“Because That’s What We’ve Always Done” It’s time to wake up a generation

April 22nd 2024


MATRIX
MOVIE CLIP

STATISTICAL PROGRAMMING

THE ART OF...

INTERNATIONAL COUNCIL FOR HARMONISATION OF TECHNICAL REQUIREMENTS FOR PHARMACEUTICALS FOR HUMAN USE

ICH HARMONISED GUIDELINE

GOOD CLINICAL PRACTICE (GCP)

E6(R3)

Draft version

Endorsed on 19 May 2023

INTERNATIONAL CONFERENCE ON HARMONISATION OF TECHNICAL REQUIREMENTS FOR REGISTRATION OF PHARMACEUTICALS FOR HUMAN USE

ICH HARMONISED TRIPARTITE GUIDELINE

STRUCTURE AND CONTENT OF CLINICAL STUDY REPORTS
E3

Current *Step 4* version

dated 30 November 1995

7.4. Statistical Programming

A copy of the statistical analysis files, derived datasets, and programs used in each interim analysis and the final analysis should be frozen and archived, preferably in separate folders.

Programs should be structured, and contain detailed descriptions and comments to enable them to be easily followed and understood by another statistician. In particular, all programs should have information identifying the trial for which they apply and a brief description of what the program does.

All analyses involving the primary endpoint should be quality controlled by an appropriately experienced person other than the trial statistician who performed the main analysis.

As a minimum this will include reviewing the data for internal consistency and consistency with previous reports (and possibly any other relevant literature) to identify clear anomalies.

Cambridge Clinical Trials Unit Box 401

This may also include a visual review of the programs used to carry out the analyses or where appropriate a repetition of the analysis of the primary endpoint from the point of reading in data.

Differing levels of quality control may be used as appropriate: reviewing by an independent statistician, reviewing of output, or a complete reprogramming of the primary analysis.

The computer software used for statistical analysis should be reliable, and will be one of the major statistical packages, for example R, Stata, SAS.

