
Specificity Value		
Protein_Content A280 (mg/mL)		
Production Date		
Expiration Date		
Target Mass		
Target Mass Unit	mg	
Select Balance		
Balance Model		
Balance Weight Range High		
Balance Weight Range Low		
Weight Range Units	mg	
Balance Check Reference	Balance Check Hyperlink	
Reagent Prep Generic Name		
Diluent Prep Reference		

Solvents	
Component	Solvent 1
Grade	
Vendor	
Lot Number	

Preparation	
	Entry
Weighed Mass	
Weighed Mass UOM	mg
Preparation Container	
Container Volume (mL)	
Concentration	
Large Molecule Concentration	
Concentration UOM	mg/mL

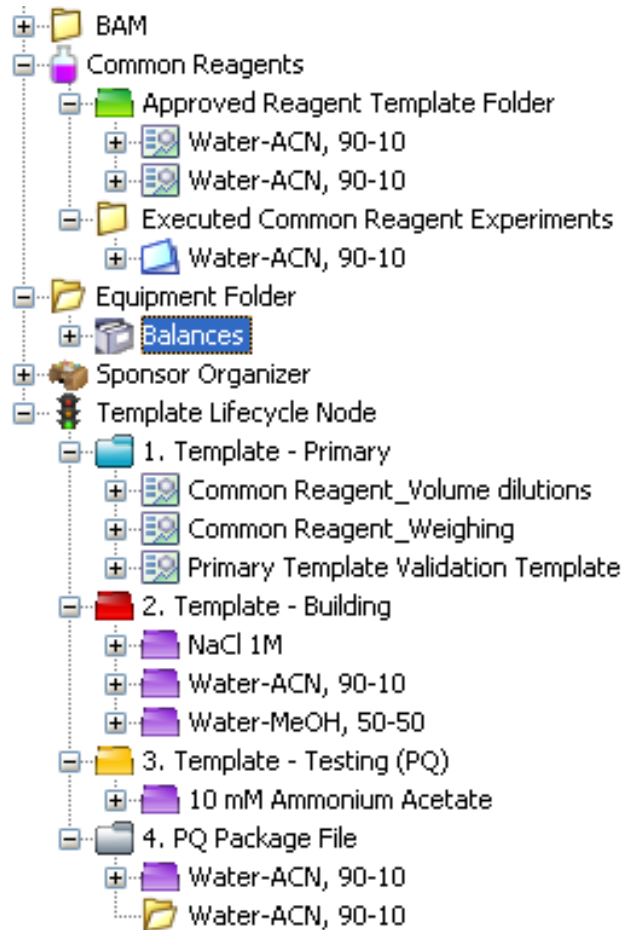
Storage	
	Entry
Storage Conditions	
Environmental Unit	
Environmental Unit Type	
Temperature (°C)	
Site	
Storage Container	
Prepared By	
Date	5-Oct-2009
Preparation Time	
Expiration Date	

Label Generator	
	Label Fields
labelType	Reagent:
labelValue	
reference	
preparationDate	10/5/2009
expirationDate	
storeRoomTemp	
storeRefrigerated	
storeFrozen	
scientist	
templateName	bioanalysis_reagent

Status	
Stock Solution Prep ID	
All Mandatory Fields Complete?	No
Passed All Field Checks?	Yes
User Entered Issue Comment	
Project_ID	JC project
Measurement Entry Witness	

ELN Workflow for stock solution

Reference std receipt	Validation ensemble: stability , matrix factor, specificity, recovery
Stock solutions	Study summary
Mixed spiking solutions	Sample preparation
Reagents	Instrumental analysis (system suitability check)
pH, weighing operations	Scientific review (carryover, blanks)
Equipment receipt, qualification, maintenance, repair, retirement	PI run review
Matrix receipt, pooling	Issue log
Making calibration stds, QC's	QA audit reports
Shipment receipt	QA master schedule
Sample accessioning, discrepancy resolution	
Sample disposal	Extensive bar-coding all items

