



BAYER'S ALYCE: ADVANCING DRUG DEVELOPMENT WITH DATA INTELLIGENCE

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CDS & A
Clinical Data Sciences & Analytics

June 2024



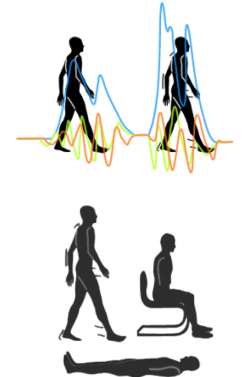
Data collected at on-site visits

- // Demographics
- // Weight, Height
- // Vital Signs
- // Single 12 Lead ECGs
- // Adverse Events, Medical History
- // ...

Data from Digital Health Technologies collected at optimal time points e.g.:

Actigraphy devices

- // Physical Activity
- // Energy Expenditure
- // Sleep Activity
- // Body Posture



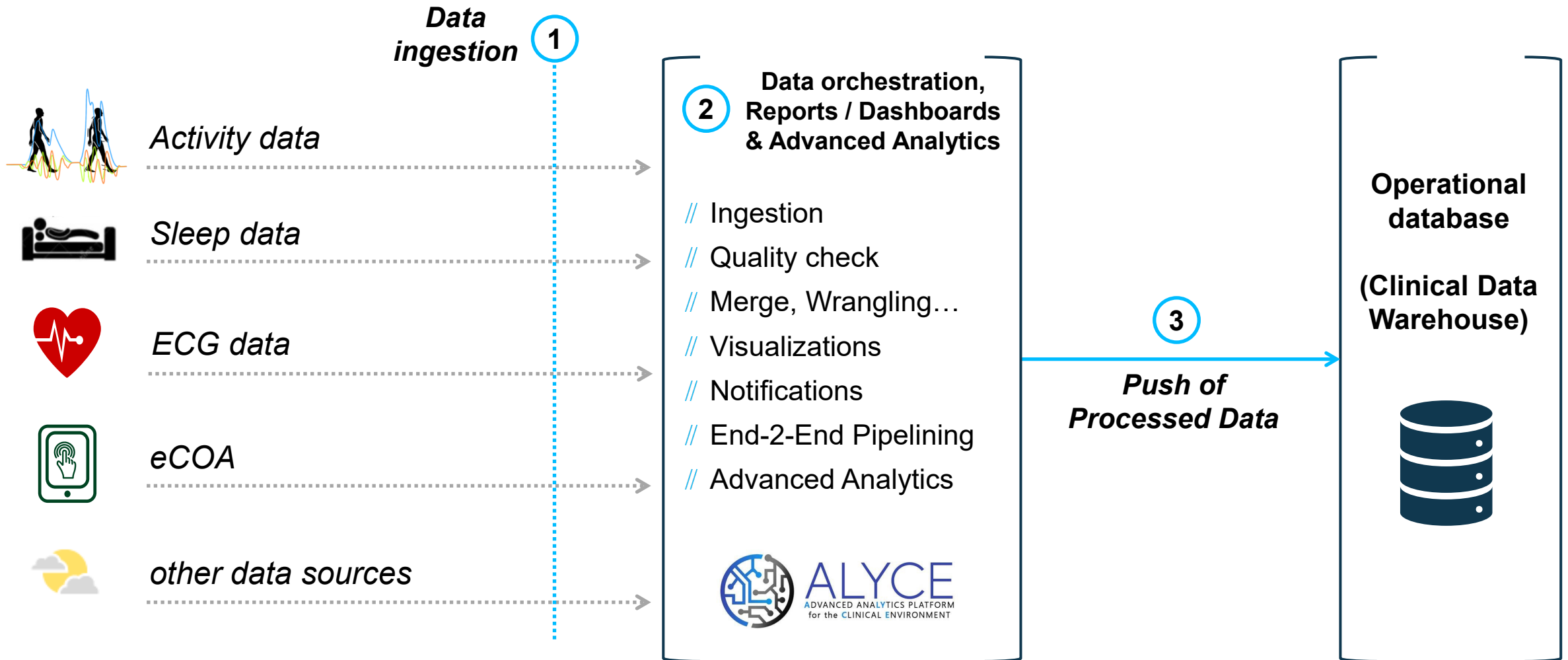
ECG Patches

- // Heart Rate
- // Respiratory Rate
- // R-to-R Interval
- // Fluid Status



Volume, Speed and Complexity of generated data will increase

Ingesting / Wrangling / Analysing





Therapeutic Area Overarching (TAO) dashboards (AE)

Pages

- Home
- Study Landing Page
- Baseline Characteristics
- Adverse Events**
- Labs
- Medical History
- Prior and Concomitant ...
- ECG
- Vital Signs
- Study Status & Visits
- Study Drug Information
- Procedures

File Export Share Chat in Teams Get insights Subscribe to report
Bay Number Study Number Default View

Adverse Events

Subjects with AE: 17
Subjects with TEAE: 14
Subjects with SAE: 5
Subjects with TESAE: 4
Subjects with AE Fatal: 0
Subjects with TEAE Fatal: 0

Graph Category: Worst Intensity

Summary | Graphs | Tables

Subject

Search

Select all

- 888851001
- 888851239
- 888852606
- 888852607
- 888852608
- 888852609
- 888852611
- 888852612
- 888852619
- 888852620
- 888852622

of AEs Related to Any SD

N: 25, Y: 2

of AEs Related to PP

(B...): 17, N: 8

of AEs per Outcome of Event

RECOVERING/RESOLVING: 27

RECOVERED/RESOLVED: 18

RECOVERED/RESOLVED WITH SEQUE...: 10

FATAL: 7

NOT RECOVERED/NOT RESOLVED: 6

UNKNOWN: 2

Adverse Events - Tables

| System Organ Class | # of Terms | % of Terms |
|---|------------|------------|
| | 19 | 70.37% |
| Nervous system disorders | 4 | 14.81% |
| Infections and infestations | 2 | 7.41% |
| Musculoskeletal and connective tissue disorders | 1 | 3.70% |
| Skin and subcutaneous tissue disorders | 1 | 3.70% |

of AEs per Action Taken

null: 16

DOSE NOT CHANGED: 7

NOT APPLICABLE: 2

DRUG INTERRUPTED: 1

DRUG WITHDRAWN: 1

of AEs per MedDRA Terminology

Worst Intensity: (Blank) MILD MODERATE SEVERE

MedDRA SOC: (Blank) 8, Nervous system disorders 3, Infections and infestations 1, Musculoskeletal and connective ... 1

