16th EBF Open Symposium – Barcelona 2023

Case study on the implementation of a regulatory compliant data platform for planning and execution, collaboration, review and reporting of bioanalytical studies.

Norbert Bittner

15-Nov-2023

up to data

or - Teaching Old Dogs New Tricks

„Take it from us - the only thing stopping our pets learning through life is our own prejudices.“

https://www.walkervillevet.com.au/blog/myth-10-you-cant-teach-an-old-dog-new-tricks/

Topics

01 What does „Cloud Computing“ mean

02 Cloud System vs. „in the Cloud“ System – what makes a difference

03 Cloud System Case Studies on Small and Midsized Labs:

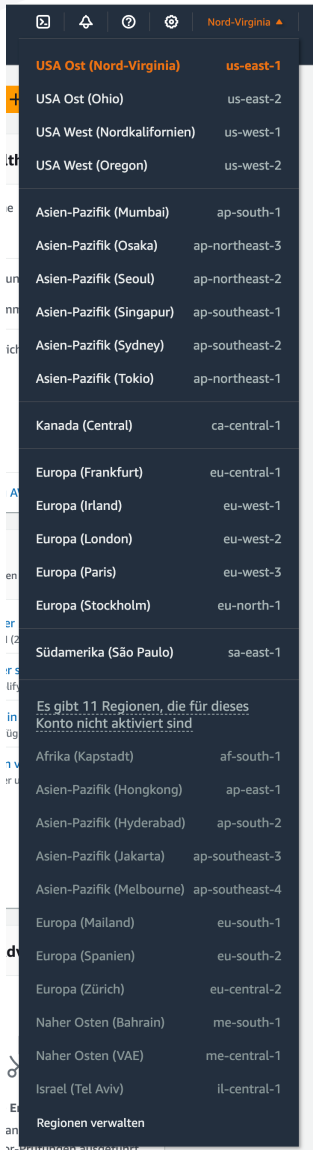
- Capture data where created
- Enable investigation of data
- Enable data communication between sponsor and lab
- Create a long-term archive

Is this „the cloud“?

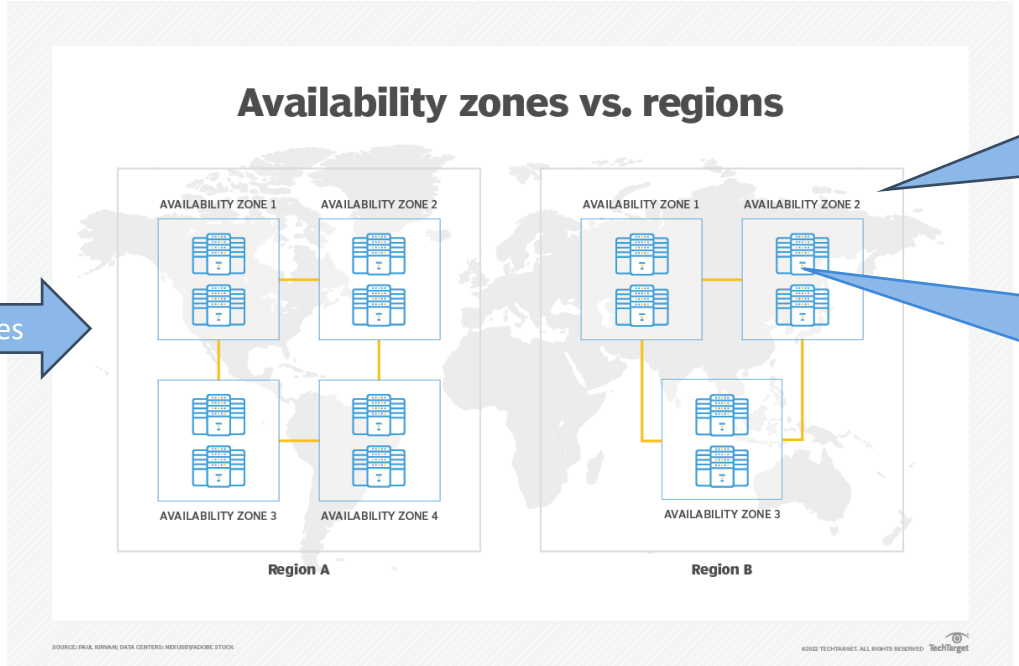
- AWS Data Center Oregon

up to data

Region – Availability Zone - Data Center



Zones



The AWS Cloud spans 102 Availability Zones within 32 geographic regions around the world, with announced plans for 15 more Availability Zones and 5 more AWS Regions in Canada, Germany, Malaysia, New Zealand, and Thailand.

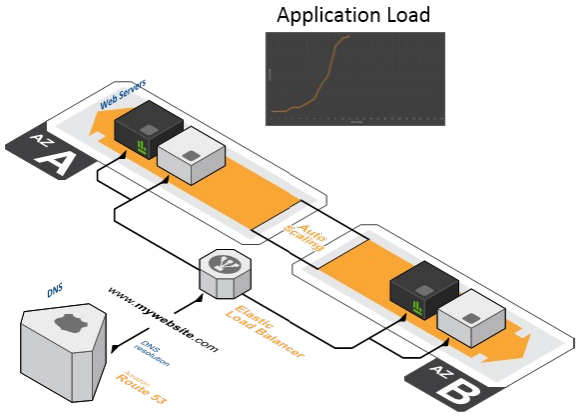
„A common misconception is that a single zone equals a single data center. In fact, each zone is backed by one or more physical data centers, with the largest backed by five.“

https://docs.aws.amazon.com/whitepapers/latest/aws-overview/global-infrastructure.html

https://baxtel.com/data-center/aws-eu-frankfurt-region-eu-central-1

Example services within and across zones and regions

- load balancing
- failover redundancy
- backups



up to data

Cloud computing - defined

Cloud computing is the **on-demand** delivery of **IT resources** over the **Internet** with **pay-as-you-go pricing**.

https://aws.amazon.com/what-is-cloud-computing/?nc1=h_ls

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Cloud computing - defined

Cloud computing is the **on-demand** delivery of **IT resources** over the **Internet** with **pay-as-you-go pricing**.

Instead of buying, owning, and maintaining physical data centers and servers, you can access technology services, such as computing power, storage, and databases, on an as-needed basis from a cloud provider like Amazon Web Services (AWS).

https://aws.amazon.com/what-is-cloud-computing/?nc1=h_ls

Cloud system vs. „in the Cloud“ system – what makes the difference

Move existing systems „in the cloud“:

Server virtualization

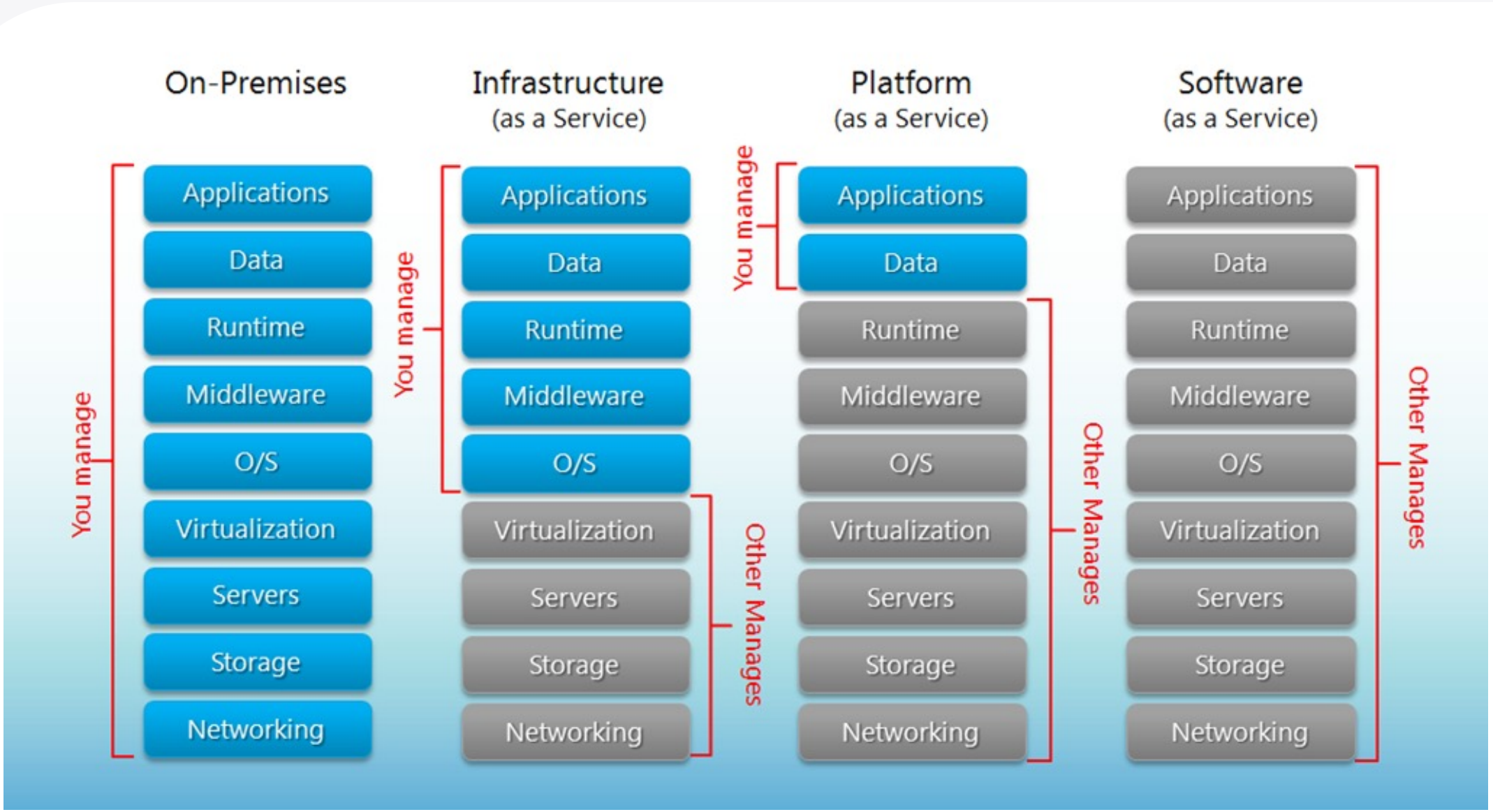
- „Run the Software on someone else‘s hardware“
- Benefits
  - Some services
  - Delegate responsibility
- **IaaS (Infrastructure as a service)**

or

- **PaaS (Platform as a service)**

up to data

Cloud Systems - Shared Responsibility



https://www.researchgate.net/figure/Shared-responsibility-model-of-cloud-computing-Source_fig1_352285658

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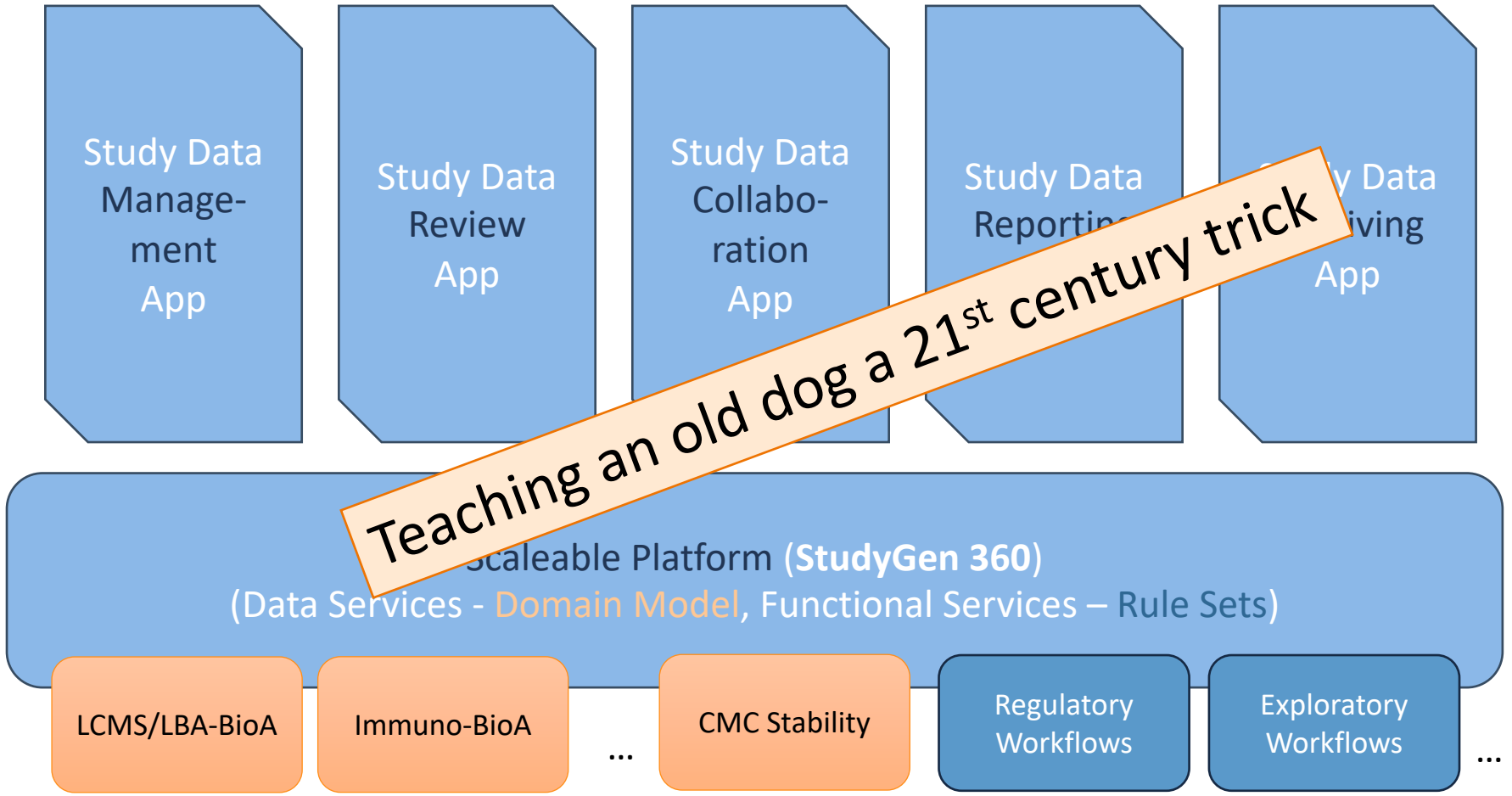
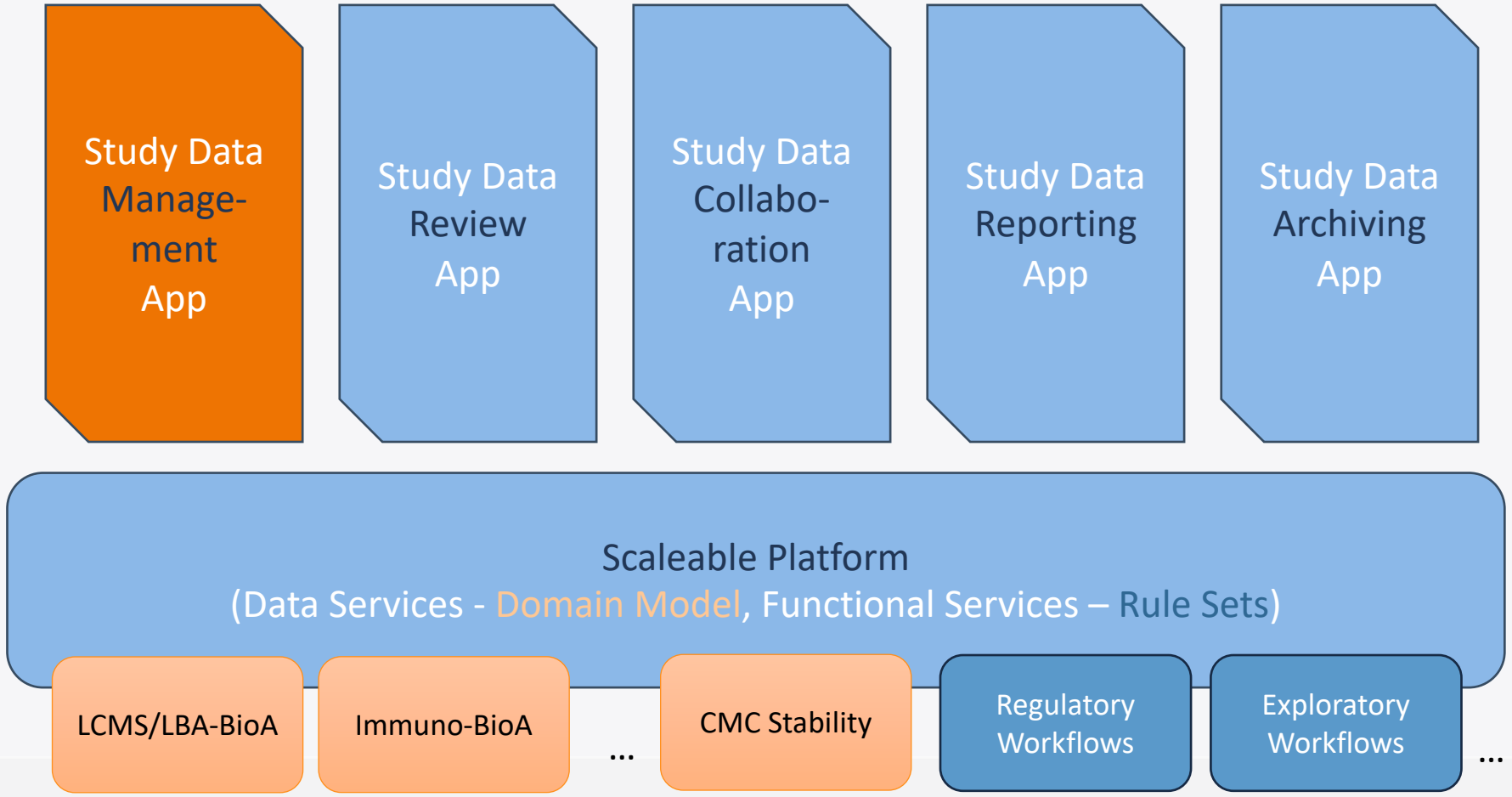
Cloud System – Study Data Management Architecture