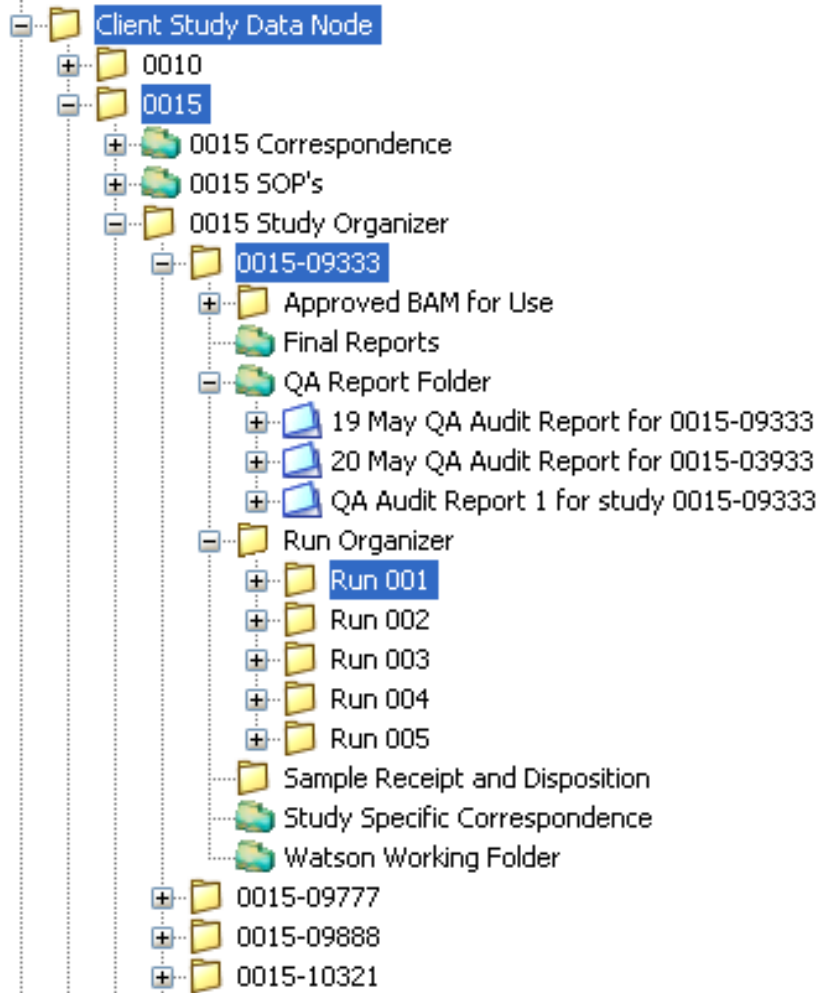


- Lifecycle management controlled by hierarchy
- Primary templates build specific draft templates
- Testing phase (PQ) according to test plan
- PQ data stored as electronic experiment (each test point can be saved as a version in the history)
- QA review, management approve the PQ experiment
- Template moved to Approved Template folder for use



AIT Bioscience

Regulated Study Layout in E-WorkBook



Sponsor node > Sponsor-specific entities and studies

Study node > Study-specific entities, including data

Only approved templates allowed



- ELN sniffs for new Watson activity (project, study, run) and creates mirror entities in ELN
- ELN automates a directed review of each run's system suitability data prior to sample injections.
- Post run, ELN looks at control and carryover samples relative to LLOQ samples and determines pass/fail status of run.



Use QC/QA Resources Up Front Instead of After the Fact

- All ELN templates are validated and controlled.
- Errors prevented, corrected in real time.
- ‘Audit by Exception’ greatly reduces QC review time.
- Less rework & review means faster turnaround.



- QA vendor audit in Feb 2010
- Risk assessment
- Validation plan
 - IQ (done)
 - Full OQ, but focus on select scripts (done)
 - PQ: hierarchy, catalog, roles/authorities, access
 - Template PQ: master templates, secondary templates