1972

North Carolina


DOMINO

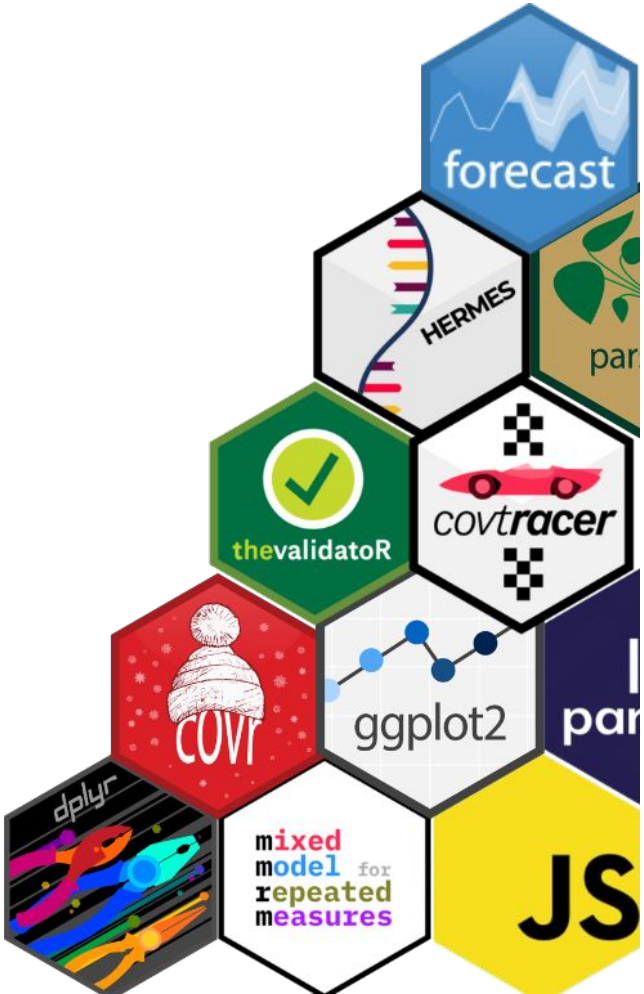

python™


R Studio®


jupyter


R


sas


forecast
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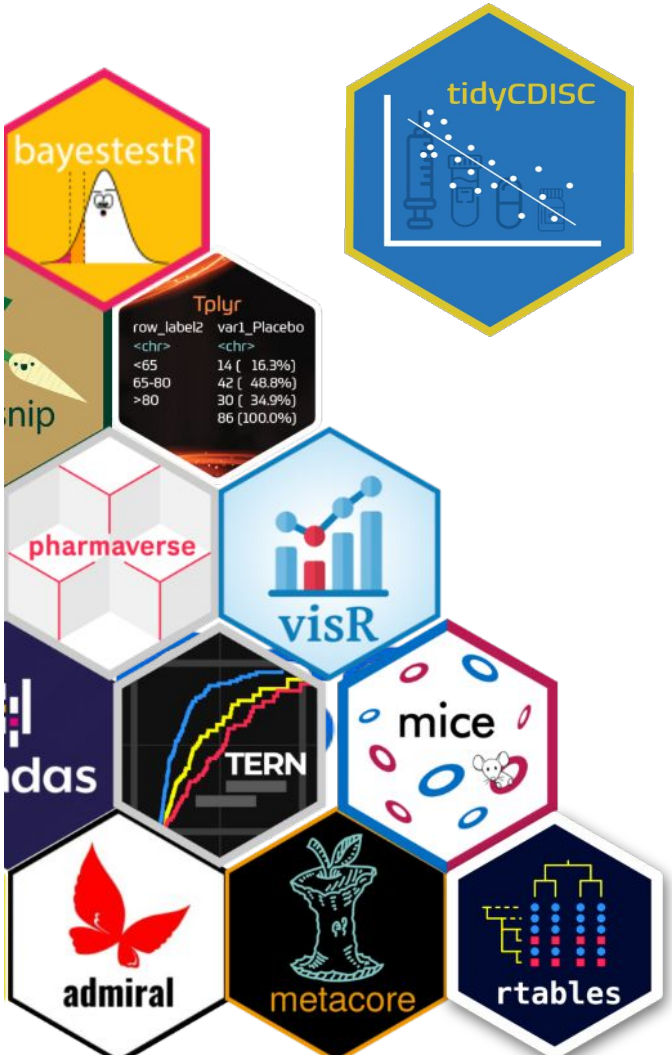
OPEN SOURCE ALLIANCE