EU Funded

up to data



Study Data Management

Case Study: Capture data where created

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Manual Workflow - without LIMS

Sample
Demographic

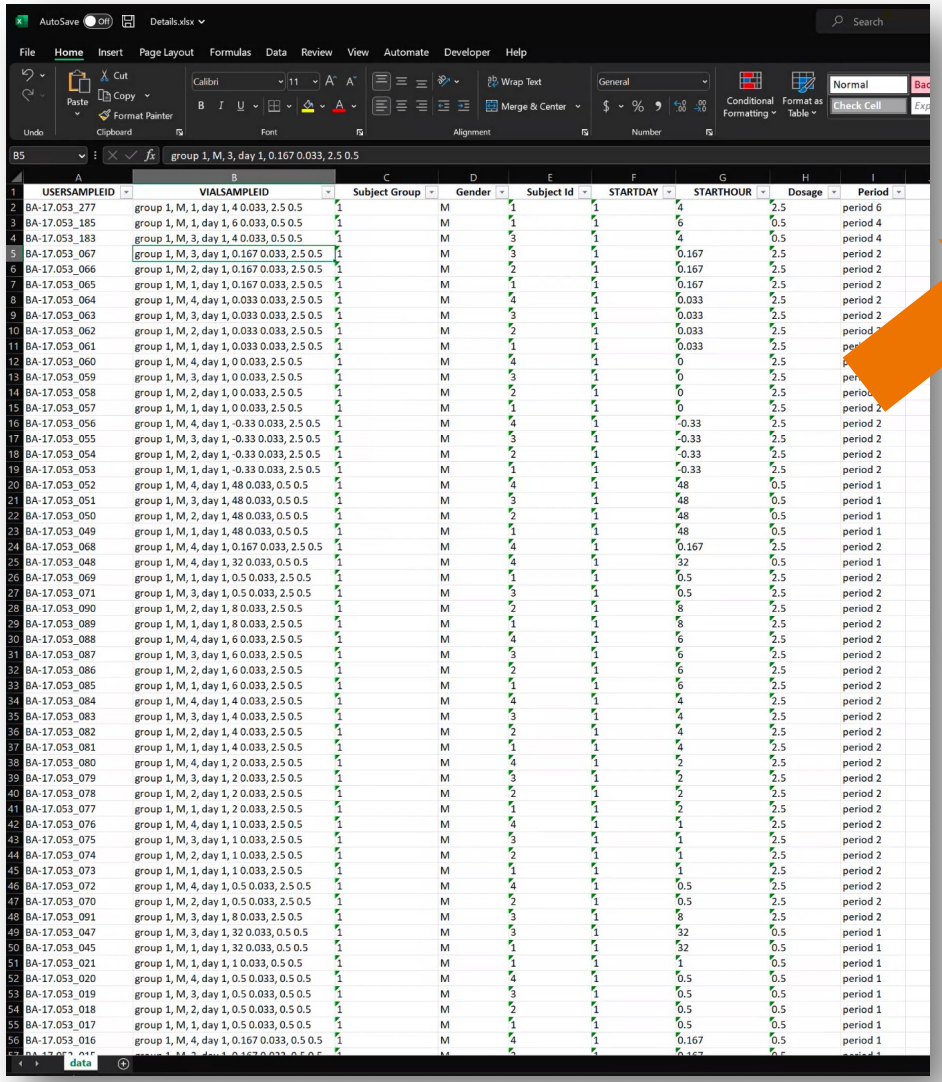
BA number:	BA-17.053			Sample check under sodium light:	no				
Study no.:	20135531			Samples checked by:	A . Steurer				
Project:	CXCR3			from - to:	1 - 367				
Matrix:	plasma and urine								
Species:	dog			Date and signature:					
* Labeling and general condition of each sample will be checked (see SOP-000312). Only, if conditions of the sample are non-standard or unexpected, these will be recorded in this column.									
no manual entry in this column		Enter in these columns the exact sample identity as presented on the tubes							
original sample identification plus dose test facility / CRO	sample identification	group	sex	animal ID	occasion [day]	time point h	dose mg/kg	comments	sample inspection
group 1, M, 1, day 1, -0,33 h, 0,5 mg/kg	BA-17.053_001	1	M	1	1	-0,33	0,5	period 1	
group 1, M, 2, day 1, -0,33 h, 0,5 mg/kg	BA-17.053_002	1	M	2	1	-0,33	0,5	period 1	
group 1, M, 3, day 1, -0,33 h, 0,5 mg/kg	BA-17.053_003	1	M	3	1	-0,33	0,5	period 1	
group 1, M, 4, day 1, -0,33 h, 0,5 mg/kg	BA-17.053_004	1	M	4	1	-0,33	0,5	period 1	
group 1, M, 1, day 1, 0 h, 0,5 mg/kg	BA-17.053_005	1	M	1	1	0	0,5	period 1	
group 1, M, 2, day 1, 0 h, 0,5 mg/kg	BA-17.053_006	1	M	2	1	0	0,5	period 1	
group 1, M, 3, day 1, 0 h, 0,5 mg/kg	BA-17.053_007	1	M	3	1	0	0,5	period 1	
group 1, M, 4, day 1, 0 h, 0,5 mg/kg	BA-17.053_008	1	M	4	1	0	0,5	period 1	
group 1, M, 1, day 1, 0,033 h, 0,5 mg/kg	BA-17.053_009	1	M	1	1	0,033	0,5	period 1	
group 1, M, 2, day 1, 0,033 h, 0,5 mg/kg	BA-17.053_010	1	M	2	1	0,033	0,5	period 1	
group 1, M, 3, day 1, 0,033 h, 0,5 mg/kg	BA-17.053_011	1	M	3	1	0,033	0,5	period 1	
group 1, M, 4, day 1, 0,033 h, 0,5 mg/kg	BA-17.053_012	1	M	4	1	0,033	0,5	period 1	
group 1, M, 1, day 1, 0,167 h, 0,5 mg/kg	BA-17.053_013	1	M	1	1	0,167	0,5	period 1	
group 1, M, 2, day 1, 0,167 h, 0,5 mg/kg	BA-17.053_014	1	M	2	1	0,167	0,5	period 1	
group 1, M, 3, day 1, 0,167 h, 0,5 mg/kg	BA-17.053_015	1	M	3	1	0,167	0,5	period 1	
group 1, M, 4, day 1, 0,167 h, 0,5 mg/kg	BA-17.053_016	1	M	4	1	0,167	0,5	period 1	
group 1, M, 1, day 1, 0,5 h, 0,5 mg/kg	BA-17.053_017	1	M	1	1	0,5	0,5	period 1	
group 1, M, 2, day 1, 0,5 h, 0,5 mg/kg	BA-17.053_018	1	M	2	1	0,5	0,5	period 1	
group 1, M, 3, day 1, 0,5 h, 0,5 mg/kg	BA-17.053_019	1	M	3	1	0,5	0,5	period 1	
group 1, M, 4, day 1, 0,5 h, 0,5 mg/kg	BA-17.053_020	1	M	4	1	0,5	0,5	period 1	
group 1, M, 1, day 1, 1 h, 0,5 mg/kg	BA-17.053_021	1	M	1	1	1	0,5	period 1	
group 1, M, 2, day 1, 1 h, 0,5 mg/kg	BA-17.053_022	1	M	2	1	1	0,5	period 1	
group 1, M, 3, day 1, 1 h, 0,5 mg/kg	BA-17.053_023	1	M	3	1	1	0,5	period 1	
group 1, M, 3, day 1, 8 h, 0,5 mg/kg	BA-17.053_039	1	M	3	1	8	0,5	period 1	
group 1, M, 4, day 1, 8 h, 0,5 mg/kg	BA-17.053_040	1	M	4	1	8	0,5	period 1	
group 1, M, 1, day 1, 24 h, 0,5 mg/kg	BA-17.053_041	1	M	1	1	24	0,5	period 1	
group 1, M, 2, day 1, 24 h, 0,5 mg/kg	BA-17.053_042	1	M	2	1	24	0,5	period 1	
group 1, M, 3, day 1, 24 h, 0,5 mg/kg	BA-17.053_043	1	M	3	1	24	0,5	period 1	
group 1, M, 4, day 1, 24 h, 0,5 mg/kg	BA-17.053_044	1	M	4	1	24	0,5	period 1	
group 1, M, 1, day 1, 32 h, 0,5 mg/kg	BA-17.053_045	1	M	1	1	32	0,5	period 1	
group 1, M, 2, day 1, 32 h, 0,5 mg/kg	BA-17.053_046	1	M	2	1	32	0,5	period 1	
group 1, M, 3, day 1, 32 h, 0,5 mg/kg	BA-17.053_047	1	M	3	1	32	0,5	period 1	
group 1, M, 4, day 1, 32 h, 0,5 mg/kg	BA-17.053_048	1	M	4	1	32	0,5	period 1	
group 1, M, 1, day 1, 48 h, 0,5 mg/kg	BA-17.053_049	1	M	1	1	48	0,5	period 1	
group 1, M, 2, day 1, 48 h, 0,5 mg/kg	BA-17.053_050	1	M	2	1	48	0,5	period 1	
group 1, M, 3, day 1, 48 h, 0,5 mg/kg	BA-17.053_051	1	M	3	1	48	0,5	period 1	
group 1, M, 4, day 1, 48 h, 0,5 mg/kg	BA-17.053_052	1	M	4	1	48	0,5	period 1	
group 1, M, 1, day 1, -0,33 h, 2,5 mg/kg	BA-17.053_053	1	M	1	1	-0,33	2,5	period 2	
group 1, M, 2, day 1, -0,33 h, 2,5 mg/kg	BA-17.053_054	1	M	2	1	-0,33	2,5	period 2	
group 1, M, 3, day 1, -0,33 h, 2,5 mg/kg	BA-17.053_055	1	M	3	1	-0,33	2,5	period 2	

sample identification	group	sex	animal ID	occasion [day]	time point h	dose mg/kg
BA-17.053_001	1	M	1	1	-0,33	0,5
BA-17.053_002	1	M	2	1	-0,33	0,5