Adverse Event Details

| Subject | AE # | Reported Term | MedDRA SOC | MedDRA HLGT | MedDRA HLT | MedDRA PT | MedDRA LLT | Category | Age | Sex | Race | Ev |
|-----------|------|-----------------------------|------------------------------|------------------------------|------------------------------|------------------|--------------------|-----------|----------|-----|------|----|
| 888856003 | 1 | epilepsy | Nervous system disorders | Seizures (incl subtypes) | Seizures and seizure diso... | Epilepsy | Epilepsy | OTHER | 82 YEARS | F | | 20 |
| 888856003 | 2 | headache | Nervous system disorders | Headaches | Headaches NEC | Headache | Headache | OTHER | 82 YEARS | F | | 20 |
| 888856003 | 3 | Liver event test1 | | | | | | OTHER | 82 YEARS | F | | 20 |
| 888856001 | 2 | Flu | Infections and infestatio... | Viral infectious disorders | Influenza viral infections | Influenza | Flu | OTHER | 75 YEARS | F | | 20 |
| 888856001 | OE1 | Skin bleeding | Skin and subcutaneous ... | Skin vascular abnormaliti... | Skin haemorrhages | Skin haemorrh... | Skin bleeding | BLEEDI... | 75 YEARS | F | | 20 |
| 888856001 | 1 | Worsening of knee arthro... | Musculoskeletal and co... | Joint disorders | Osteoarthritis | Osteoarthritis | Osteoarthritis ... | OTHER | 75 YEARS | F | | 20 |

Filters

Search

- Serious is (All)
- Special Interest is (All)
- IME is (All)
- ATC Codes is (All)
- Drug Category is (All)
- ECG Test is (All)
- Ingredients is (All)
- LAB SubjectID is (All)
- MH Preferred Term is (All)

Filters on all pages

Treatment Group is (All)



Therapeutic Area Overarching (TAO) dashboards (Labs)

Pages

- Home
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- Baseline Characteristics
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- Labs**
- Medical History
- Prior and Concomitant ...
- ECG
- Vital Signs
- Study Status & Visits
- Study Drug Information
- Procedures

File | Export | Share | Chat in Teams | Get insights | Subscribe to report
Bay Number | Study Number | Default View

MIRA
Medical Insights, Review & Analytics

Category: GENERAL CHEMISTRY

Labs

Scatter Plot | Lab Flag | Summary Statistics

Filters

Search

Subject

Search

- Select all
- (Blank)
- 380043003
- 470053003
- 888851001
- 888851003
- 888851006
- 888851237
- 888851238
- 888851239
- 888852010
- 888852023
- 888852601
- 888852602

Test

Search

- Select all
- Alanine Aminot...
- Albumin
- Alkaline Phosp...
- Aspartate Amin...
- Bilirubin
- Blood Urea Nitr...
- C Reactive Prot...
- Cholesterol
- Cholinesterase
- Creatine Kinase
- Creatine Kinase...
- Creatine Kinase...
- Creatine Kinase...

Lab Results Over Time

Filters on this visual

- Baseline is (All)
- Excluded (4)**
Glucose (LBTEST) + 837 (LBDY) + 888888 (LBSTRESN), Glucose (LBTEST) + 837 (LBDY) + 888888 (LBSTRESN),...
- Test is (All)
- Treatment Day is (All)
- Visit Name is (All)

Filters on this page

- Subcategory is (All)

Filters on all pages

- Treatment Group is (All)
- Actual Treatment Arm is (All)
- Site is (All)
- Country is (All)
- Age Group is (All)
- Randomized

Lab Details

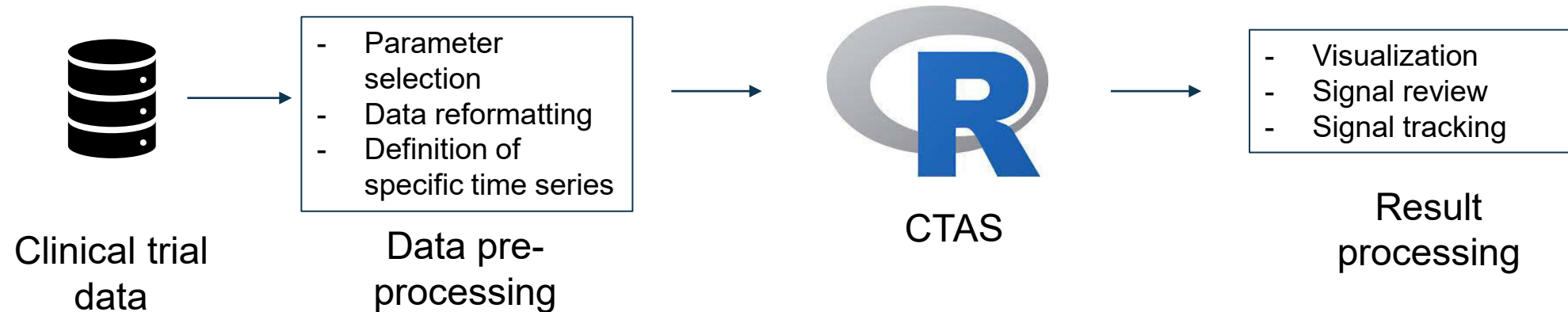
| Subject | Visit Date | Visit Num./Name | Category | Subcategory | Test | Rel S | Rel E | Baseline | Standard Result | Standard Unit | Standard LLN | Standard ULN |
|-----------|------------|----------------------|-------------------|---------------|----------------------------|-------|-------|----------|-----------------|---------------|--------------|--------------|
| 888851239 | 2022-01-03 | 900000.0-UNSCHEДУLED | GENERAL CHEMISTRY | | Potassium | 1 | | | 222.00 | mmol/L | 3.50 | 5.00 |
| 888851239 | 2022-01-03 | 900000.0-UNSCHEДУLED | GENERAL CHEMISTRY | | Sodium | 1 | | | 245.00 | mmol/L | 135.00 | 145.00 |
| 888851239 | 2022-01-03 | 900000.0-UNSCHEДУLED | GENERAL CHEMISTRY | | Aspartate Aminotransferase | 1 | | | 245.00 | U/L | 20.00 | 48.00 |
| 888851239 | 2022-01-03 | 900000.0-UNSCHEДУLED | GENERAL CHEMISTRY | | Albumin | 1 | | | 324.00 | g/dL | 3.50 | 4.80 |
| 888851239 | 2022-12-28 | | GENERAL CHEMISTRY | LIVER EVEN... | Glucose | 360 | | | 214.00 | mg/dL | 115.00 | 140.00 |
| 888851239 | 2022-12-28 | | GENERAL CHEMISTRY | LIVER EVEN... | Albumin | 360 | | | 234.00 | g/dL | 3.50 | 4.80 |

5

/// DATA+AI SUMMIT /// June 2024

Clinical Trial Anomaly Spotter (CTAS)

- CTAS (Clinical Trial Anomaly Spotter) is a CSM (Central Statistical Monitoring) tool focused on identifying anomalous time series of continuous variables.
- “Unsupervised” tool which does not use pre-specified KRIs. The identified anomalies can be such that were not anticipated during study design.
- Originally developed by Bayer where it is available for all company studies.
 - The Bayer-internal tool was presented in PHUSE EU Connect 23. Please see refs. [1] and [2] for details.
- Code base shared with IMPALA for co-development in July 2023.