admiral


pharmaverse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<65 14 (16.3%)
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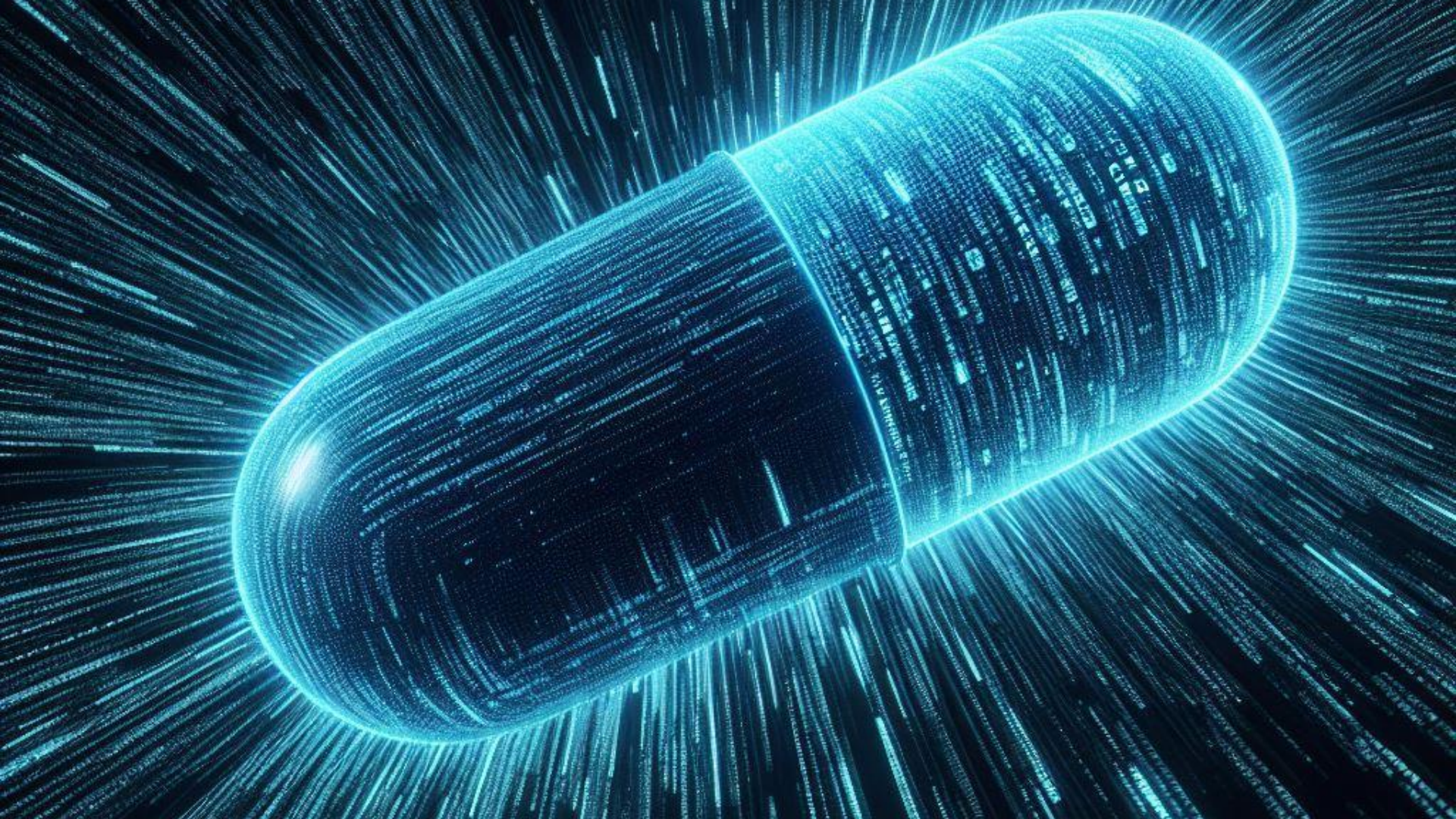
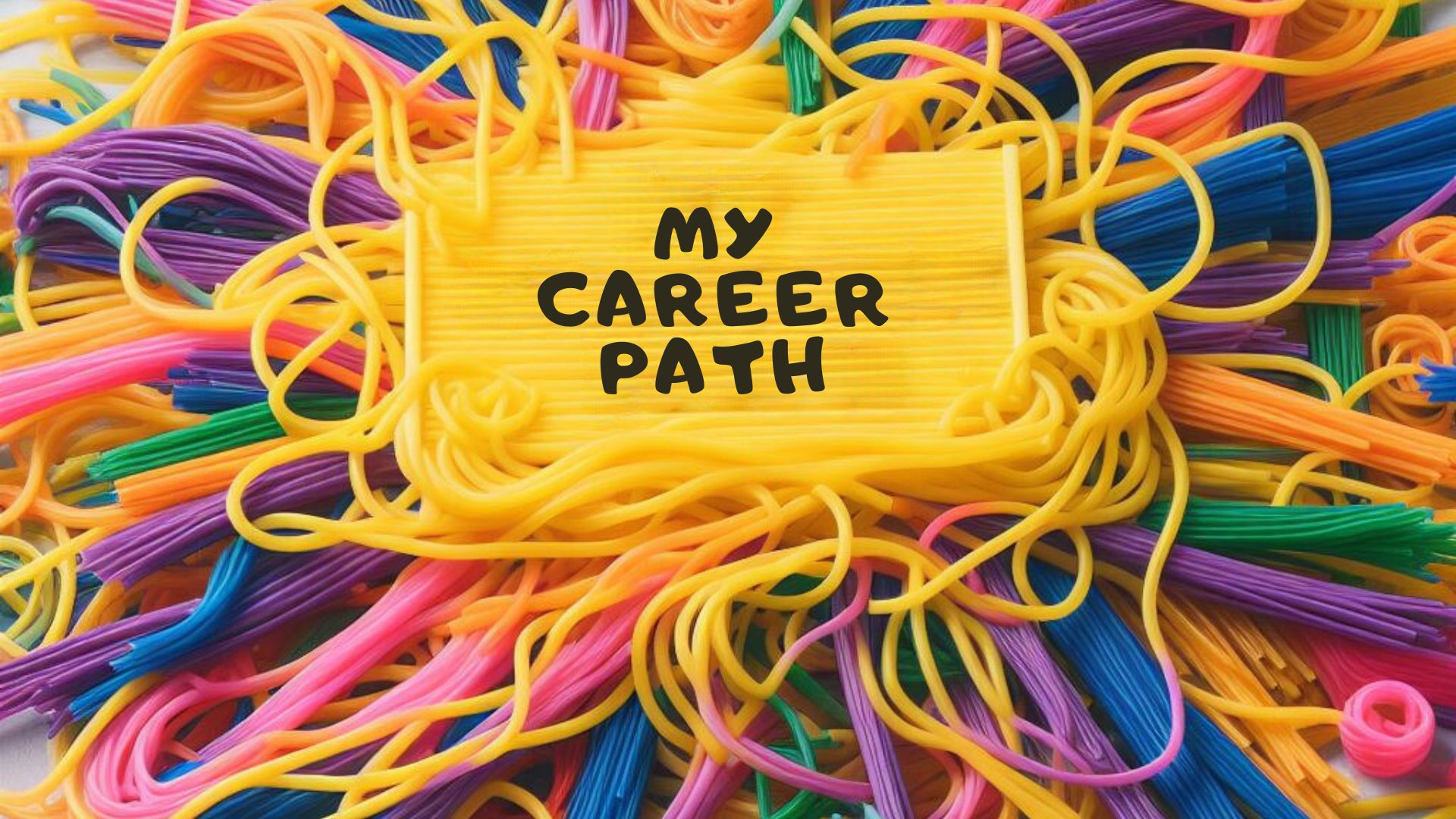
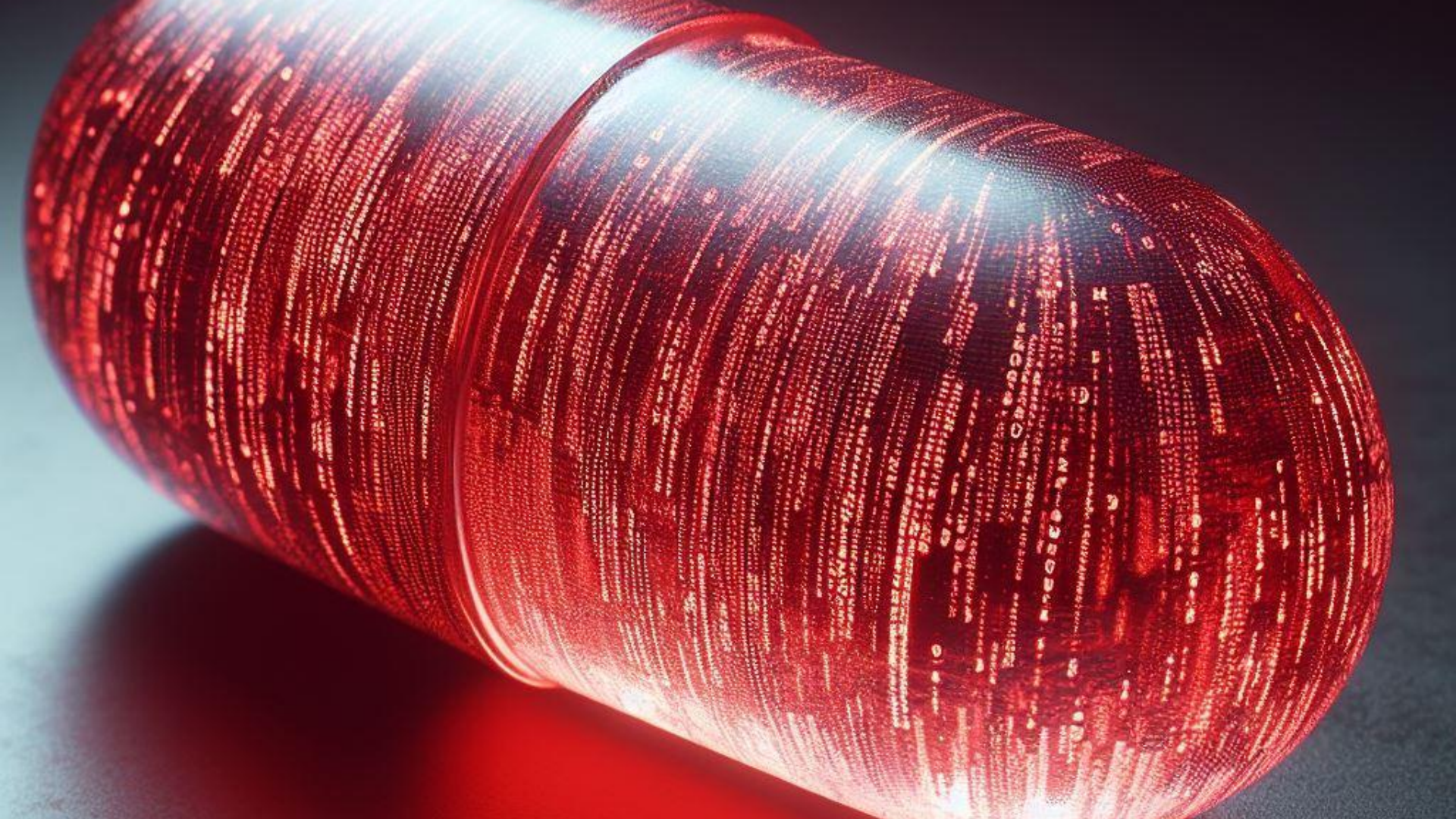