Seite 1

up to data

Either Uploading Data (Demographics) or …



USERSAMPLEID	VIALSAMPLEID	Subject Group	Gender	Subject Id	STARTDAY	STARTHOUR	Dosage	Period
BA-17.053_277	group 1, M, 1, day 1, 4 0.033, 2.5 0.5	1	M	1	1	4	2.5	period 6
BA-17.053_185	group 1, M, 1, day 1, 6 0.033, 0.5 0.5	1	M	1	1	6	0.5	period 4
BA-17.053_183	group 1, M, 3, day 1, 4 0.033, 0.5 0.5	1	M	3	1	4	0.5	period 4
BA-17.053_067	group 1, M, 3, day 1, 0.167 0.033, 2.5 0.5	1	M	3	1	0.167	2.5	period 2
BA-17.053_066	group 1, M, 2, day 1, 0.167 0.033, 2.5 0.5	1	M	2	1	0.167	2.5	period 2
BA-17.053_065	group 1, M, 1, day 1, 0.167 0.033, 2.5 0.5	1	M	1	1	0.167	2.5	period 2
BA-17.053_064	group 1, M, 4, day 1, 0.033 0.033, 2.5 0.5	1	M	4	1	0.033	2.5	period 2
BA-17.053_063	group 1, M, 3, day 1, 0.033 0.033, 2.5 0.5	1	M	3	1	0.033	2.5	period 2
BA-17.053_062	group 1, M, 2, day 1, 0.033 0.033, 2.5 0.5	1	M	2	1	0.033	2.5	period 2
BA-17.053_061	group 1, M, 1, day 1, 0.033 0.033, 2.5 0.5	1	M	1	1	0.033	2.5	period 2
BA-17.053_060	group 1, M, 4, day 1, 0 0.033, 2.5 0.5	1	M	4	1	0	2.5	period 2
BA-17.053_059	group 1, M, 3, day 1, 0 0.033, 2.5 0.5	1	M	3	1	0	2.5	period 2
BA-17.053_058	group 1, M, 2, day 1, 0 0.033, 2.5 0.5	1	M	2	1	0	2.5	period 2
BA-17.053_057	group 1, M, 1, day 1, 0 0.033, 2.5 0.5	1	M	1	1	0	2.5	period 2
BA-17.053_056	group 1, M, 4, day 1, -0.33 0.033, 2.5 0.5	1	M	4	1	-0.33	2.5	period 2
BA-17.053_055	group 1, M, 3, day 1, -0.33 0.033, 2.5 0.5	1	M	3	1	-0.33	2.5	period 2
BA-17.053_054	group 1, M, 2, day 1, -0.33 0.033, 2.5 0.5	1	M	2	1	-0.33	2.5	period 2
BA-17.053_053	group 1, M, 1, day 1, -0.33 0.033, 2.5 0.5	1	M	1	1	-0.33	2.5	period 2
BA-17.053_052	group 1, M, 4, day 1, 48 0.033, 0.5 0.5	1	M	4	1	48	0.5	period 1
BA-17.053_051	group 1, M, 3, day 1, 48 0.033, 0.5 0.5	1	M	3	1	48	0.5	period 1
BA-17.053_050	group 1, M, 2, day 1, 48 0.033, 0.5 0.5	1	M	2	1	48	0.5	period 1
BA-17.053_049	group 1, M, 1, day 1, 48 0.033, 0.5 0.5	1	M	1	1	48	0.5	period 1
BA-17.053_068	group 1, M, 4, day 1, 0.167 0.033, 2.5 0.5	1	M	4	1	0.167	2.5	period 2
BA-17.053_048	group 1, M, 4, day 1, 32 0.033, 0.5 0.5	1	M	4	1	32	0.5	period 1
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BA-17.053_071	group 1, M, 3, day 1, 0.5 0.033, 2.5 0.5	1	M	3	1	0.5	2.5	period 2
BA-17.053_090	group 1, M, 2, day 1, 8 0.033, 2.5 0.5	1	M	2	1	8	2.5	period 2
BA-17.053_089	group 1, M, 1, day 1, 8 0.033, 2.5 0.5	1	M	1	1	8	2.5	period 2
BA-17.053_088	group 1, M, 4, day 1, 6 0.033, 2.5 0.5	1	M	4	1	6	2.5	period 2
BA-17.053_087	group 1, M, 3, day 1, 6 0.033, 2.5 0.5	1	M	3	1	6	2.5	period 2
BA-17.053_086	group 1, M, 2, day 1, 6 0.033, 2.5 0.5	1	M	2	1	6	2.5	period 2
BA-17.053_085	group 1, M, 1, day 1, 6 0.033, 2.5 0.5	1	M	1	1	6	2.5	period 2
BA-17.053_084	group 1, M, 4, day 1, 4 0.033, 2.5 0.5	1	M	4	1	4	2.5	period 2
BA-17.053_083	group 1, M, 3, day 1, 4 0.033, 2.5 0.5	1	M	3	1	4	2.5	period 2
BA-17.053_082	group 1, M, 2, day 1, 4 0.033, 2.5 0.5	1	M	2	1	4	2.5	period 2
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BA-17.053_080	group 1, M, 4, day 1, 2 0.033, 2.5 0.5	1	M	4	1	2	2.5	period 2
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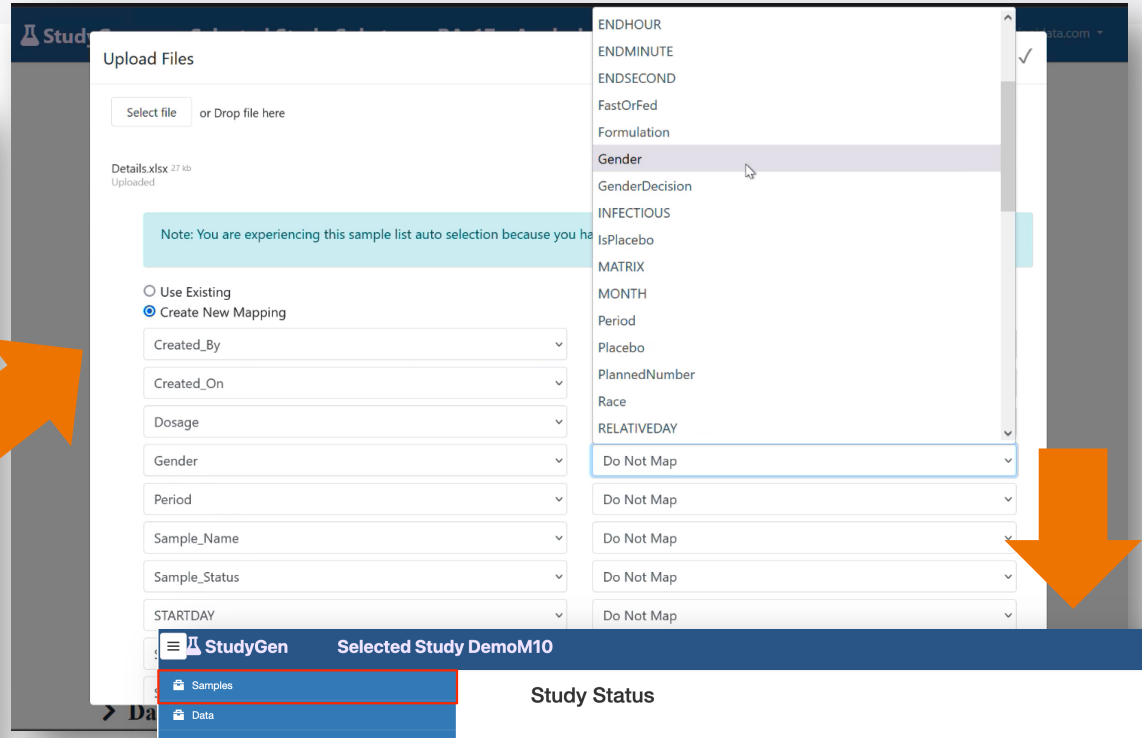
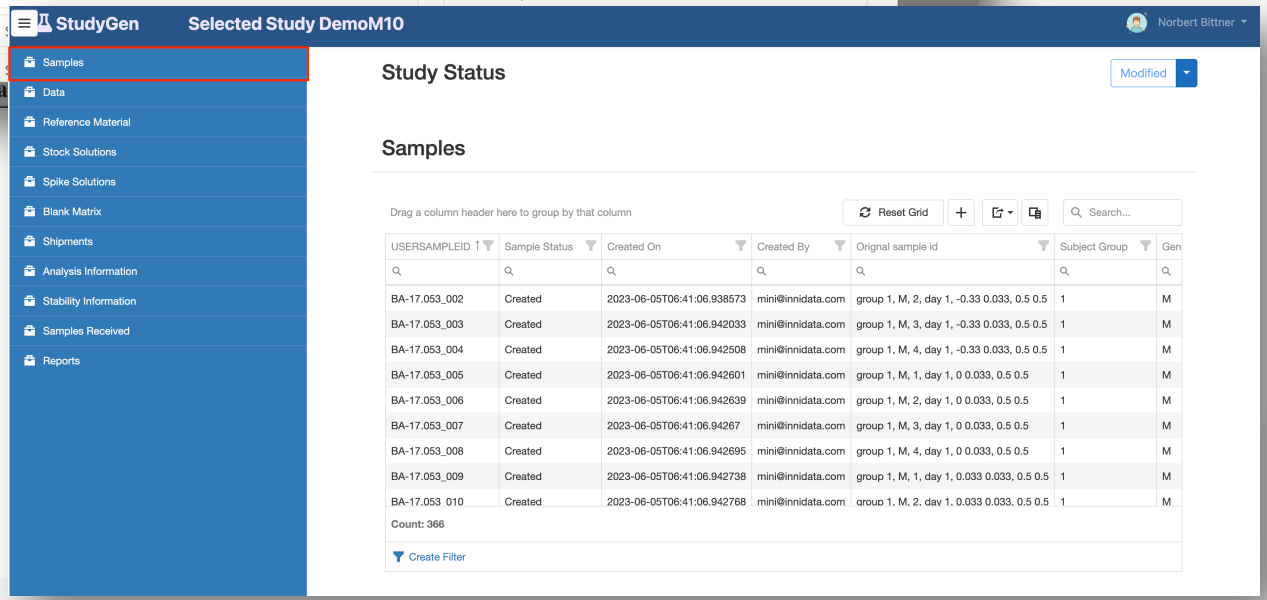
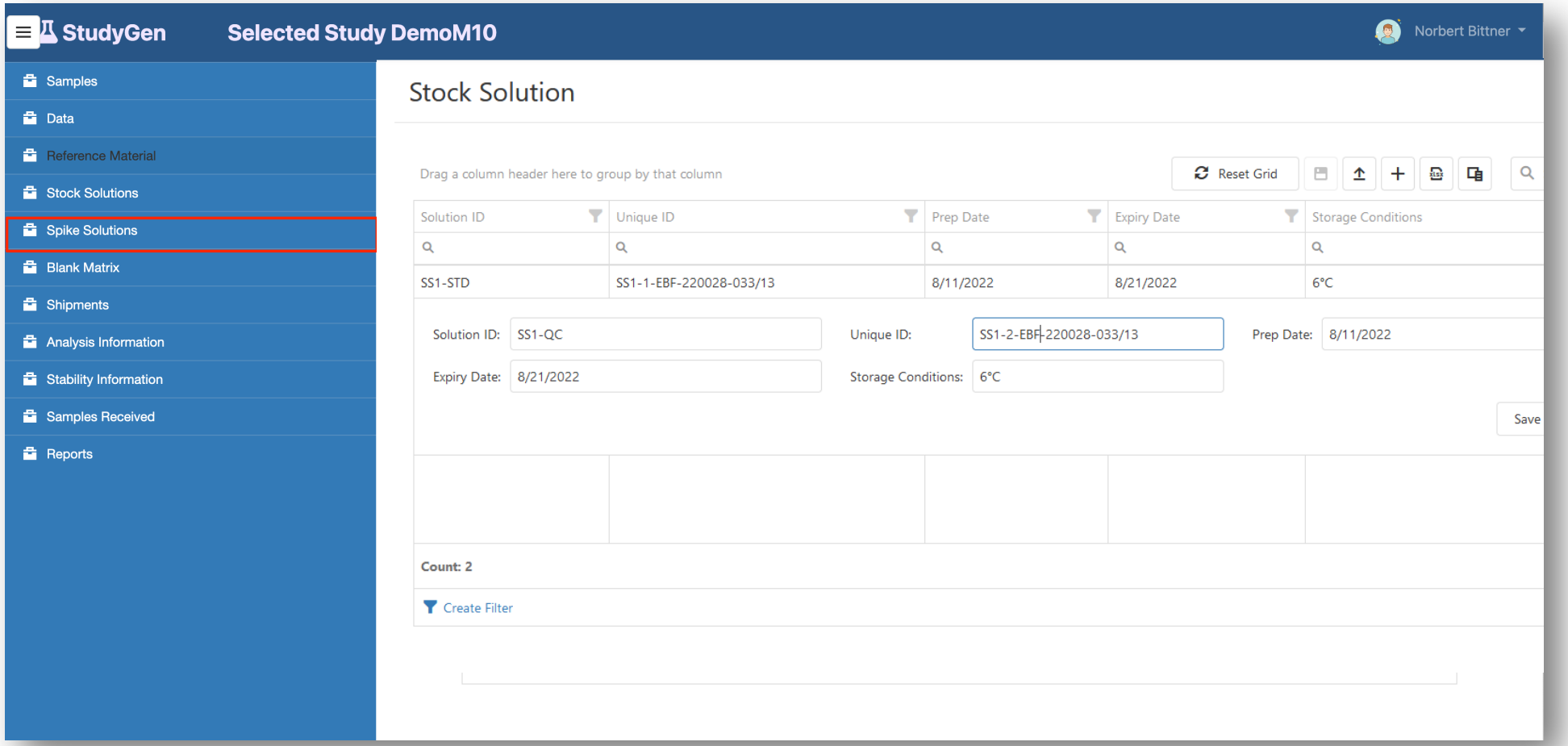
BA-17.053_077	group 1, M, 1, day 1, 2 0.033, 2.5 0.5	1	M	1	1	2	2.5	period 2
BA-17.053_076	group 1, M, 4, day 1, 1 0.033, 2.5 0.5	1	M	4	1	1	2.5	period 2
BA-17.053_075	group 1, M, 3, day 1, 1 0.033, 2.5 0.5	1	M	3	1	1	2.5	period 2
BA-17.053_074	group 1, M, 2, day 1, 1 0.033, 2.5 0.5	1	M	2	1	1	2.5	period 2
BA-17.053_073	group 1, M, 1, day 1, 1 0.033, 2.5 0.5	1	M	1	1	1	2.5	period 2
BA-17.053_072	group 1, M, 4, day 1, 0.5 0.033, 2.5 0.5	1	M	4	1	0.5	2.5	period 2
BA-17.053_070	group 1, M, 2, day 1, 0.5 0.033, 2.5 0.5	1	M	2	1	0.5	2.5	period 2
BA-17.053_091	group 1, M, 3, day 1, 8 0.033, 2.5 0.5	1	M	3	1	8	2.5	period 2
BA-17.053_047	group 1, M, 3, day 1, 32 0.033, 0.5 0.5	1	M	3	1	32	0.5	period 1
BA-17.053_045	group 1, M, 1, day 1, 32 0.033, 0.5 0.5	1	M	1	1	32	0.5	period 1
BA-17.053_021	group 1, M, 1, day 1, 1 0.033, 0.5 0.5	1	M	1	1	1	0.5	period 1
BA-17.053_020	group 1, M, 4, day 1, 0.5 0.033, 0.5 0.5	1	M	4	1	0.5	0.5	period 1
BA-17.053_019	group 1, M, 3, day 1, 0.5 0.033, 0.5 0.5	1	M	3	1	0.5	0.5	period 1
BA-17.053_018	group 1, M, 2, day 1, 0.5 0.033, 0.5 0.5	1	M	2	1	0.5	0.5	period 1
BA-17.053_017	group 1, M, 1, day 1, 0.5 0.033, 0.5 0.5	1	M	1	1	0.5	0.5	period 1
BA-17.053_016	group 1, M, 4, day 1, 0.167 0.033, 0.5 0.5	1	M	4	1	0.167	0.5	period 1