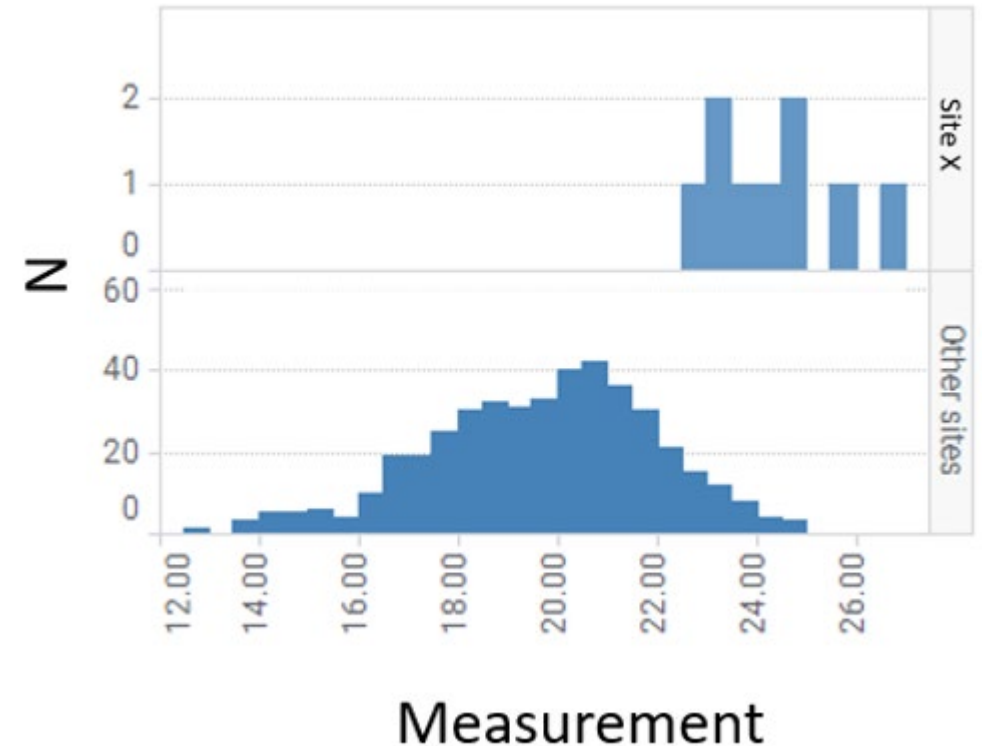
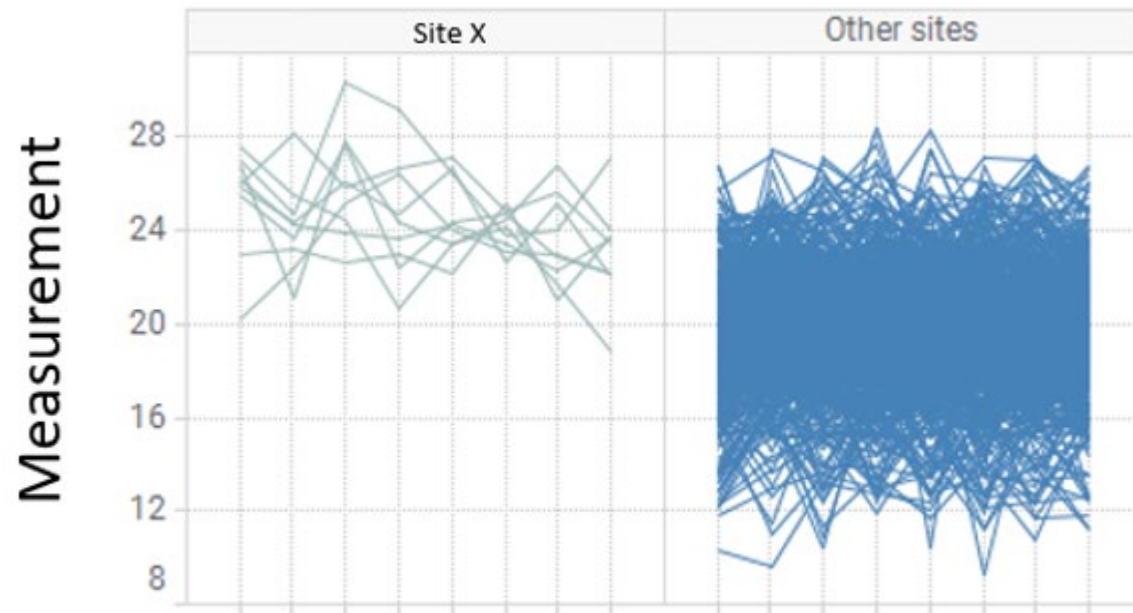


[1] https://phuse.s3.eu-central-1.amazonaws.com/Archive/2022/Connect/EU/Belfast/PRE_AR04.pdf

[2] https://phuse.s3.eu-central-1.amazonaws.com/Archive/2022/Connect/EU/Belfast/PAP_AR04.pdf

Examples of anomalies identified with CTAS

Site with unusually large laboratory assay results (Bayer)



Potential reasons: bias in subject selection, in-correct assay calibration (local labs), errors in sample handling (central labs)

IMPALA consortium

- Industry consortium IMPALA has been formed to develop tools, provide training and create best practices for quality in clinical trials.
- IMPALA aims to engage with Health Authorities inspectors on defining guiding principles for the use of advanced analytics to complement, enhance and accelerate current QA practices.
- Another important activity is co-development of open-source AI/ML tools for QA.
- For more information on the IMPALA consortium, please visit <https://impala-consortium.org/>



CTAS is open source

After few months of co-development, IMPALA published CTAS as an open-source R package in December 2023.

The source code is available on the public IMPALA Github repository under the MIT License:

<https://github.com/IMPALA-Consortium/ctas>

Everyone is invited to test and use the package and report bugs and/or suggest new features.





Azure Databricks, OpenAI & Langchain for clinical GenAI experiments

Microsoft Azure | databricks

Search data, notebooks, recents, and more... CTRL + P

New

Workspace

- Recents
- Catalog
- Workflows
- Compute

SQL

- SQL Editor
- Queries
- Dashboards
- Alerts
- Query History
- SQL Warehouses

Data Engineering

- Job Runs
- Data Ingestion
- Delta Live Tables

Machine Learning

- Playground
- Experiments
- Features
- Models
- Serving

Marketplace

- Partner Connect

Collapse menu

LLMs for clinical (statistics) examples Python

File Edit View Run Help Last edit was now New cell UI: ON

Run all Terminated Schedule Share

Use of GPT4-vision to interpret clinical figures

26: Examples KM curve from survminer

```
1 import base64
2 import io
3 from matplotlib import pyplot as plt
4 import matplotlib.image as mpimg
5 import requests
6 b64 = base64.b64encode(requests.get("https://rpkgs.datanovia.com/survminer/reference/ggsurvplot-2.png").content)
7 plt.imshow(mpimg.imread(io.BytesIO(base64.b64decode(b64))), interpolation='nearest')
8 plt.show()
```

