Data management at ESBATech

LabKey User Group Meeting 2015
Stefan Moese
Group Head Screening Technology
ESBATech, a Novartis company
Overview ESBATech Pipeline

Therapeutic antibody discovery pipeline for Ophthalmology

scFv antibodies

Process Development / Production
PK/PD

Protein Engineering

Antibody Screening

Formulation & Structural Biophysics

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From Hit to Lead – Research & Development at ESBATech

Antibody discovery and lead ID

1. B-cells / animal
   - Flow cytometry
   - Confirmed hits

2. Target binding ELISA reader
   - Confirmed hits

3. Antibody design and optimization
   - Characterization
   - Affinity maturation
   - Lead candidates
ESBATech development & manufacturing
“Comprehensive technical development - in a Nutshell”

DNA

Discovery | Development | Manufacturing

High throughput & Standard production

Fermentation & purification development

GMP production API & Product (Alcon)

Protein Engineering | Assay Development | DAS Assessment | Formulation development | Preclinical | Clinic

DNA
Requirements of a data management system

“What the system should do...”

- Capture result assay data securely at central place
- Get overview about which molecules are at what stage in the development pipeline
- Organize data via molecule identifier for queries across multiple projects
- Comprehensive searches for molecule properties
- Molecule/material storage inventory
Data management solution

LabKey as hybrid open source solution / commercial solution
Requirements
“Data inside and outside of labkey”

- Instrument
  - Raw Data
- Data Analysis
- ELN Data Documentation

LabKey Data Management system

- Results Data Management
- Sample tracking

Workflow-Tracking (passive)
Who has to do what when

Lab management (e.g. Freezer inventory)

Knime, R etc
Spotfire
Rabbit IgG Screening

Example of ELISA 384-well EC50 determination

Setup:
- 4708 candidates tested in dose response (12 conc.)
- Assay performed in 50 384 well plates
- Samples in duplicates
- Total 17600 sample wells (+ 1600 controls)

Analysis:
- Plate based normalization on based standard curves

Hitselection:
- Hit candidates EC_{50} determination, Hit rate ~ 50 %
Automated Data Analysis Pipelines

Knime – Lego for biologists

Data handling and conversion via Knime, statistics & curve fitting via R

![Diagram of Knime workflow](image_url)
Basic system operations

General principle:

Sample 1 to many → Method → Sample 0 to many → Results 0 to many

Experiment

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Basic system operations

Examples

Analytical assay:
(e.g. ELISA)

Assay in pipeline:
(e.g. HPLC)

Aliquots:
(e.g. Storage of biomolecules)
Molecule hierarchy

One to many vs many to one in addition
Same molecule, multiple materials, multiple assays

Molecule 1

Format: IgG

Material:
1. DNA

Storage location

Storage position drawer/ rack etc.

Assay 1

Data: • Text • Images

Step 1

Molecule 1

Format: IgG

Material:
1. Protein

Storage location

Storage position drawer/ rack etc.

Assay 2

Data: • Text • Images

Step 2
General hierarchy structure

«It’s all about proteins.»
Workflow tracking

Passive tracking of materials and assays across departments

SampleSet
- Molecules
- Workflow table
- List1
  - Scientific Workflow
- List2
  - Operational Workflow
- List3
  - Summary level Workflow

Assays
- GPAT
- List4
  - Assay list

List5
- Team specific Workflow

SampleSet
Assay
List
ESBATech drug development process

Molecule hierarchy

Arrows: Change in molecule properties
ESBATEch drug development process

*Molecule hierarchy <-> assay hierarchy*

Arrows: Change in molecule properties
Triangles: Associated assay data

Queries for same assay type across hierarchy
LabKey
Data model
LabKey example – Department specific requirements

*Molecule / workflow management*

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**Main portal for Production Group**

**Workflowstep HTP**

View: Workflowstep_HTP

<table>
<thead>
<tr>
<th>Workflow level 1 Generic Project Plan</th>
<th>Workflow level 2 Operational Step</th>
<th>Operation Level 2 Status</th>
<th>User</th>
<th>Date</th>
</tr>
</thead>
<tbody>
<tr>
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<td>Details</td>
<td>5. Characterisation IgG SN</td>
<td>HTSP</td>
<td>open</td>
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</table>

**Workflowstep Standard Production**

View: Workflowstep_standardproduction

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<th>Workflow level 1 Generic Project Plan</th>
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<td>Stefan Moese</td>
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<td>6002</td>
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</table>
LabKey example molecule hierarchy implementation

Example: molecule hierarchy of a development candidate

Antigen for immunization
- ~15 hierarchy levels
- ~50 parent molecules

Development candidate

Clinical candidate
- ~3-5 hierarchy levels
- ~1500 children molecules

Derive sample from 3208

3802

Sample

Derive sample from 3802

3881

Derive sample from 3208

3802

3881

1405224001 1461244001 1429220001 1405224005 141124BC001 150323BC001 141126BC001 141201BC001 140825DC001
LabKey example assay implementation
Pilot project version 4 running
Assay setups established
Test dataset defined
Server performance / infrastructure testing and optimization ongoing
Test dataset integration ongoing

Business logic
Usability
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Ryan Luce
Patty Foley
Molly O’Hara
...

LabKey Server
Open Source Software for Scientists

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