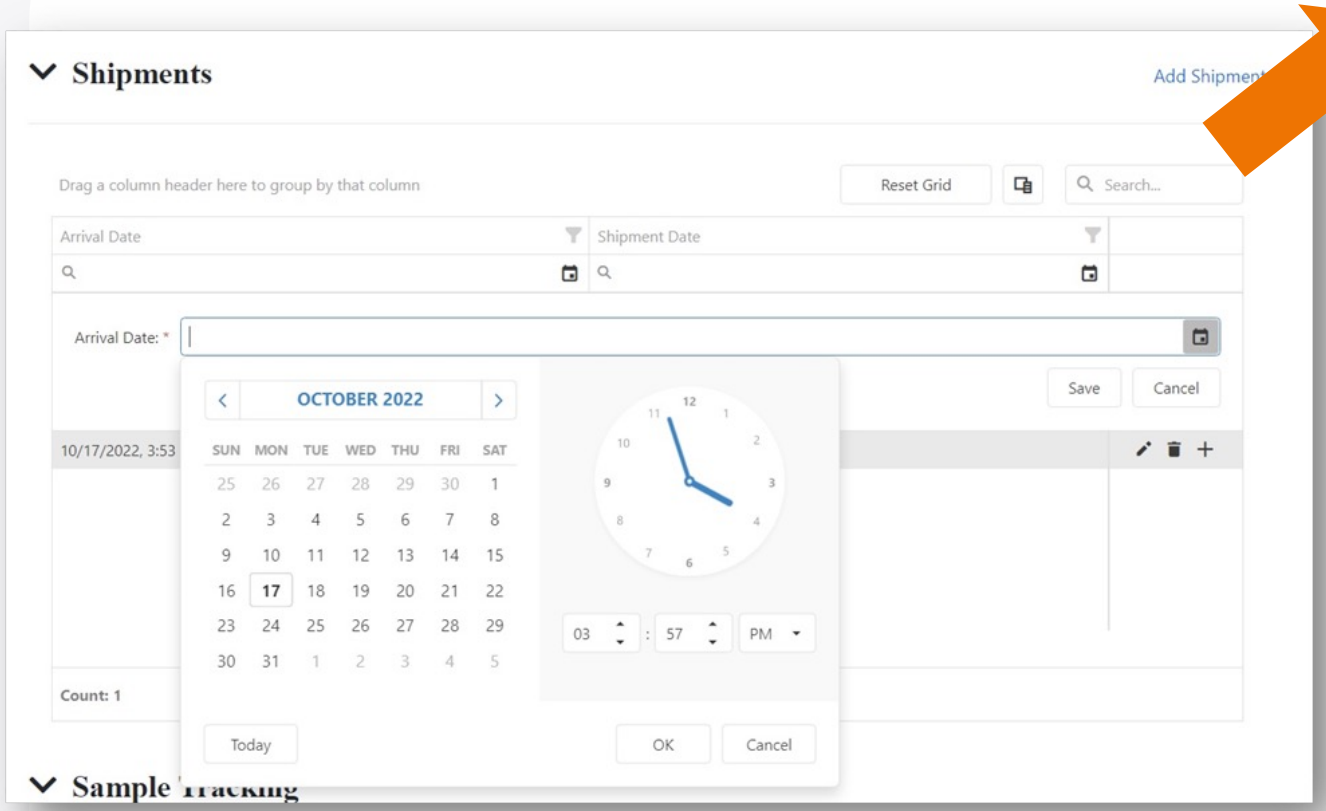
up to data

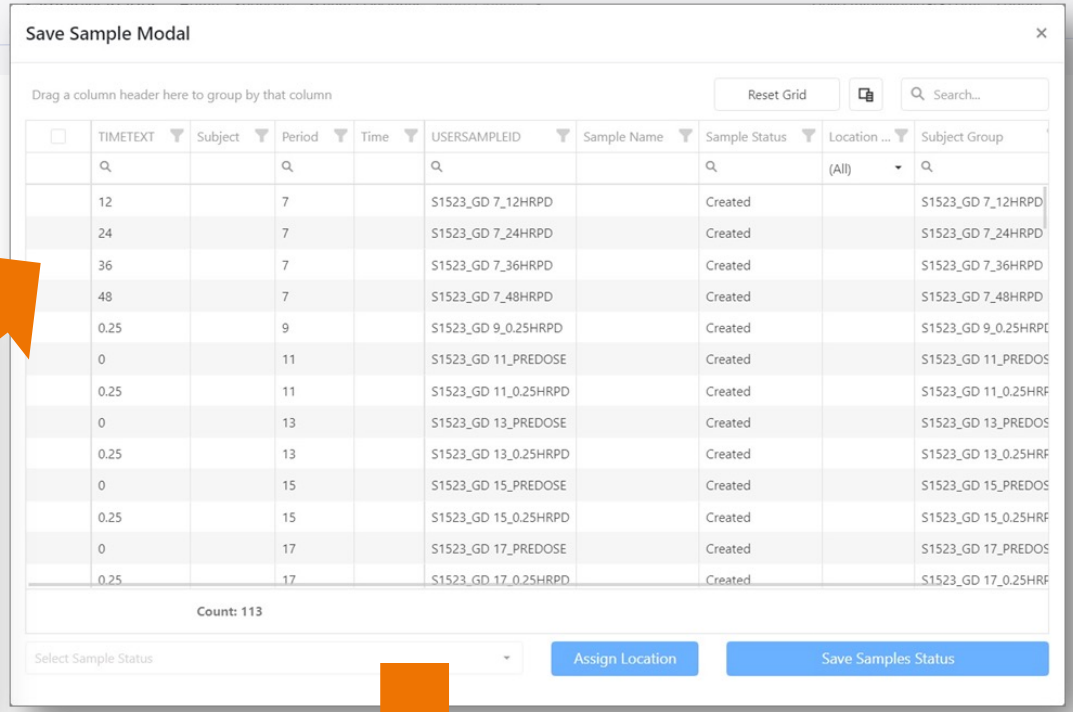
Entering Data in Forms

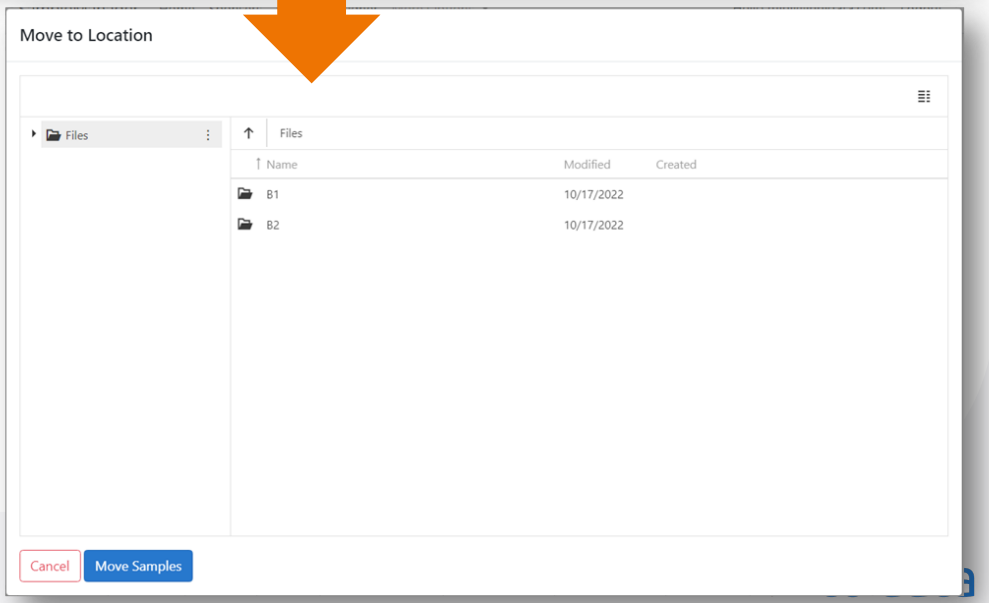


up to data

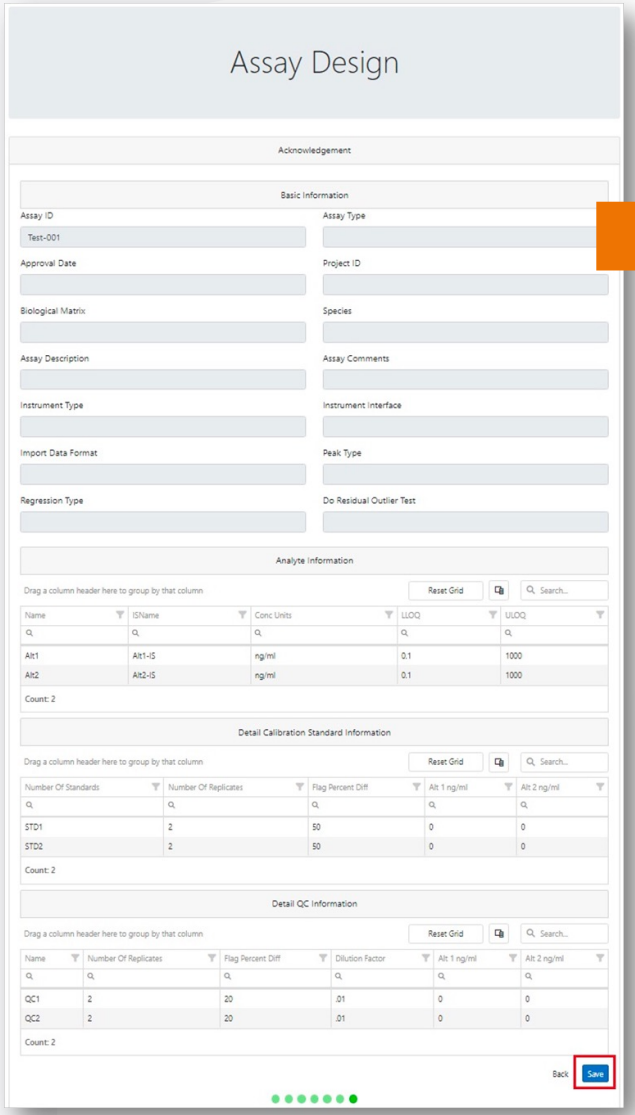
Sample Receipt and Storage



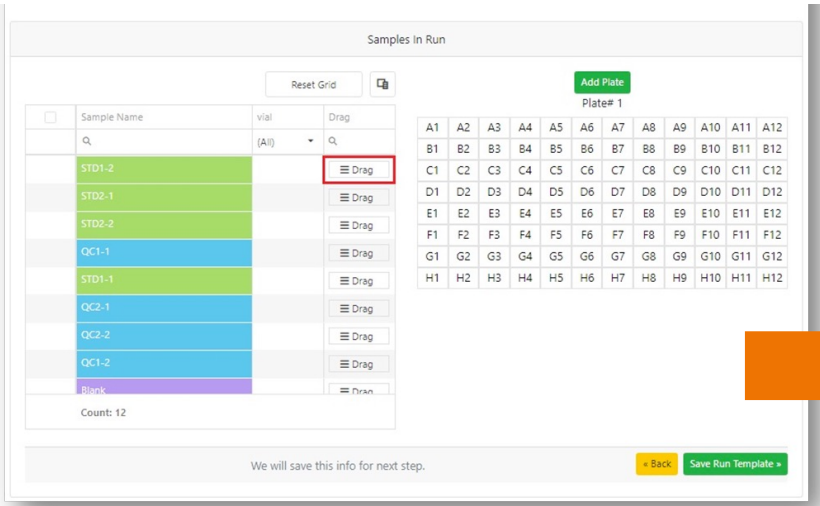




Run/Batch-Planning and Plate-Layout design



Assay to Plate-Template



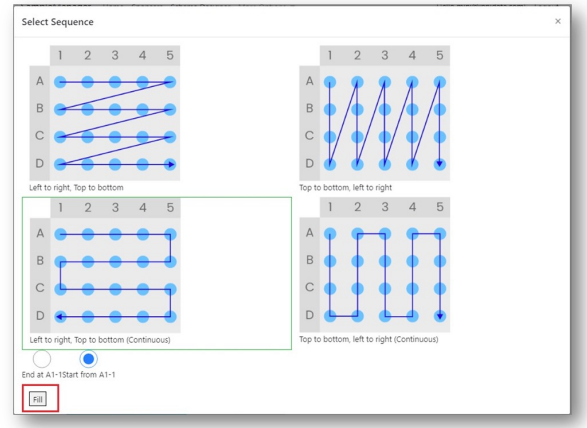
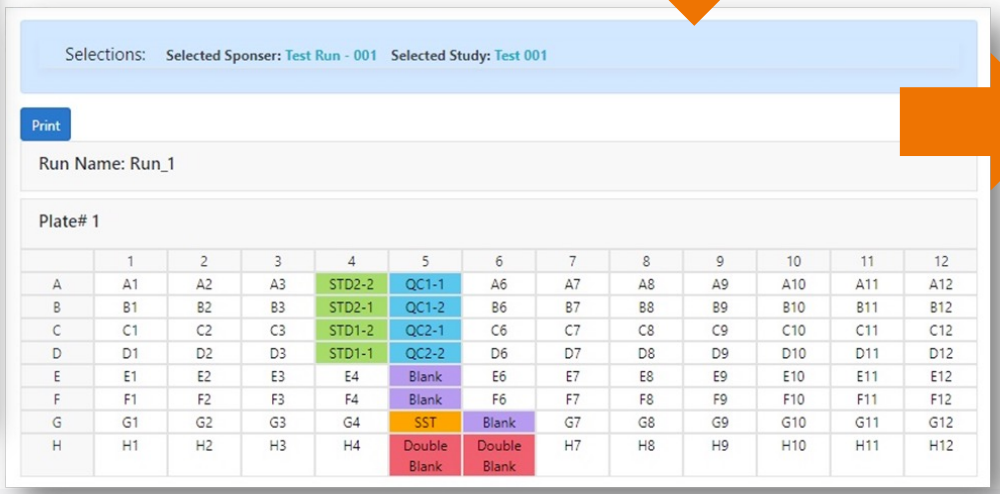
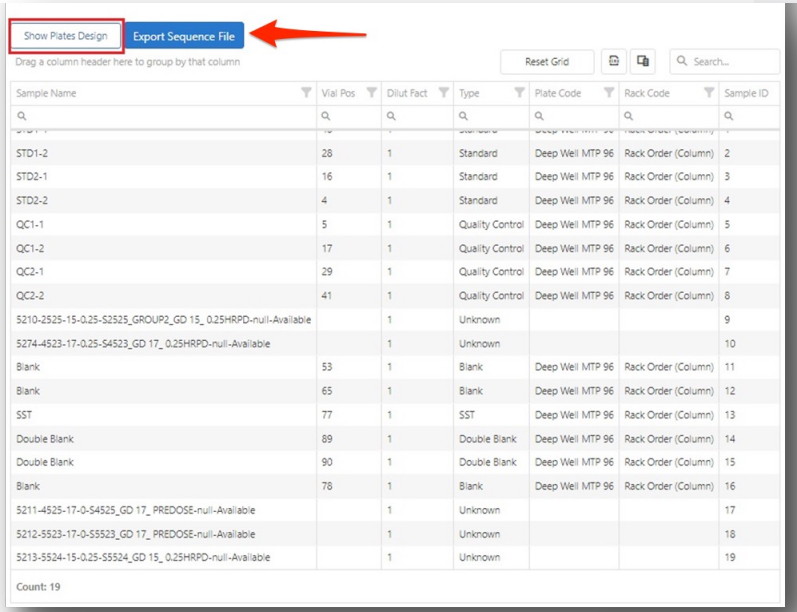
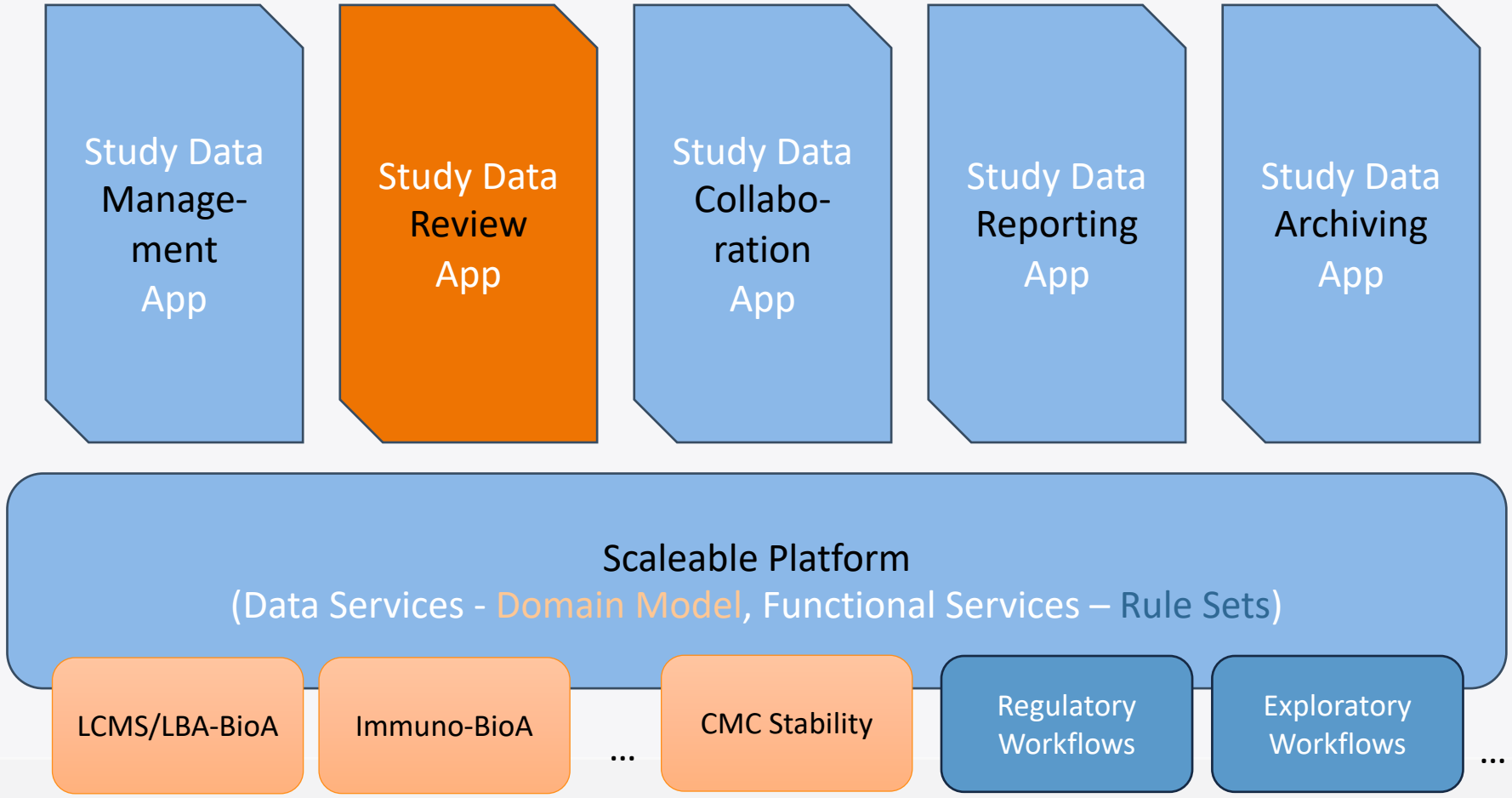