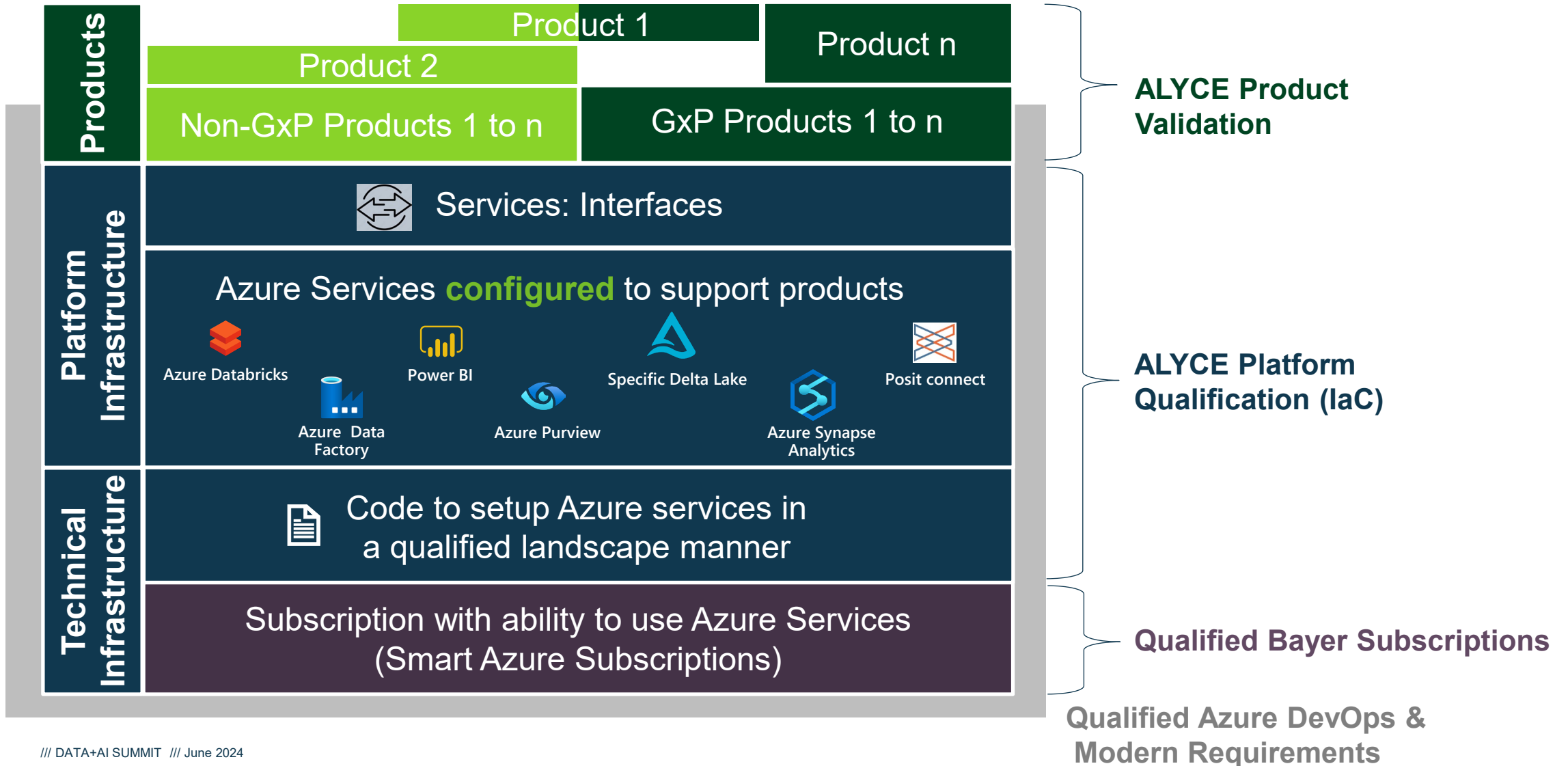
| | 0 | 200 | 400 | 600 | 800 | 1000 | 1200 |
|--------|-----|-----|-----|-----|-----|------|------|
| Male | 138 | 62 | 20 | 7 | 2 | | |
| Female | 90 | 53 | 21 | 3 | 0 | | |

27: Interpret a Kaplan Meier / survival curve with full response

```
1 chat_completion = vision_client.chat.completions.create(
```