A NORMAL CAREER PATH


MY
CAREER
PATH



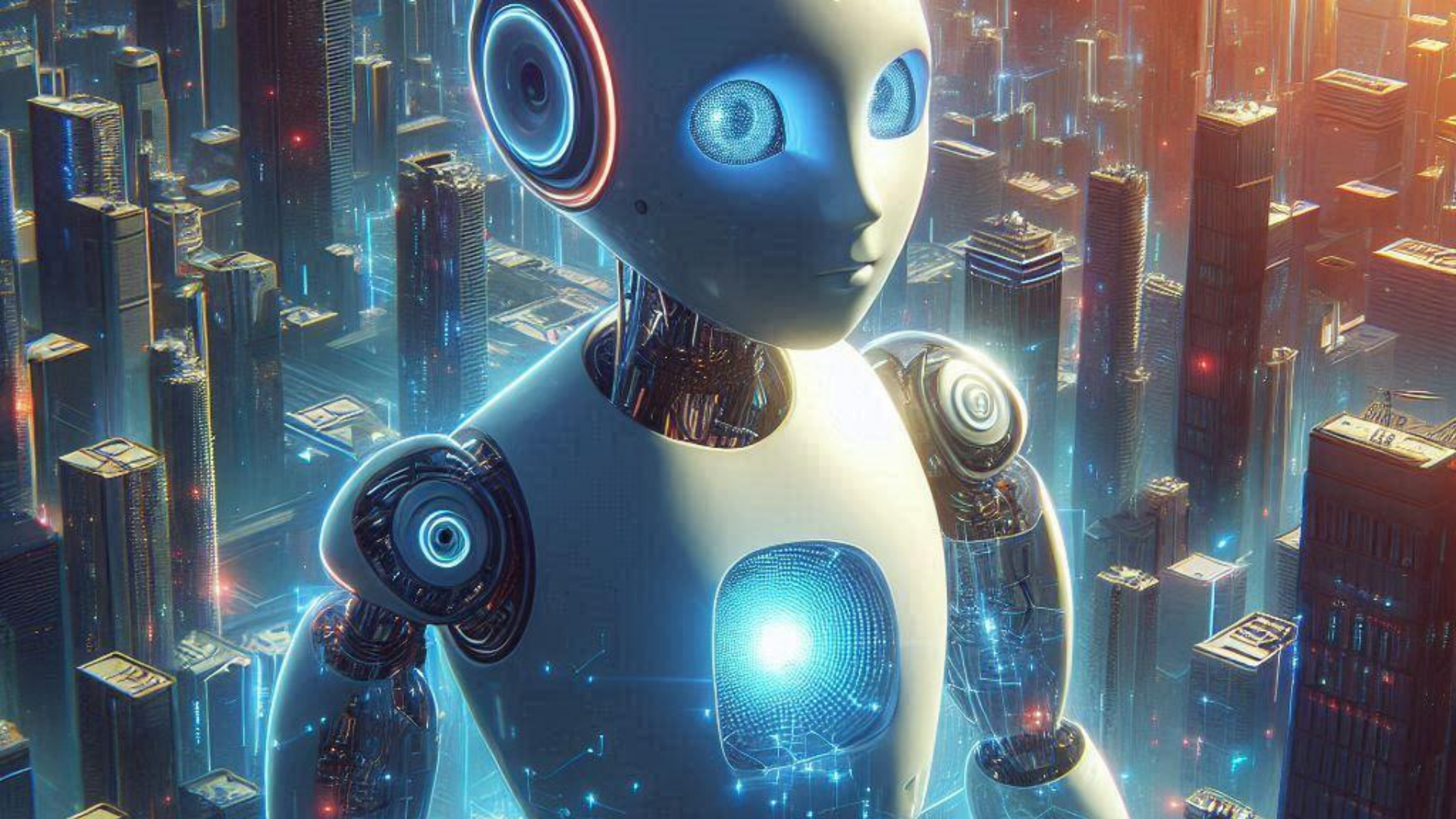
Disposition (DS) [Location: ds.xpt]

Variable	Label	Key	Type	Length	Controlled Terms or Format	Origin	Derivatio
STUDYID	Study Identifier	1	text	7		Protocol	
DOMAIN	Domain Abbreviation		text	2	["DS" = "Disposition"] <Domain Abbreviation (DS)>	Assigned	
USUBJID	Unique Subject Identifier	2	text	14		Derived	Concatena
DSSEQ	Sequence Number		integer	1		Derived	Sequential in the dom
DSTERM	Reported Term for the Disposition Event		text	34	Reported Term for the Disposition Record	CRF Pages 6 16 18	
DSDECOD	Standardized Disposition Term	6	text	21	Completion/Reason for Non-Completion	CRF Pages 6 16 18	CRF contro controlled
DSCAT	Category for Disposition Event	5	text	18	["DISPOSITION EVENT" = "Disposition Event", "PROTOCOL MILESTONE" = "Protocol Milestone"] <Category for Disposition Event>	Assigned	
EPOCH	Epoch		text	9	["SCREEN", "TREATMENT"]	Assigned	