Plate-Template and Sample to create a Sequence





up to data



Study Data Review

Case Study: Enable Scientists to Investigate Data

up to data

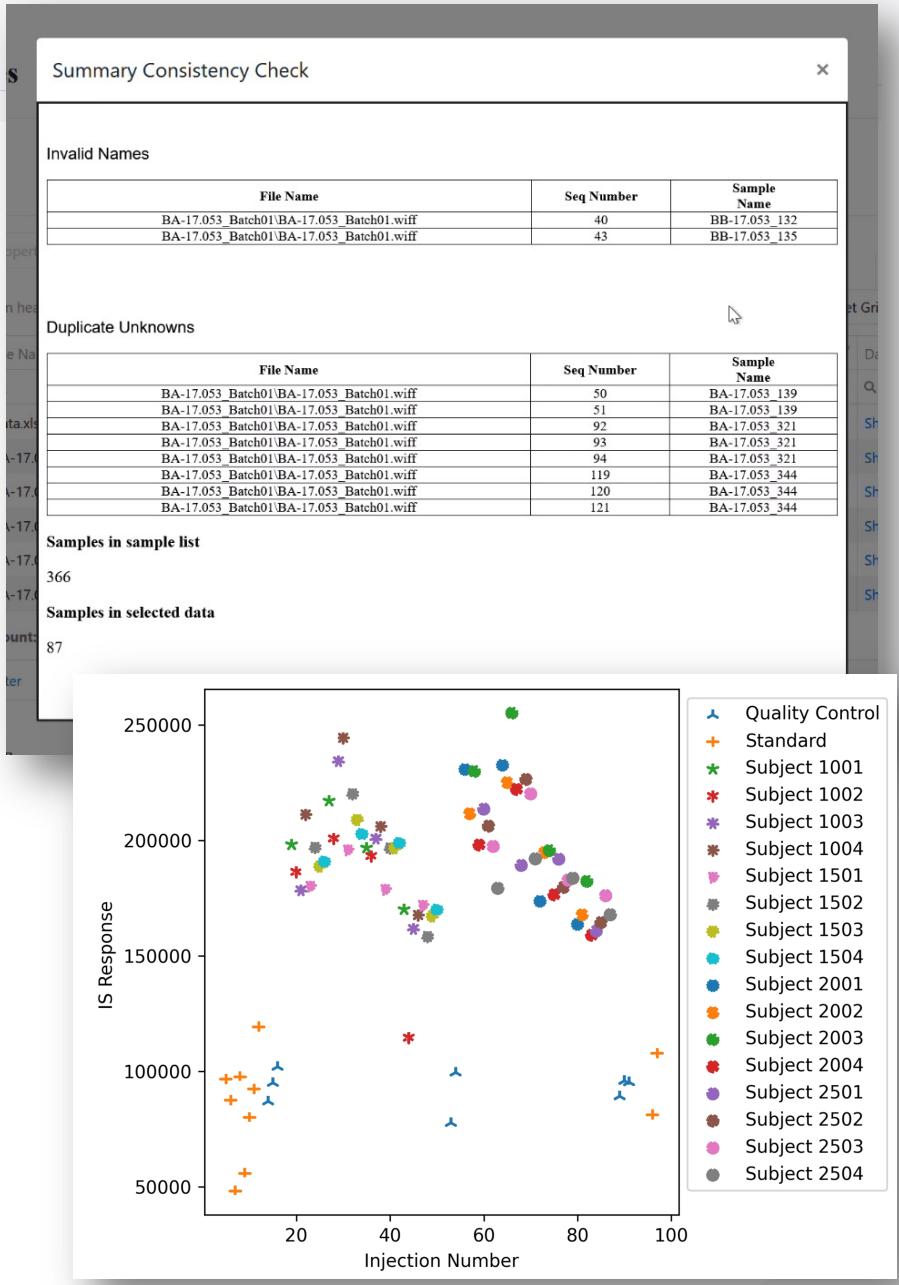
Sponsors concerns

- Quality Parameter driven data review to meet **scientific quality objectives**
  - beyond “standard” reporting provided by CRO

- Individual definition of
  - Quality Parameters (e.g)
    - Sequence of samples/injections consistent
    - Was there a stop/restart
  - Quality Attributes (e.g.)
    - Precision and Accuracy
    - Is there a cross well contamination
    - Matrix effect on STDs/QCs vs. Samples
    - Background and STDs/QC response drift and range changes (in/between runs)
    - S/N consistency
    - Specifics for LC/MS
      - Integration parameters, peak shape, IS variation, retention time variation, carryover, interference peak …

- **Templateable and reusable data analysis**

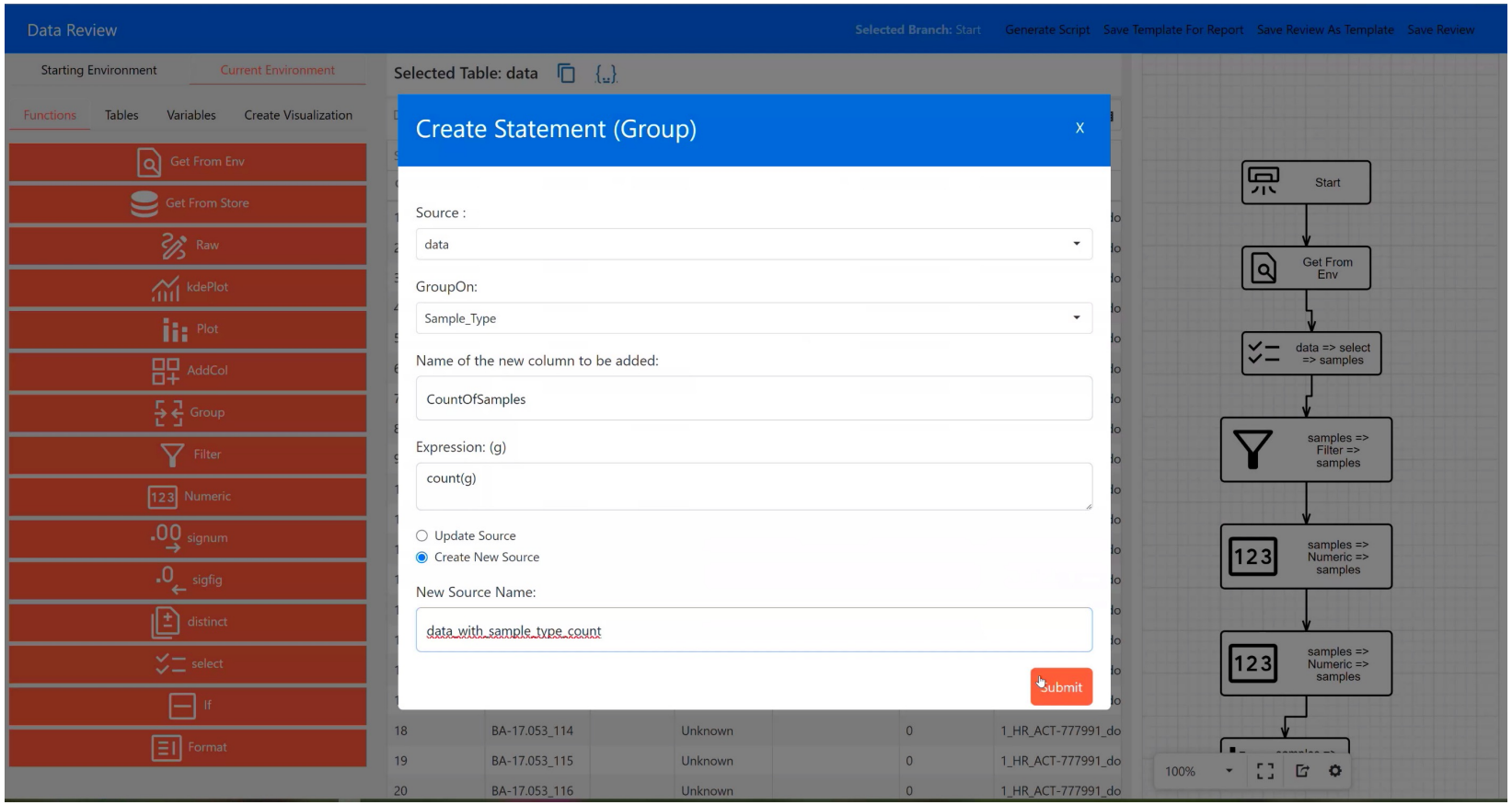
- Trackable collaboration on data-review



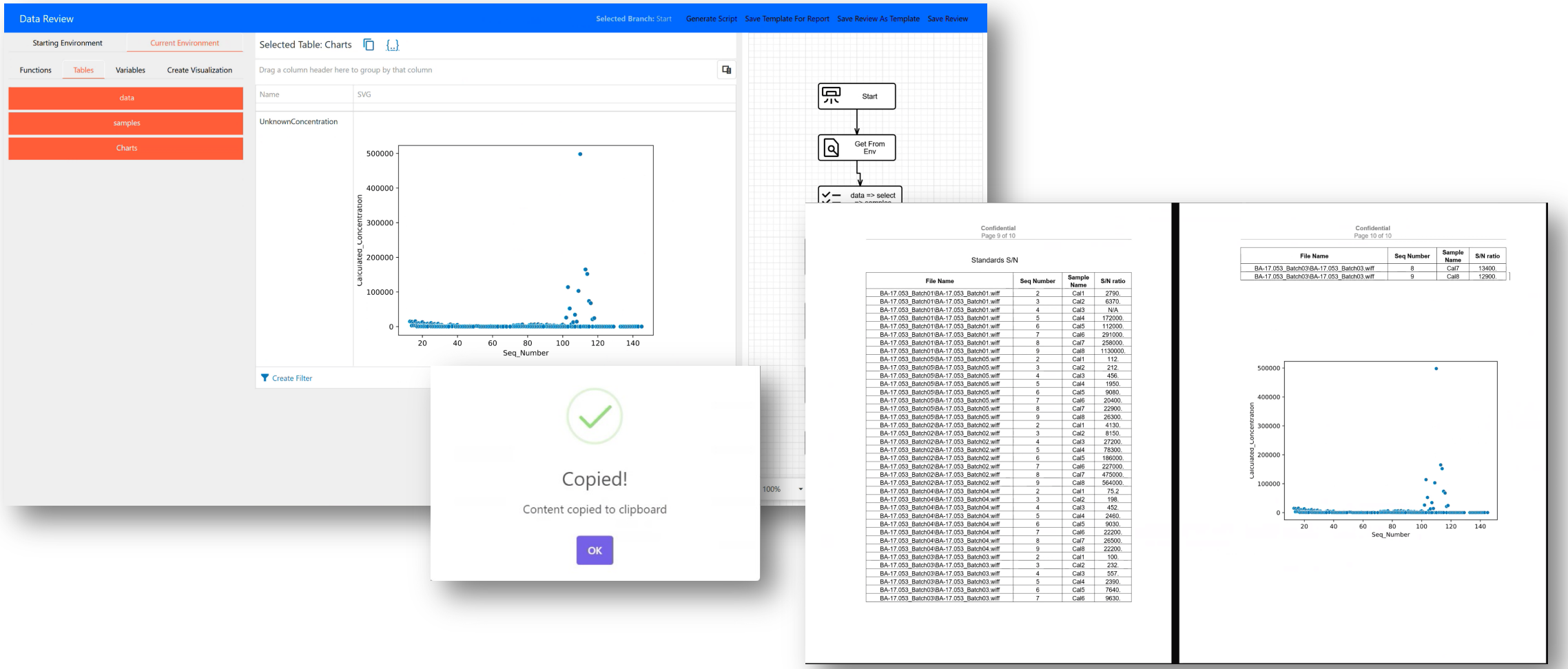
up to data

Data-Review –Templates

- Interactive Scenario-Builder to create Review-Templates
  - GUI to support configuration



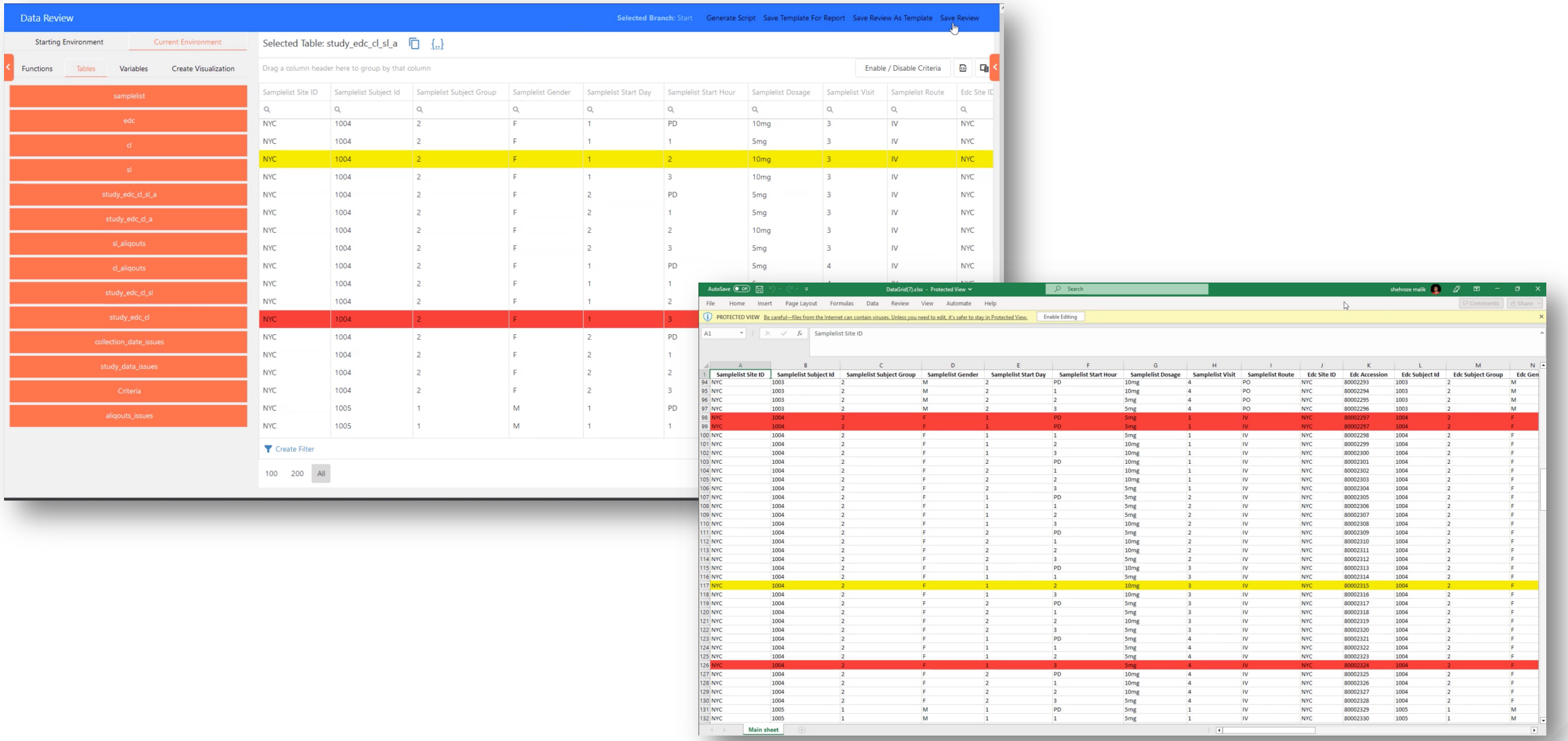
Applying a preconfigured Review-Template