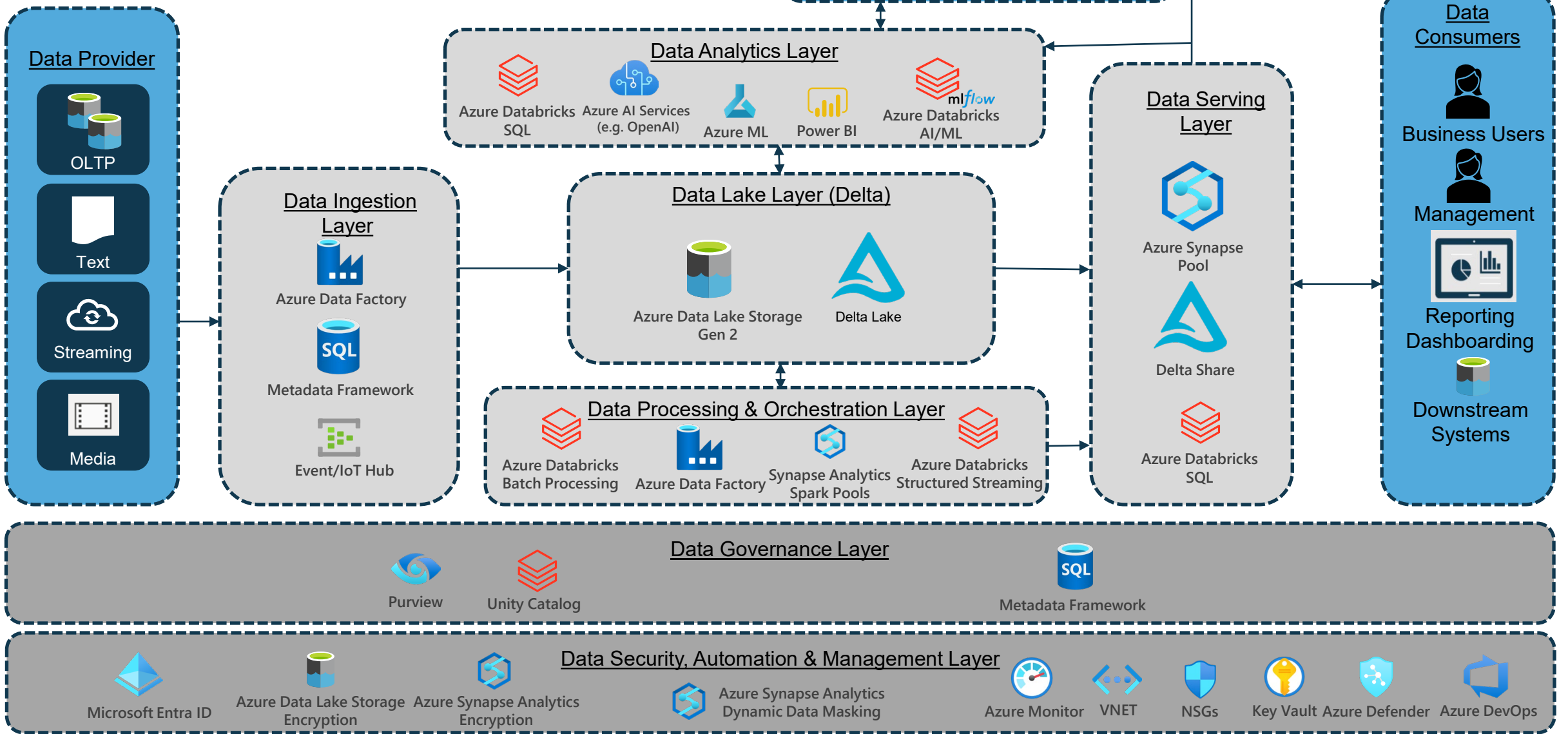


ALYCE Platform GxP Blueprint





ALYCE Data Intelligence Platform



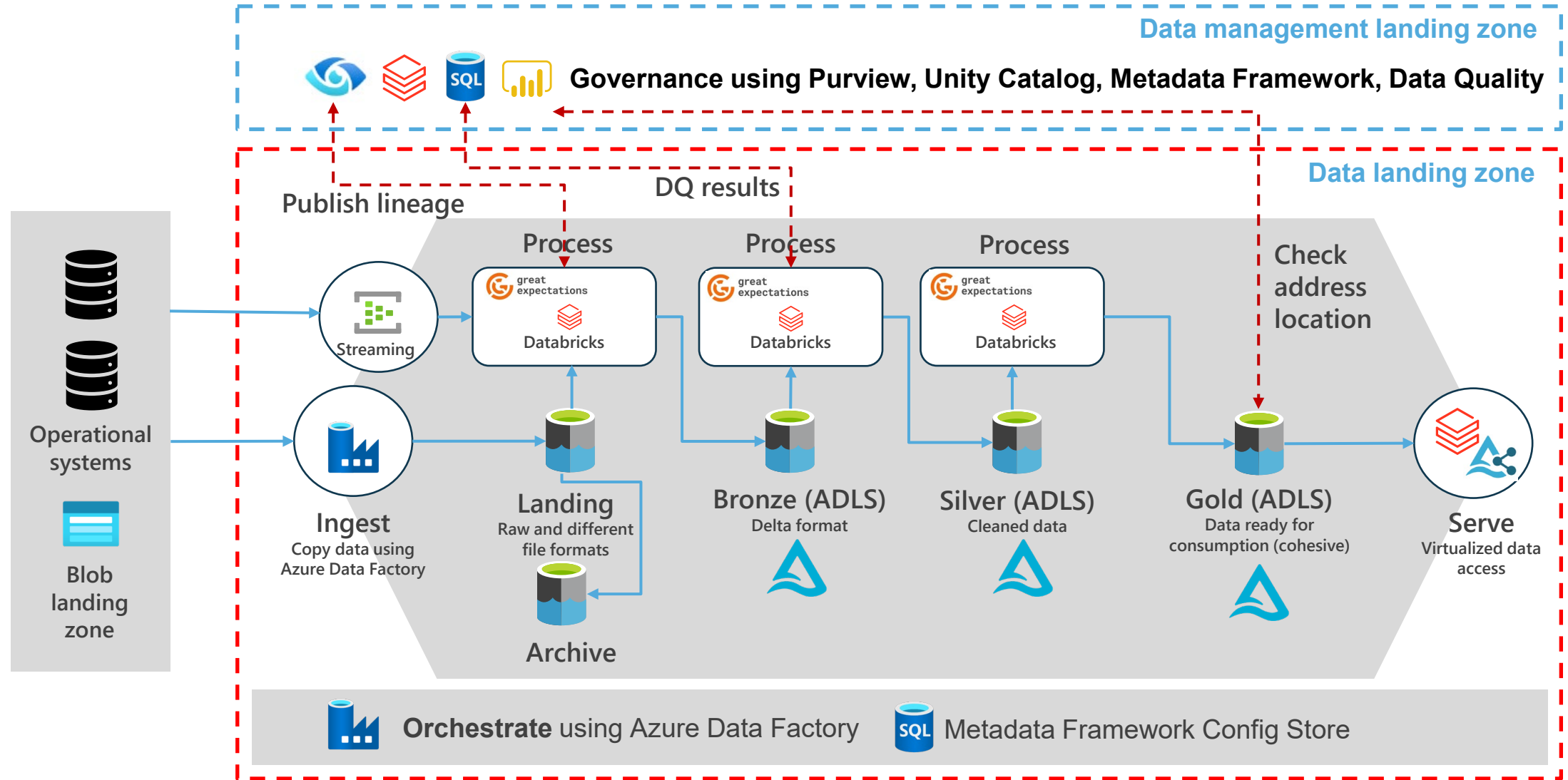
Data Consumers

- Business Users
- Management
- Reporting Dashboarding
- Downstream Systems



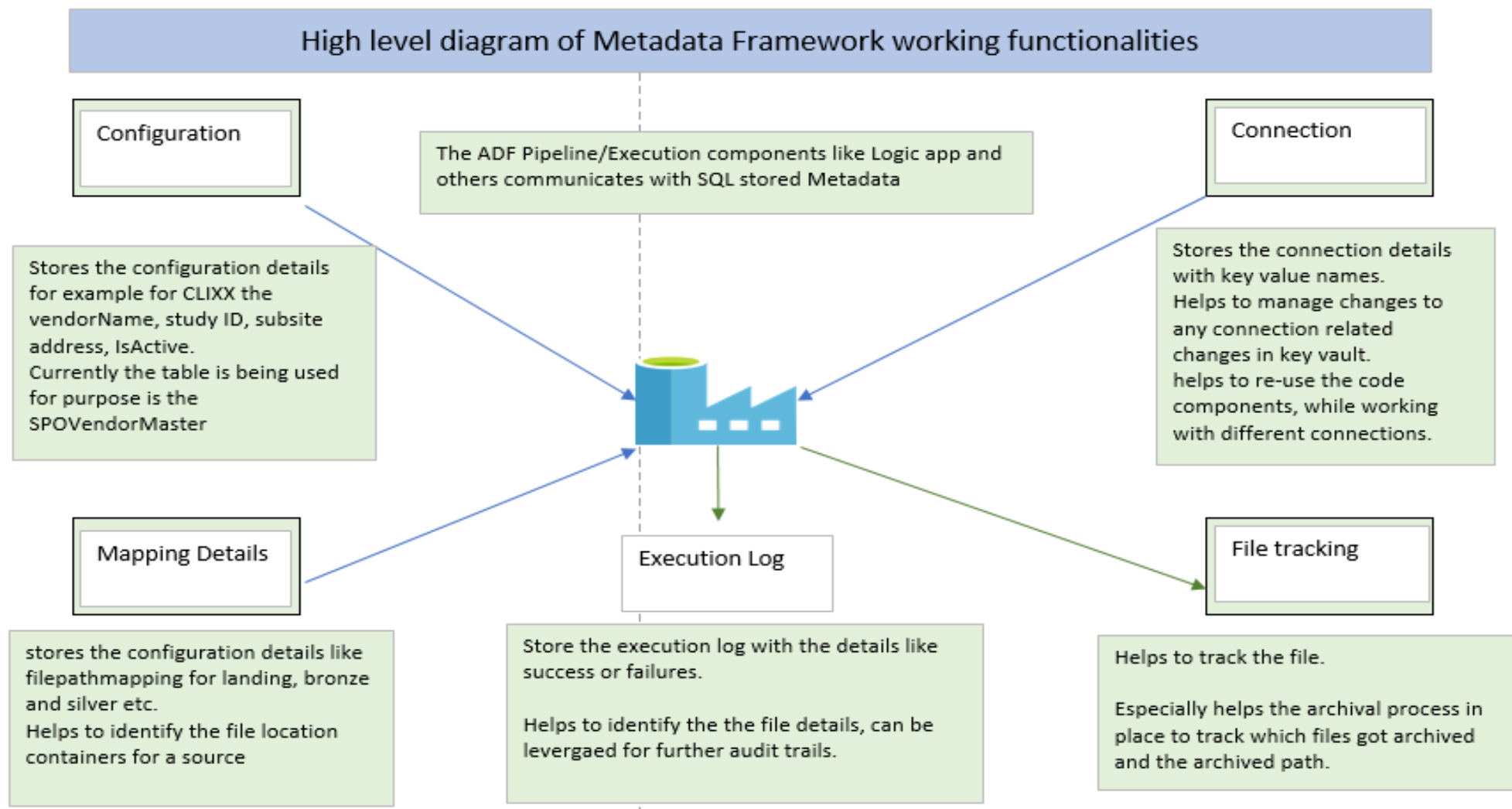
ALYCE Data Product Blueprint

Each domain get its own data product architecture for building data products at scale