- [redacted]
- [redacted]

In addition, 9 SAEs reported by 8 subjects were considered by the investigator to be potentially related to study vaccination: 2 SAEs reported for 1 subject in the HPV group, 6 SAEs in the ALU group and 1 SAE is still blinded since this event was expected based on the known safety profile of the HPV-16/18 vaccine.

- [redacted]
- [redacted]
- [redacted]
- [redacted]
- [redacted]



CRYPTOGRAPHIC HASHING

A Clinical Data Perspective

01 Configure cataloging rules and alerts

02 SDTM-DM Created

03 SDTM-DM File Hashed

*Unique Hash Derived from Content Itself
** Change file and Hash Changes

04 Hash Stored at Client Site

05 Hash Cataloged/Arranged

06 Hash Registered on an EQTY Integrity_Graph

07 Insights surfaced through reports or visual explorer

08 One-Click Authenticate Integrity by Rehashing SDTM-DM

09 Rule Flag when SDTM-DM Changes

*Hashes match = integrity
**Hashes do not match, see who, what, where, when changes made

Modernized Regulatory Review Tool

Challenge

Data quality assurances with the number of submissions and complexity increasing. Goal to review 90% of submissions in six-months*.

Solution

Enhanced confidence layer over sponsor clinical trial systems enables quality inspectors and regulatory reviewers to **trace, reproduce and trust data**. Audit reports and clickable visual explorer streamlines review and query process for capture (RWD/Labs/eCRF) and statistical analysis (SDTM, ADaM, TFL).