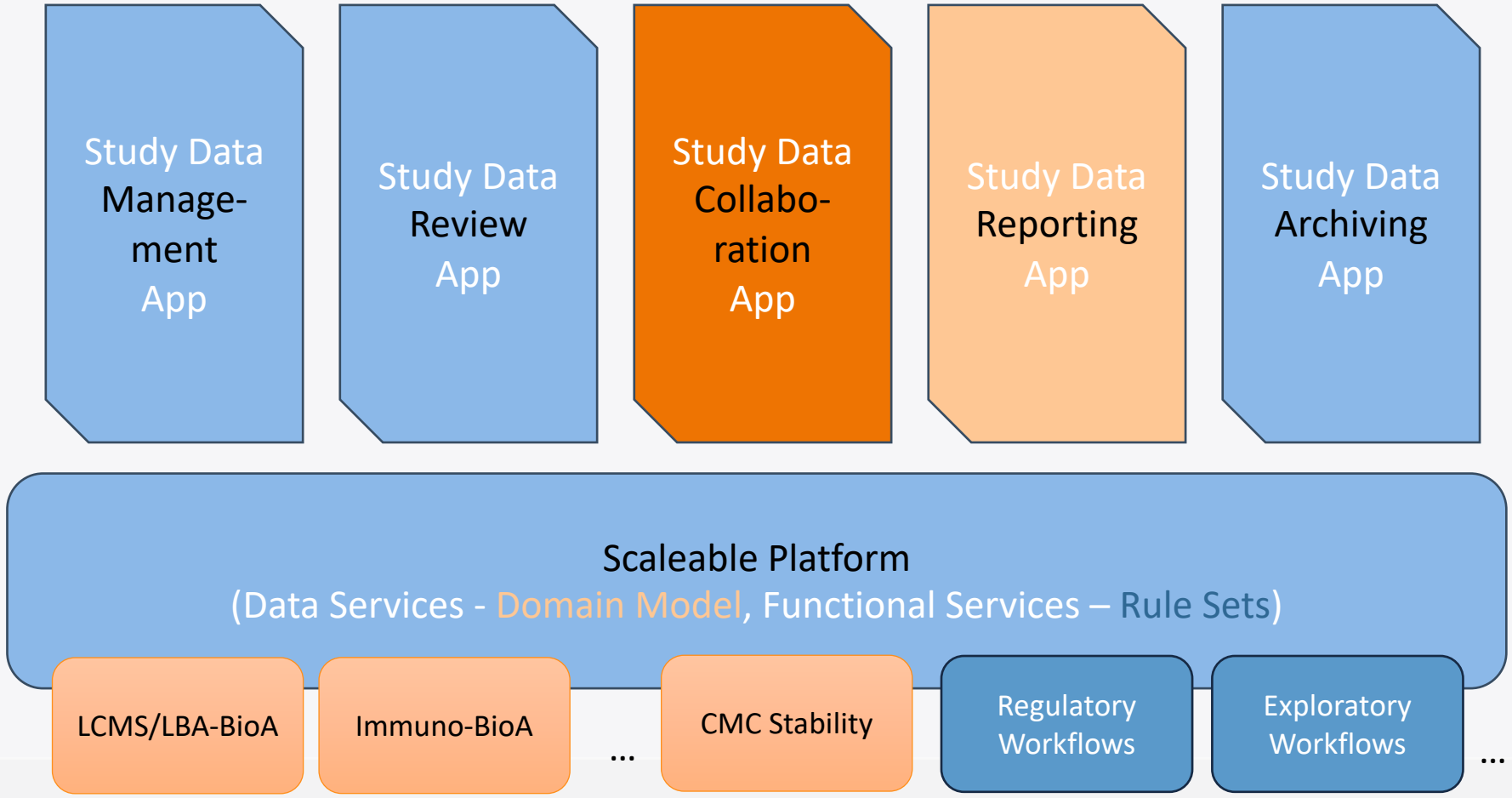


File Name	Seq Number	Sample Name	S/N ratio
BA-17.053_Batch01\BA-17.053_Batch01.wiff	2	Cal1	2790.
BA-17.053_Batch01\BA-17.053_Batch01.wiff	3	Cal2	6370.
BA-17.053_Batch01\BA-17.053_Batch01.wiff	4	Cal3	N/A
BA-17.053_Batch01\BA-17.053_Batch01.wiff	5	Cal4	172000.
BA-17.053_Batch01\BA-17.053_Batch01.wiff	6	Cal5	112000.
BA-17.053_Batch01\BA-17.053_Batch01.wiff	7	Cal6	291000.
BA-17.053_Batch01\BA-17.053_Batch01.wiff	8	Cal7	258000.
BA-17.053_Batch01\BA-17.053_Batch01.wiff	9	Cal8	1130000.
BA-17.053_Batch05\BA-17.053_Batch05.wiff	2	Cal1	112.
BA-17.053_Batch05\BA-17.053_Batch05.wiff	3	Cal2	212.
BA-17.053_Batch05\BA-17.053_Batch05.wiff	4	Cal3	456.
BA-17.053_Batch05\BA-17.053_Batch05.wiff	5	Cal4	1950.
BA-17.053_Batch05\BA-17.053_Batch05.wiff	6	Cal5	9080.
BA-17.053_Batch05\BA-17.053_Batch05.wiff	7	Cal6	20400.
BA-17.053_Batch05\BA-17.053_Batch05.wiff	8	Cal7	22900.
BA-17.053_Batch05\BA-17.053_Batch05.wiff	9	Cal8	26300.
BA-17.053_Batch02\BA-17.053_Batch02.wiff	2	Cal1	4130.
BA-17.053_Batch02\BA-17.053_Batch02.wiff	3	Cal2	8150.
BA-17.053_Batch02\BA-17.053_Batch02.wiff	4	Cal3	27200.
BA-17.053_Batch02\BA-17.053_Batch02.wiff	5	Cal4	78300.
BA-17.053_Batch02\BA-17.053_Batch02.wiff	6	Cal5	186000.
BA-17.053_Batch02\BA-17.053_Batch02.wiff	7	Cal6	227000.
BA-17.053_Batch02\BA-17.053_Batch02.wiff	8	Cal7	475000.
BA-17.053_Batch02\BA-17.053_Batch02.wiff	9	Cal8	564000.
BA-17.053_Batch04\BA-17.053_Batch04.wiff	2	Cal1	75.2
BA-17.053_Batch04\BA-17.053_Batch04.wiff	3	Cal2	198.
BA-17.053_Batch04\BA-17.053_Batch04.wiff	4	Cal3	452.
BA-17.053_Batch04\BA-17.053_Batch04.wiff	5	Cal4	2460.
BA-17.053_Batch04\BA-17.053_Batch04.wiff	6	Cal5	9030.
BA-17.053_Batch04\BA-17.053_Batch04.wiff	7	Cal6	22200.
BA-17.053_Batch04\BA-17.053_Batch04.wiff	8	Cal7	26500.
BA-17.053_Batch04\BA-17.053_Batch04.wiff	9	Cal8	22200.
BA-17.053_Batch03\BA-17.053_Batch03.wiff	2	Cal1	100.
BA-17.053_Batch03\BA-17.053_Batch03.wiff	3	Cal2	232.
BA-17.053_Batch03\BA-17.053_Batch03.wiff	4	Cal3	557.
BA-17.053_Batch03\BA-17.053_Batch03.wiff	5	Cal4	2390.
BA-17.053_Batch03\BA-17.053_Batch03.wiff	6	Cal5	7640.
BA-17.053_Batch03\BA-17.053_Batch03.wiff	7	Cal6	9630.

File Name	Seq Number	Sample Name	S/N ratio
BA-17.053_Batch03\BA-17.053_Batch03.wiff	8	Cal7	13400.
BA-17.053_Batch03\BA-17.053_Batch03.wiff	9	Cal8	12900.

Record / Field highlighting part of scenario builder to compare data





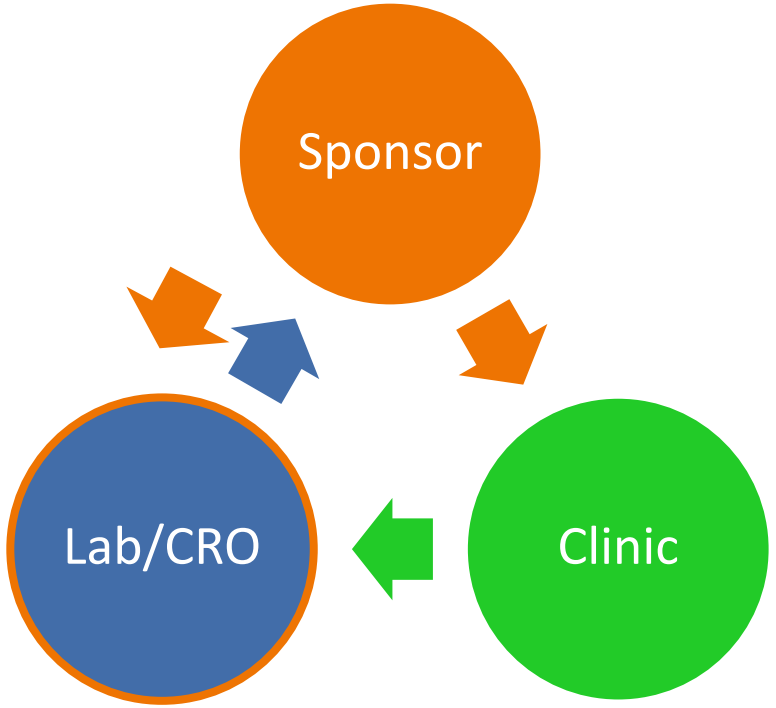
Study Data Collaboration & Reporting

Case Study: Enable Communication and Access

up to data

Who creates / is in need of what study data

- Study Data Management
  - Receive Multiple **Sample Shipment Manifest**
  - Sample **Receipt Data** Documentation
  - Handle **Demographics data** incl. „**Reconciliation**“
  - Sample Storage Documentation
  - Sample Preparation Documentation, incl. Materials
  - Run/Batch Data
    - Assay and Method Documentation
    - Run/Batch-Planning and Plate-Layout design
    - Interfacing with devices (Run-Sequence, Result-Files)
    - **Data Review and Evaluation**
    - Reassay-Handling
- Study Data Reporting
  - **Regulatory Reporting** (BioA-Report, Validation-Report)
  - **DTA Files**
  - **SEND PC-Domain Files**



up to data

DTA Files

- Configurable per Sponsor/DTA
- Consitent with any other reports

	A	B	C	D	E	F	G	H	I	J	K	L
4	Actual Sampling Date/Time	Analyte	Subject	Subject Group	Time Text	Nominal Time (Design)	Run Id	Biological Matrix Abbreviation	Concentration	Concentration (Rounded)	Concentration (Sig.Figs.)	Concentration Units
6	25-Jan-2019	Analyte1	101-001	1	D2 24H	48	1	PLM				ng/mL
7	25-Jan-2019	Analyte1	101-001	1	D2 24H	48	1	PLM				ng/mL
8	25-Jan-2019	Analyte1	101-001	1	D2 24H	48	1	PLM				ng/mL
9	25-Jan-2019	Analyte1	101-001	1	D2 24H	48	1	PLM				ng/mL
10	25-Jan-2019	Analyte1	101-001	1	D2 24H	48	1	PLM				ng/mL
11	25-Jan-2019	Analyte1	101-001	1	D2 24H	48	1	PLM				ng/mL
12	25-Jan-2019	Analyte1	101-001	1	D2 24H	48	1	PLM				ng/mL
13	25-Jan-2019	Analyte1	101-001	1	D2 24H	48	1	PLM				ng/mL
14	25-Jan-2019	Analyte1	101-001	1	D2 24H	48	1	PLM				ng/mL
15	25-Jan-2019	Analyte1	101-001	1	D2 24H	48	1	PLM				ng/mL
16	25-Jan-2019	Analyte1	101-001	1	D2 24H	48	1	PLM				ng/mL
17	25-Jan-2019	Analyte1	101-001	1	D2 24H	48	1	PLM				ng/mL
18	25-Jan-2019	Analyte1	101-001	1	D2 24H	48	1	PLM				ng/mL
19	25-Jan-2019	Analyte1	101-001	1	D2 24H	48	1	PLM				ng/mL
20	25-Jan-2019	Analyte1	101-001	1	D2 24H	48	1	PLM				ng/mL
21	25-Jan-2019	Analyte1	101-001	1	D2 24H	48	1	PLM				ng/mL
22	25-Jan-2019	Analyte1	101-001	1	D2 24H	48	1	PLM				ng/mL
23	25-Jan-2019	Analyte1	101-001	1	D2 24H	48	1	PLM	14,1752135556753	14,18	14	ng/mL
24	25-Jan-2019	Analyte1	101-001	1	D2 24H	48	1	PLM	14,1752135556753	14,18	14	ng/mL
25	25-Jan-2019	Analyte1	101-001	1	D2 24H	48	1	PLM	14,1752135556753	14,18	14	ng/mL
26	25-Jan-2019	Analyte1	101-001	1	D2 24H	48	1	PLM	14,1752135556753	14,18	14	ng/mL
27	25-Jan-2019	Analyte1	101-001	1	D2 24H	48	1	PLM	14,1752135556753	14,18	14	ng/mL
28	25-Jan-2019	Analyte1	101-001	1	D2 24H	48	1	PLM	14,1752135556753	14,18	14	ng/mL
29	25-Jan-2019	Analyte1	101-001	1	D2 24H	48	1	PLM	14,1752135556753	14,18	14	ng/mL
30	25-Jan-2019	Analyte1	101-001	1	D2 24H	48	1	PLM	14,1752135556753	14,18	14	ng/mL
31	25-Jan-2019	Analyte1	101-001	1	D2 24H	48	1	PLM	14,1752135556753	14,18	14	ng/mL
32	25-Jan-2019	Analyte1	101-001	1	D2 24H	48	1	PLM	14,1752135556753	14,18	14	ng/mL
33	25-Jan-2019	Analyte1	101-001	1	D2 24H	48	1	PLM	14,1752135556753	14,18	14	ng/mL
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35	25-Jan-2019	Analyte1	101-001	1	D2 24H	48	1	PLM	14,1752135556753	14,18	14	ng/mL
36	25-Jan-2019	Analyte1	101-001	1	D2 24H	48	1	PLM	14,1752135556753	14,18	14	ng/mL
37	25-Jan-2019	Analyte1	101-001	1	D2 24H	48	1	PLM	14,1752135556753	14,18	14	ng/mL
38	25-Jan-2019	Analyte1	101-001	1	D2 24H	48	1	PLM	14,1752135556753	14,18	14	ng/mL
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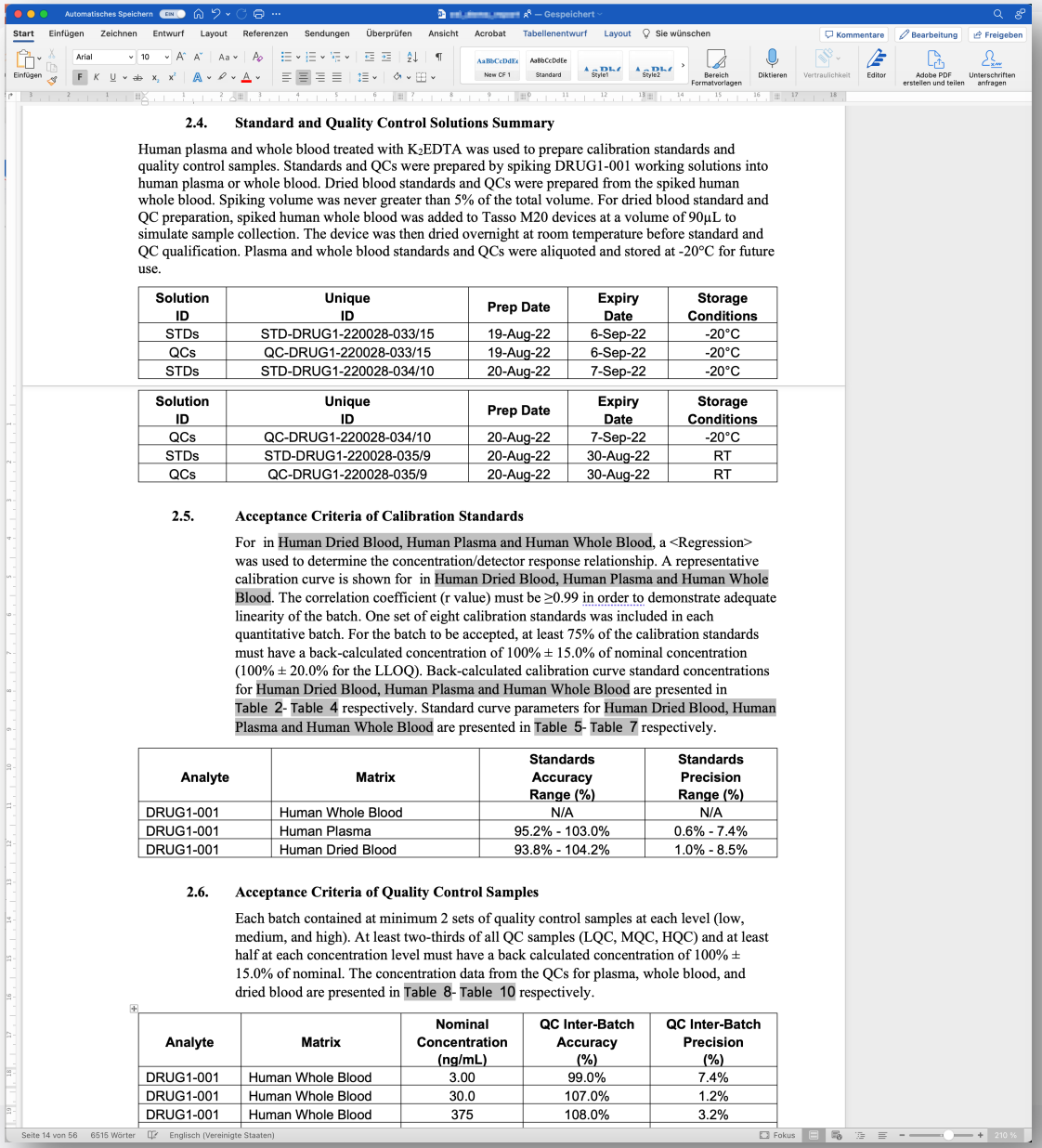
40	25-Jan-2019	Analyte1	101-001	1	D2 24H	48	1	PLM	14,1752135556753	14,18	14	ng/mL
41	25-Jan-2019	Analyte1	101-001	1	D2 24H	48	1	PLM	14,1752135556753	14,18	14	ng/mL
42	25-Jan-2019	Analyte1	101-001	1	D2 24H	48	1	PLM	14,1752135556753	14,18	14	ng/mL
43	25-Jan-2019	Analyte1	101-001	1	D2 24H	48	1	PLM	14,1752135556753	14,18	14	ng/mL
44	25-Jan-2019	Analyte1	101-001	1	D2 24H	48	1	PLM	14,1752135556753	14,18	14	ng/mL