Metadata Framework Config Store

Implementation design of Metadata Framework



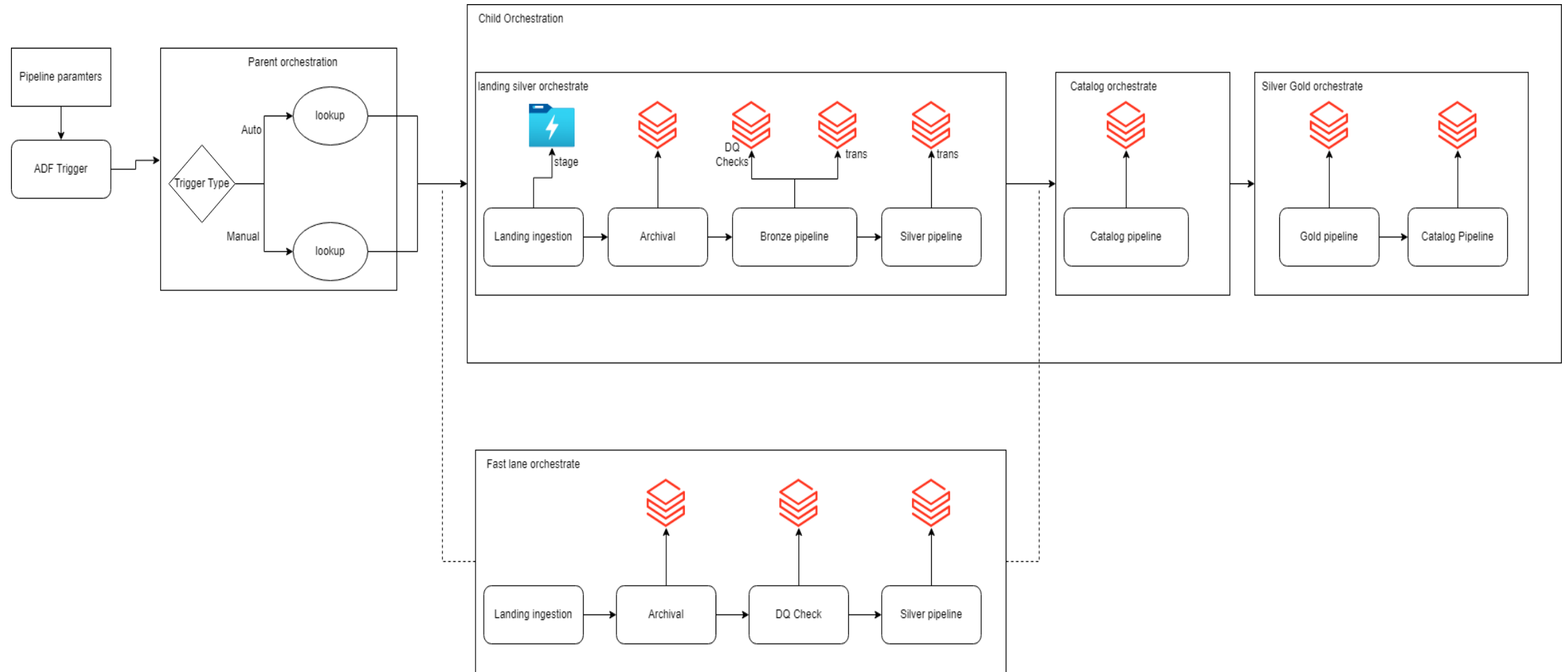


Azure ADF Generalized Pipeline





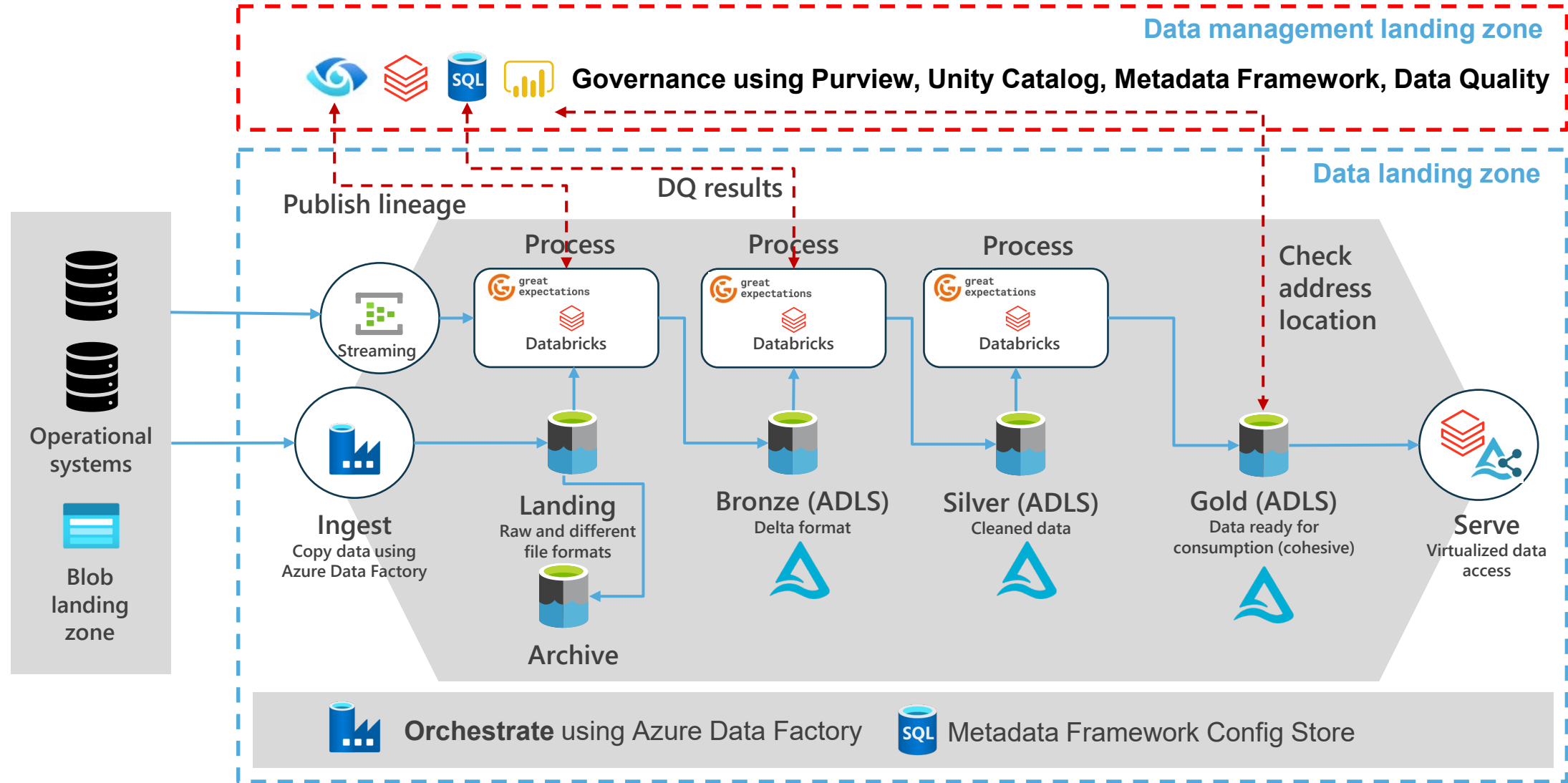