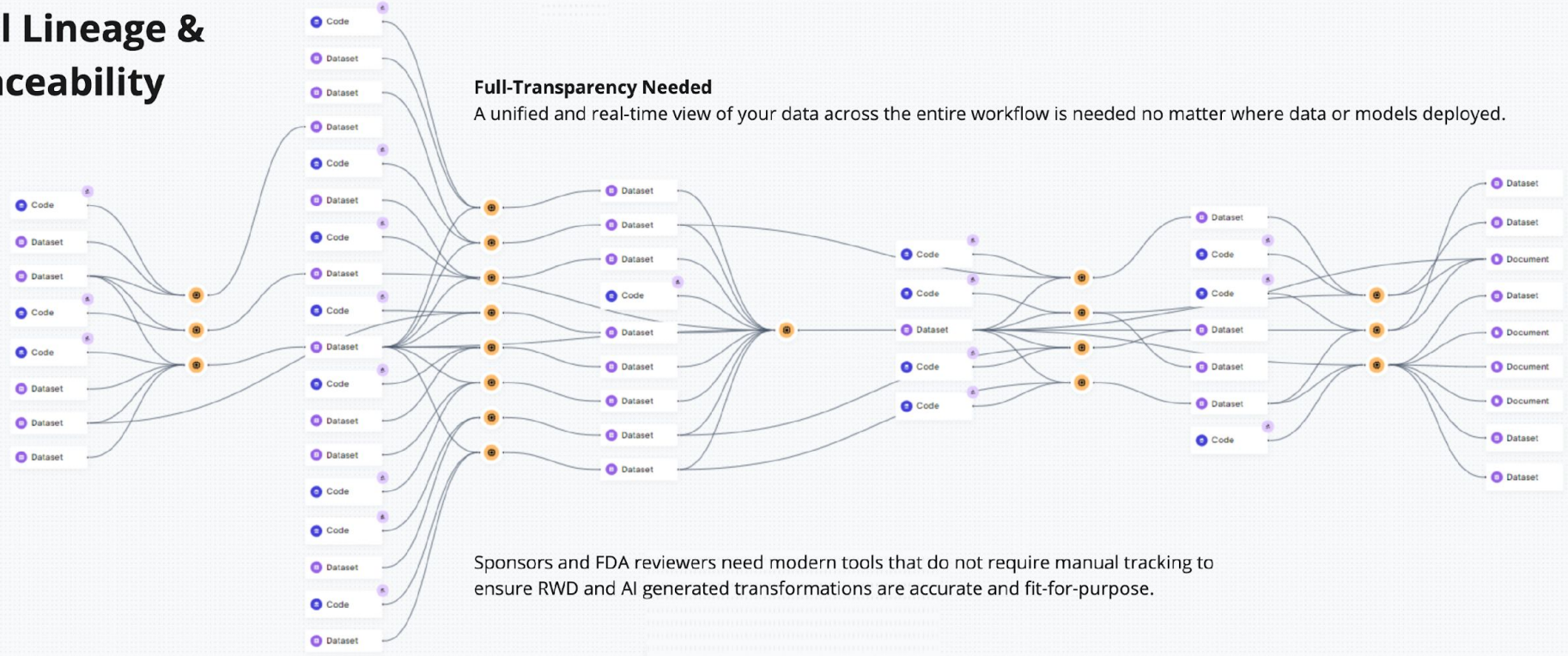
Outcome

End to end third-party integrity of clinical trial data and sponsor processes. Sponsors can enable faster regulatory reviews by proving governance controls over quality and providing auditors proof of lineage and traceability back to provenance.

* PDUFA VII - Commitment Letter - 08192021

Multi-System Lineage Explorer

Full Lineage & Traceability



Full-Transparency Needed

A unified and real-time view of your data across the entire workflow is needed no matter where data or models deployed.

Sponsors and FDA reviewers need modern tools that do not require manual tracking to ensure RWD and AI generated transformations are accurate and fit-for-purpose.

RWD/RWE Streamlined Submission

Challenge

Prove healthcare data is representative of population, ethically curated and analyzed at **from capture to submission.**

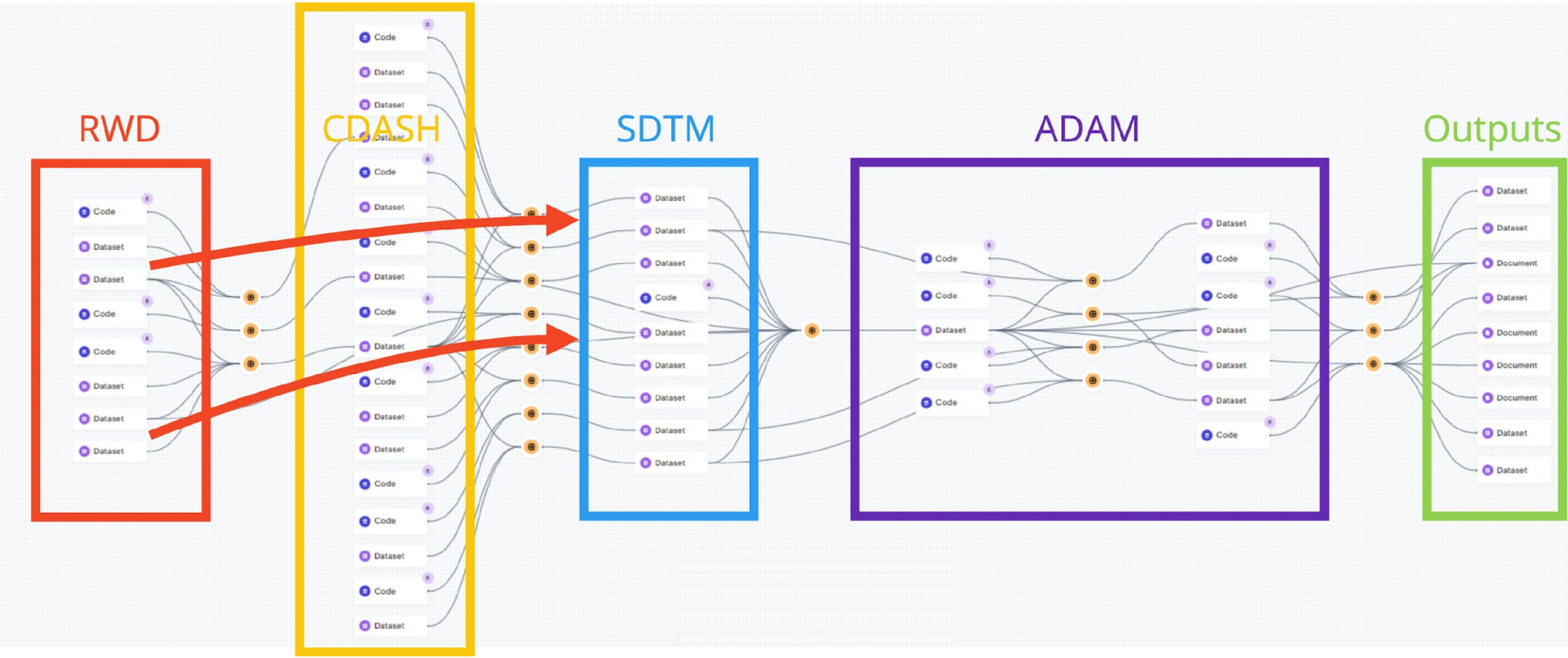
Solution

An Integrity Graph provides sponsors, data providers and EHR vendors ability to **prove data and process integrity to regulators**, ensuring **fit-for-purpose RWE submissions**.