Regulatory Reporting (M10 Scope)



2.4. Standard and Quality Control Solutions Summary

Human plasma and whole blood treated with K_2EDTA was used to prepare calibration standards and quality control samples. Standards and QCs were prepared by spiking DRUG1-001 working solutions into human plasma or whole blood. Dried blood standards and QCs were prepared from the spiked human whole blood. Spiking volume was never greater than 5% of the total volume. For dried blood standard and QC preparation, spiked human whole blood was added to Tasso M20 devices at a volume of 90µL to simulate sample collection. The device was then dried overnight at room temperature before standard and QC qualification. Plasma and whole blood standards and QCs were aliquoted and stored at -20°C for future use.

Solution ID	Unique ID	Prep Date	Expiry Date	Storage Conditions
STDs	STD-DRUG1-220028-033/15	19-Aug-22	6-Sep-22	-20°C
QCs	QC-DRUG1-220028-033/15	19-Aug-22	6-Sep-22	-20°C
STDs	STD-DRUG1-220028-034/10	20-Aug-22	7-Sep-22	-20°C

Solution ID	Unique ID	Prep Date	Expiry Date	Storage Conditions
QCs	QC-DRUG1-220028-034/10	20-Aug-22	7-Sep-22	-20°C
STDs	STD-DRUG1-220028-035/9	20-Aug-22	30-Aug-22	RT
QCs	QC-DRUG1-220028-035/9	20-Aug-22	30-Aug-22	RT

2.5. Acceptance Criteria of Calibration Standards

For in Human Dried Blood, Human Plasma and Human Whole Blood, a <Regression> was used to determine the concentration/detector response relationship. A representative calibration curve is shown for in Human Dried Blood, Human Plasma and Human Whole Blood. The correlation coefficient (r value) must be ≥0.99 in order to demonstrate adequate linearity of the batch. One set of eight calibration standards was included in each quantitative batch. For the batch to be accepted, at least 75% of the calibration standards must have a back-calculated concentration of 100% ± 15.0% of nominal concentration (100% ± 20.0% for the LLOQ). Back-calculated calibration curve standard concentrations for Human Dried Blood, Human Plasma and Human Whole Blood are presented in Table 2- Table 4 respectively. Standard curve parameters for Human Dried Blood, Human Plasma and Human Whole Blood are presented in Table 5- Table 7 respectively.

Analyte	Matrix	Standards Accuracy Range (%)	Standards Precision Range (%)
DRUG1-001	Human Whole Blood	N/A	N/A
DRUG1-001	Human Plasma	95.2% - 103.0%	0.6% - 7.4%
DRUG1-001	Human Dried Blood	93.8% - 104.2%	1.0% - 8.5%

2.6. Acceptance Criteria of Quality Control Samples

Each batch contained at minimum 2 sets of quality control samples at each level (low, medium, and high). At least two-thirds of all QC samples (LQC, MQC, HQC) and at least half at each concentration level must have a back calculated concentration of 100% ± 15.0% of nominal. The concentration data from the QCs for plasma, whole blood, and dried blood are presented in Table 8- Table 10 respectively.

Analyte	Matrix	Nominal Concentration (ng/mL)	QC Inter-Batch Accuracy (%)	QC Inter-Batch Precision (%)
DRUG1-001	Human Whole Blood	3.00	99.0%	7.4%
DRUG1-001	Human Whole Blood	30.0	107.0%	1.2%
DRUG1-001	Human Whole Blood	375	108.0%	3.2%

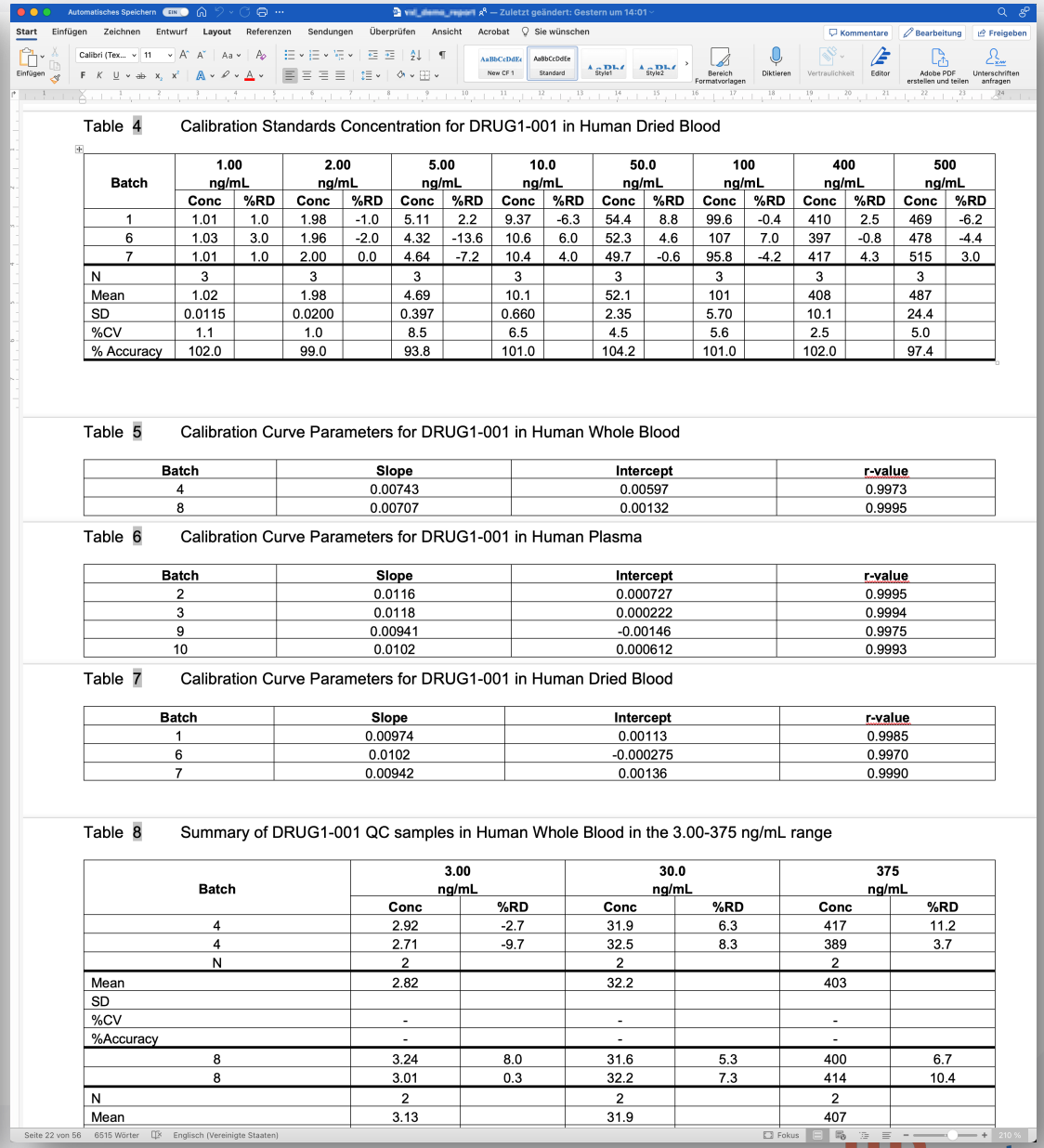


Table 4 Calibration Standards Concentration for DRUG1-001 in Human Dried Blood

Batch	1.00 ng/mL		2.00 ng/mL		5.00 ng/mL		10.0 ng/mL		50.0 ng/mL		100 ng/mL		400 ng/mL		500 ng/mL	
	Conc	%RD	Conc	%RD	Conc	%RD	Conc	%RD	Conc	%RD	Conc	%RD	Conc	%RD	Conc	%RD
1	1.01	1.0	1.98	-1.0	5.11	2.2	9.37	-6.3	54.4	8.8	99.6	-0.4	410	2.5	469	-6.2
6	1.03	3.0	1.96	-2.0	4.32	-13.6	10.6	6.0	52.3	4.6	107	7.0	397	-0.8	478	-4.4
7	1.01	1.0	2.00	0.0	4.64	-7.2	10.4	4.0	49.7	-0.6	95.8	-4.2	417	4.3	515	3.0
N	3		3		3		3		3		3		3		3	
Mean	1.02		1.98		4.69		10.1		52.1		101		408		487	
SD	0.0115		0.0200		0.397		0.660		2.35		5.70		10.1		24.4	
%CV	1.1		1.0		8.5		6.5		4.5		5.6		2.5		5.0	
% Accuracy	102.0		99.0		93.8		101.0		104.2		101.0		102.0		97.4	

Table 5 Calibration Curve Parameters for DRUG1-001 in Human Whole Blood

Batch	Slope	Intercept	r-value
4	0.00743	0.00597	0.9973
8	0.00707	0.00132	0.9995

Table 6 Calibration Curve Parameters for DRUG1-001 in Human Plasma

Batch	Slope	Intercept	r-value
2	0.0116	0.000727	0.9995
3	0.0118	0.000222	0.9994
9	0.00941	-0.00146	0.9975
10	0.0102	0.000612	0.9993

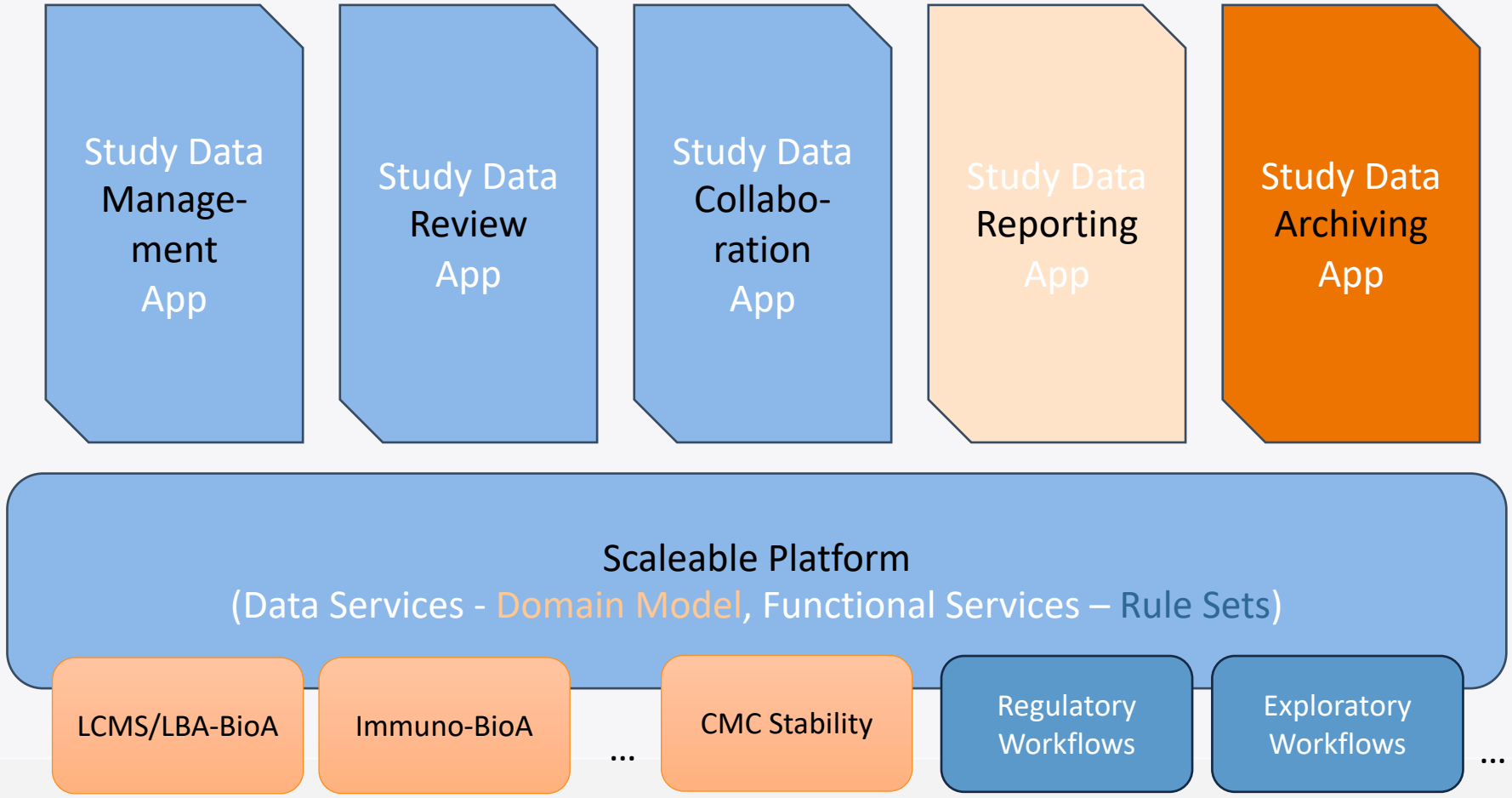
Table 7 Calibration Curve Parameters for DRUG1-001 in Human Dried Blood