ALYCE Orchestration Blueprint





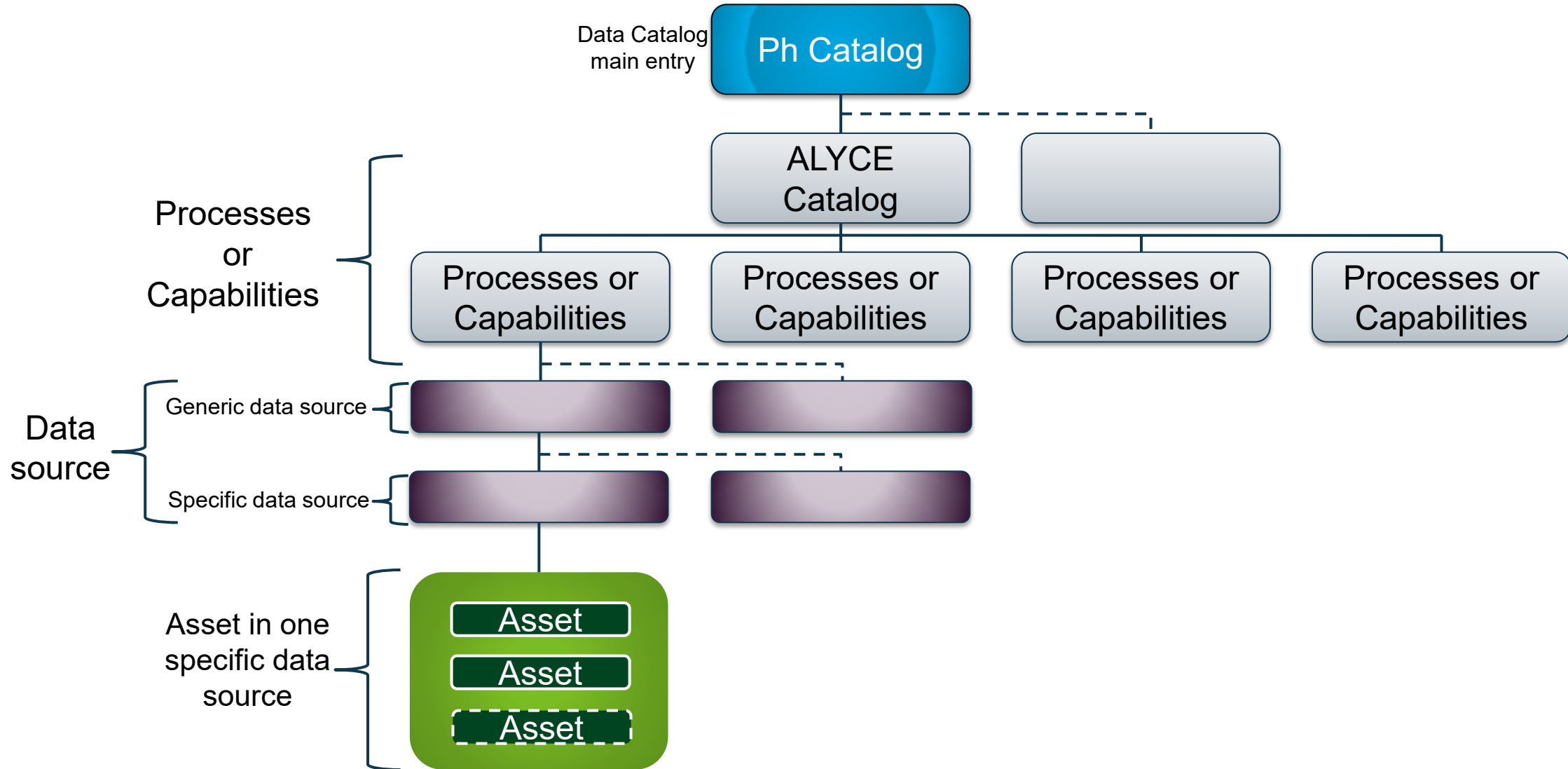
ALYCE Data Product Blueprint

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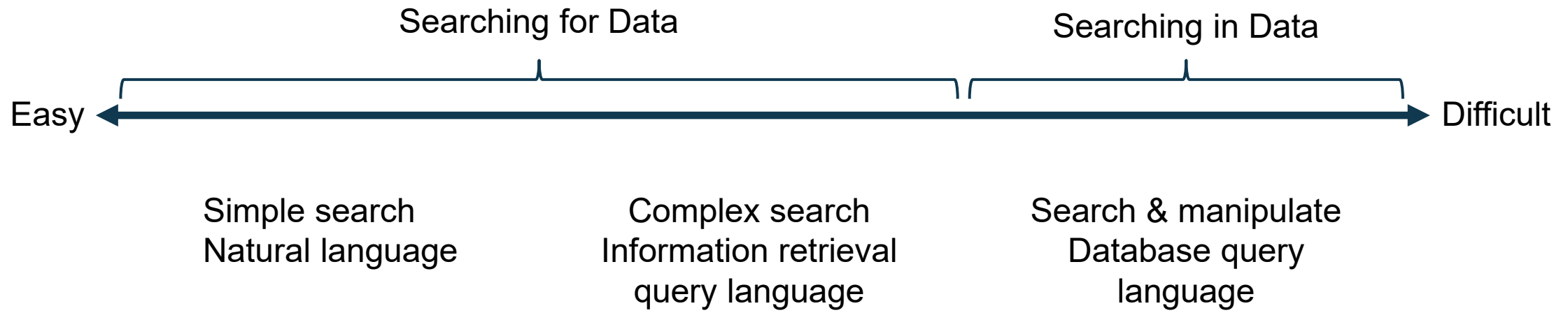
ALYCE Data Catalog Blueprint