Outcome

The **quality score of real world data has third-party integrity through mathematical proof.** Digital twins and RWE integrated submissions have end-to-end verified trust for use as a control/placebo.

Enable RWD usage



AI Governance
Trial Design and SAP

TransCelerate BIOPHARMA INC.

Challenge

Transparency, reproducibility and proof of control over training, inferences and security of data and model.

Solution

Prove trustworthiness of an **LLM that generates a protocol and statistical analysis plan**, future-proofing it for connection to clinical analysis via CDISC USDM affiliation.

Outcome

Tangible proof-of-concept that illustrates our capabilities to **control artificial intelligence for regulated submissions by sponsors.**

AI Governance
COVID Safety Monitoring

Challenge

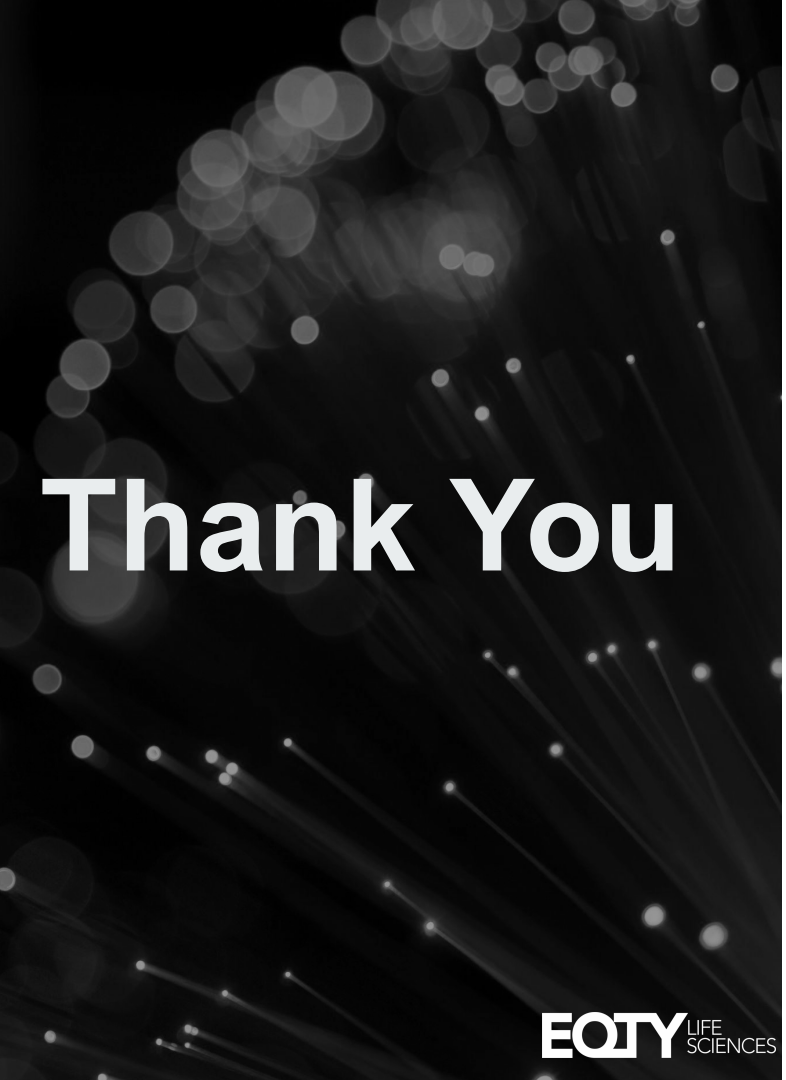
Predictive AI models that monitor long-term responses to vaccines and surface interventions require higher levels of integrity that prove responsibility.

Solution

Using an Integrity Graph, AI models that utilize RWD for post marketing surveillance or to predict events can be trusted by regulatory agencies and shape public perspective on long-term vaccine data.

Outcome

Our AI Integrity solution, provides proveable audit trails for models that ensure compliance, adherence to standards for higher levels of confidence.



Smash those black boxes!

If you would like to learn more:

- Ali Dootson: Ali@eqtylab.io

If you would like to visit our website or explore our products:

- EQTYLab.io
- Open Source Lineage Explorer
  [https://huggingface.co/spaces/EQTYLab/lineage-explorer]