Batch	Slope	Intercept	r-value
1	0.00974	0.00113	0.9985
6	0.0102	-0.000275	0.9970
7	0.00942	0.00136	0.9990

Table 8 Summary of DRUG1-001 QC samples in Human Whole Blood in the 3.00-375 ng/mL range

Batch	3.00 ng/mL		30.0 ng/mL		375 ng/mL	
	Conc	%RD	Conc	%RD	Conc	%RD
4	2.92	-2.7	31.9	6.3	417	11.2
4	2.71	-9.7	32.5	8.3	389	3.7
N	2		2		2	
Mean	2.82		32.2		403	
SD						
%CV	-		-		-	
%Accuracy	-		-		-	
8	3.24	8.0	31.6	5.3	400	6.7
8	3.01	0.3	32.2	7.3	414	10.4
N	2		2		2	
Mean	3.13		31.9		407	

up to data



Study Data Archiving

Mission: A New Approach to Archiving

up to data

Study Archiving Framework

- Refer to https://www.fda.gov/media/75414/download
- US FDA Guidance for Industry: „21 CFR Part 11; Electronic Records; Electronic Signatures; Maintenance of Electronic Records“ was **withdrawn** (line 100)
  - Section 11.10 (b) was requesting: “The ability to generate accurate and complete copies of records in **both human readable and electronic** form suitable for inspection, review, and copying by the agency“
  - Replaced with **recommendation** (line 284ff):

    “We recommend that you supply **copies of electronic records** by: …

    Using established automated conversion or export methods, where available, to make copies **in a more common format** (examples of such formats include, but are not limited to, PDF, XML, or SGML).

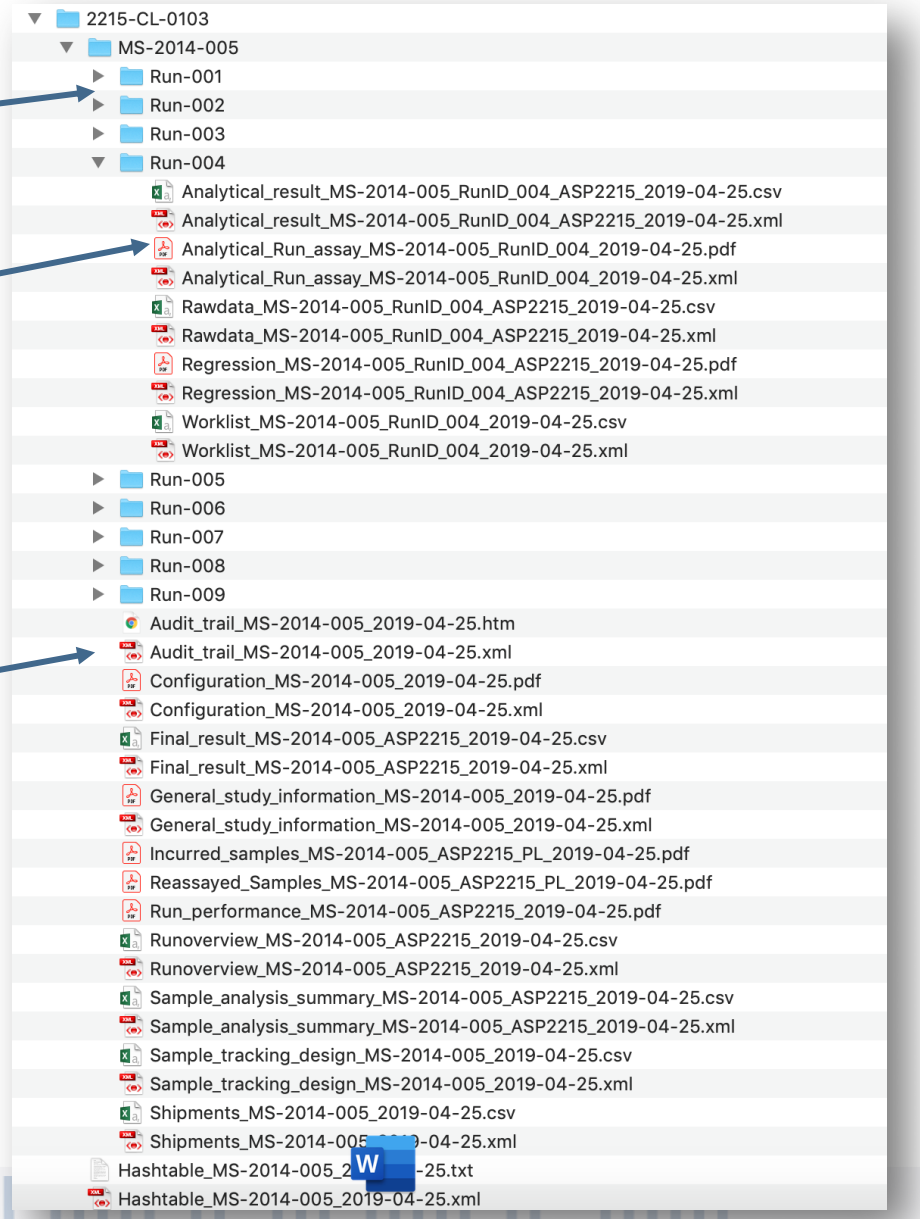
    …

    In each case, we recommend that the copying process used produces copies that preserve the content and meaning of the record. …”

- Case Study: Create Study Archive mechanism that is
  - human readable for fast review without addtl. software
  - consistent with prior submission documents (statistics, comments, ...)
  - as light-weight as possible
  - makes all data accessible to be further processed without knowledge of any software

Human Readable

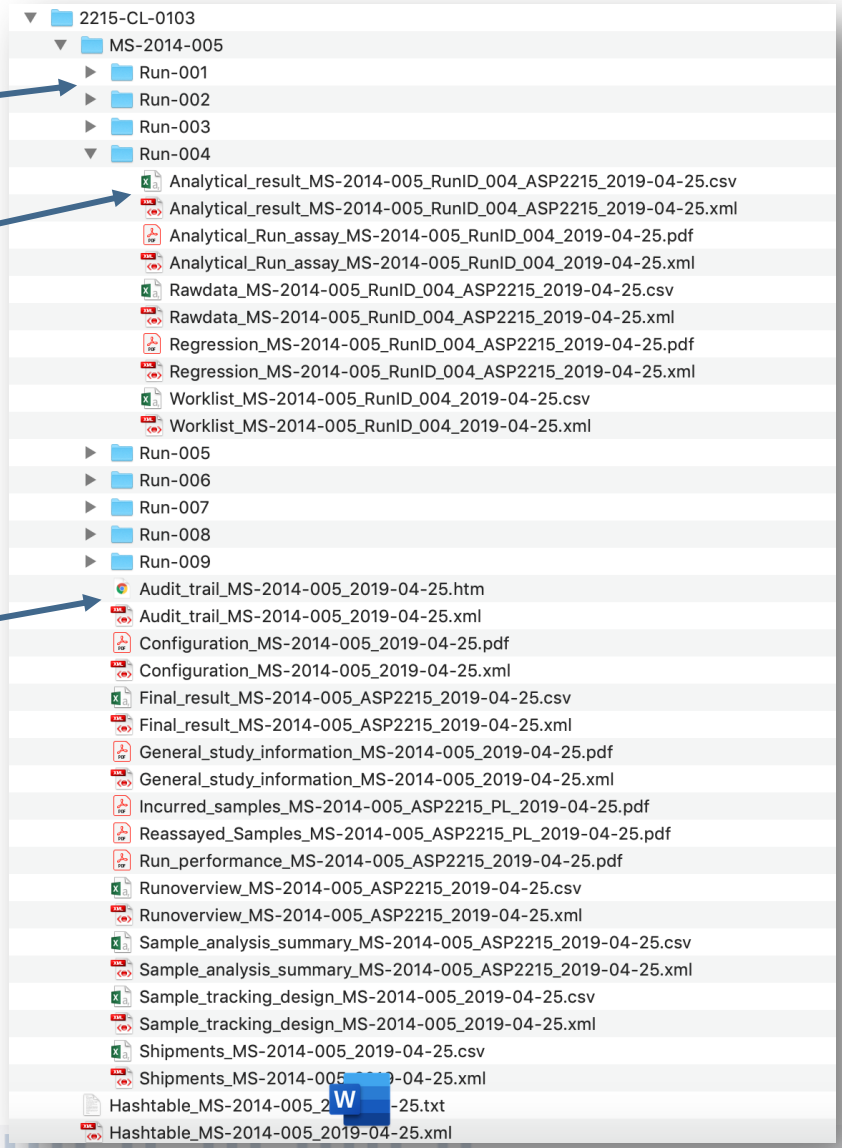
- PDF document stack
  - Structure by RUN
  - Individual analyte reports
    - with "raw" response value tabulation
    - calibration data (regression info)
    - processing information
    - ...
  - Structure by STUDY
    - Audit trail
    - …



up to data

Accessible Data

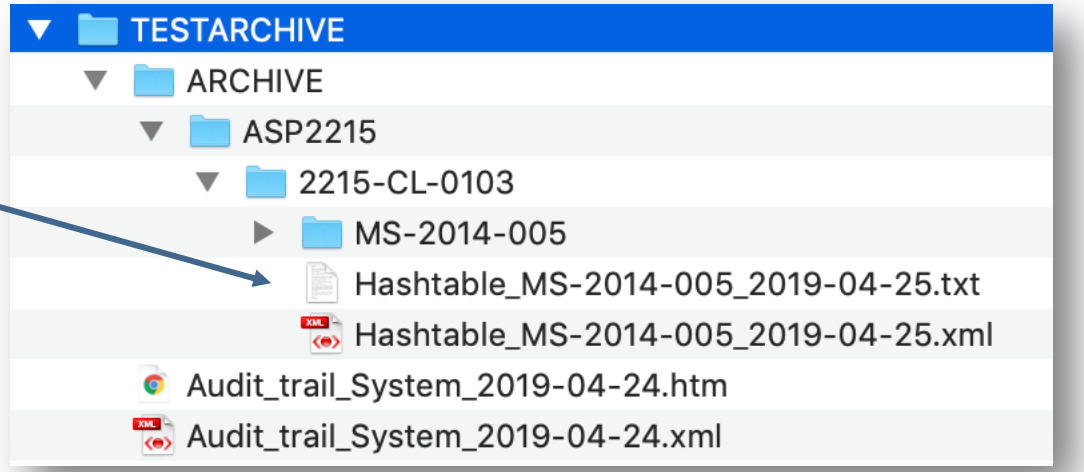
- XML and/or CSV file stack
  - Structure by RUN
  - Individual analyte data
    - with "raw" response value tabulation
    - calibration data (regression info)
    - processing information
    - ...
  - Structure by STUDY
    - Audit trail



up to data

Data Integrity

- File with checksum of all files
  - Hash-values of files
- Checksum of this file in processing protocol
  - Hash of Hashes



Algorithm	Hash	Path
SHA256	8e8b22f10cf4516115796809041a2e54df9970a3520ee7ada03dd38056577530	ASP2215\2215-CL-0103\MS-2014-005\Run-001\Analytical_Run_assay_MS-2014-005_RunID_001_2019-04-25.pdf
SHA256	c4dadba6c5234df7d299c914348e9ec537fc5842266b03453cb4f240ea072fc7	ASP2215\2215-CL-0103\MS-2014-005\Run-001\Analytical_Run_assay_MS-2014-005_RunID_001_2019-04-25.xml
SHA256	8b51c10e1746a14fa46085fa067b16a01293765e6dc904cc27a37d3c2aab03a0	ASP2215\2215-CL-0103\MS-2014-005\Run-002\Analytical_Run_assay_MS-2014-005_RunID_002_2019-04-25.pdf
SHA256	adb248c5c4f4d788817f9464786d9dbd562917881714ea11736a68eed6d1bc78	ASP2215\2215-CL-0103\MS-2014-005\Run-002\Analytical_Run_assay_MS-2014-005_RunID_002_2019-04-25.xml
SHA256	98364a74f43e9105604166c1f33da8f0dbdfd5b33c3a953e59be7c1db5c86448	ASP2215\2215-CL-0103\MS-2014-005\Run-003\Analytical_Run_assay_MS-2014-005_RunID_003_2019-04-25.pdf
SHA256	83e10afa4adbb3b5a79880dbfaa7d7764343b8cfce23a5e5d0708b3784cce9bb	ASP2215\2215-CL-0103\MS-2014-005\Run-003\Analytical_Run_assay_MS-2014-005_RunID_003_2019-04-25.xml
SHA256	5c6d45a2c5f6824363619d18d424e63fa8177f184bce4a01dedcb24f332424b1	ASP2215\2215-CL-0103\MS-2014-005\Run-004\Analytical_Run_assay_MS-2014-005_RunID_004_2019-04-25.pdf
SHA256	3fcd126fb6f0fb01d467b3ab97e16b992647b098e41a2ab6b84f0f9ad5d12001	ASP2215\2215-CL-0103\MS-2014-005\Run-004\Analytical_Run_assay_MS-2014-005_RunID_004_2019-04-25.xml
SHA256	4f2726ea14f1f639f0a5f24f0b8f144b0a0f782b97444395080c4dd987cd1421	ASP2215\2215-CL-0103\MS-2014-005\Run-005\Analytical_Run_assay_MS-2014-005_RunID_005_2019-04-25.pdf
SHA256	7b5ee1be9c160e74bcd5d387935534055a6f02aa5420541c316ee5fe793ce16c	ASP2215\2215-CL-0103\MS-2014-005\Run-005\Analytical_Run_assay_MS-2014-005_RunID_005_2019-04-25.xml
SHA256	fc8ed60f0024733c2af619474843808bb574cdf9da4767ddab84d9c4a3594cb0	ASP2215\2215-CL-0103\MS-2014-005\Run-006\Analytical_Run_assay_MS-2014-005_RunID_006_2019-04-25.pdf
SHA256	b2c7f88286b9a852cfb4bb52972926a587bb955b060b5903670739682c4f8ff6	ASP2215\2215-CL-0103\MS-2014-005\Run-006\Analytical_Run_assay_MS-2014-005_RunID_006_2019-04-25.xml
SHA256	47293e719e61a39eff593fb833cff1613de1a7d34de293724105fc49ca89958f	ASP2215\2215-CL-0103\MS-2014-005\Run-007\Analytical_Run_assay_MS-2014-005_RunID_007_2019-04-25.pdf
SHA256	6e10ecdfda1a49a4760ca9d5cfe7f6e4fd08a85c8501ed7ad28a7f8005b2a60c	ASP2215\2215-CL-0103\MS-2014-005\Run-007\Analytical_Run_assay_MS-2014-005_RunID_007_2019-04-25.xml
SHA256	0755d7cf2d11eb67ee1c3e9f034bbb7331b1cb4785c6c3061bccaba67e40df38	ASP2215\2215-CL-0103\MS-2014-005\Run-008\Analytical_Run_assay_MS-2014-005_RunID_008_2019-04-25.pdf

Thank you for your attention

Contact for questions/comments

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