ALYCE Data Catalog Search

Spectrum of Search





Example of Clinical Model Asset (SDTM Model)

Microsoft Azure | databricks

Search data, notebooks, recents, and more... CTRL + P

Catalog Explorer [Send feedback](#)

+ Add Browse DBFS ALYCE-POC-DEV Serverless S

Catalogs > alyce_silver_poc_catalog > **alyce_silver_poc_catalog**

Overview Sample Data Details Permissions History Lineage Insights Quality

Filter columns...

| Column | Type | Comment | Tags |
|---------------------|--------|--|------|
| STUDYID | string | Study ID | |
| DOMAIN | string | Domain of data | |
| USUBJID | string | Unique subject identifier | |
| AESEQ | int | Adverse event sequence number | |
| AEGRPID | string | Adverse event group identifier | |
| AESPID | string | Adverse event subject identifier | |
| AELNKID | string | Adverse event linked identifier | |
| DATAPAGEID | int | Data page ID | |
| RECORDID | int | Record ID | |
| SUBJECTNAME | string | Subject name | |
| SUBJECTUUID | string | Subject UUID | |
| STUDYEVENTREPEATKEY | string | Study event repeat key | |
| STUDYEVENTNUM | double | Study event number | |
| AEEPRLI | string | Adverse event pre-relationship to study drug | |
| AETERM | string | Adverse event term | |
| AETERMCV | string | Adverse event term (MedDRA coding version) | |

About this table

Owner: unknown

Data source format: [Delta](#)

Popularity: all

Tags: [Add tags](#)

Comment

The Adverse Events AE table contains data related to adverse events reported during a clinical trial. It includes information such as the study ID, subject ID, event sequence number, event term, severity, and outcome. This table is important for monitoring the safety of the study and ensuring that any adverse events are properly documented and addressed. It can also be used for analysis of safety data and identification of potential safety concerns.



ALYCE Platform Automation Blueprint



Infrastructure Pipeline

Deploy Databricks
Run on agent

- Create or Update Databricks Workspace with Vnet Injec...
ARM template deployment
- Create firewall rule for KeyVault to allow connection fro...
Disabled: Azure CLI
- Download the Secret for Databricks cluster
Disabled: Azure Key Vault
- Create or Update ADF Databricks Lineage Solution Acc...
Disabled: ARM template deployment
- Removal of Carriage return from the script before exec...
Disabled: Azure CLI
- Install Databricks Custom Type Objects in Purview
Disabled: Azure CLI
- Remove Databricks Custom Type Objects in Purview
Disabled: Azure CLI
- Create Or Update SQL Warehouse in Databricks
Disabled: Azure CLI
- Create Access Connector for Manage Location
ARM template deployment
- Create Access Connector for External Location
ARM template deployment
- Delete firewall rule of KeyVault to deny connection fro...
Disabled: Azure CLI

Data Pipeline

Deploy Databricks NoteBooks and Cluster Config files to the ET...
Run on agent

- Use Python 3.8
Disabled: Use Python version
- Create firewall rule for KeyVault to allow connection fro...
Azure CLI
- Download Secret from KeyVault for databricks workspace
Azure Key Vault
- Delete firewall rule for KeyVault to allow connection fro...
Azure CLI
- Databricks Notebooks deployment - Prod
Disabled: Databricks Deploy Notebooks
- Databricks Notebooks deployment - Non-Prod
Disabled: Databricks Deploy Notebooks
- Upload Cluster Config files to Databricks DBFS
Disabled: Databricks files to DBFS
- Upload Cluster Config files to Databricks Workspace
Azure CLI
- Copy Notebooks to Databricks Workspace - Prod
Azure CLI
- Copy Notebooks to Databricks Workspace- Non Prod
Azure CLI

Access Pipeline

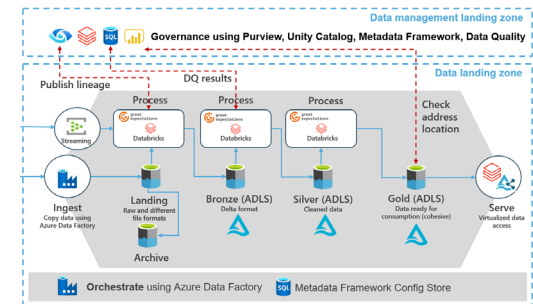
Deploy Unity Catalog Object and Access management.
Run on agent

- Create firewall rule for KeyVault to allow connection fro...
Azure CLI
- Instaling Databricks SQL CLI
Azure CLI
- Download Secret from KeyVault
Azure Key Vault
- Create Manage and External Location
Azure CLI
- Create Unity Catalog
Azure CLI
- Schema Creation for Unity Catalog
Azure CLI
- Grant Access on Unity Object
Azure CLI
- Access Configuration on Unity Catalog Schema
Azure CLI
- Owner Access on Unity Catalog Object
Azure CLI
- Remove firewall rule for KeyVault to allow connection fr...
Azure CLI

Operational Change Pipeline

SQL Metadata Changes
Run on agent

- Create firewall rule for KeyVault to allow connection fro...
Azure CLI
- Download the Secret for SQLDB Admin
Azure Key Vault
- SQL Meta Data Modification
Azure SQL Database deployment
- Delete firewall rule of KeyVault to deny connection fro...
Azure CLI





ALYCE in a Nutshell

Management summary



Revolutionize (Clinical) Data Management: Shatter Data Silos and Boost Medical Review Speed by 10x and beyond.

Unleash the power of your R&D and organizational data by dismantling data silos and consolidating it using the Databricks Lakehouse platform. Witness a remarkable 10x acceleration in Medical Review efficiency, enabling faster, data-driven decisions.

Elevate your organization with the advanced Databricks Data Intelligence Platform, streamlining data analytics and decision-making processes.

Utilize the same data assets gathered through your comprehensive data pipelines for consistent, globally compliant medical reporting. Transform your organization's data capabilities and secure a competitive advantage in the rapidly evolving medical industry. Next step will be Clinical Data Repository (CDR).



DATA+AI SUMMIT 2024

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BY databricks

Thank you!

