

DIGITAL **TRANSFORMATION** INITIATIVE IN SAFETY **SURVEILLANCE**

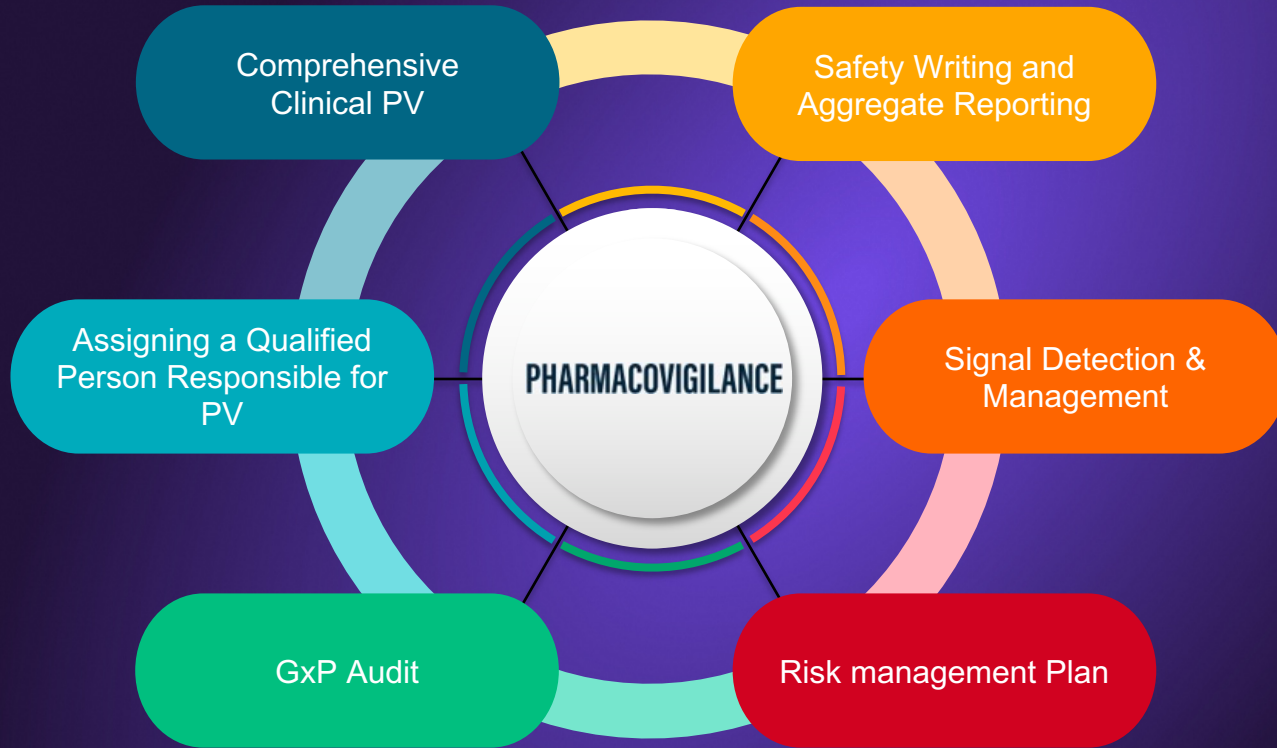
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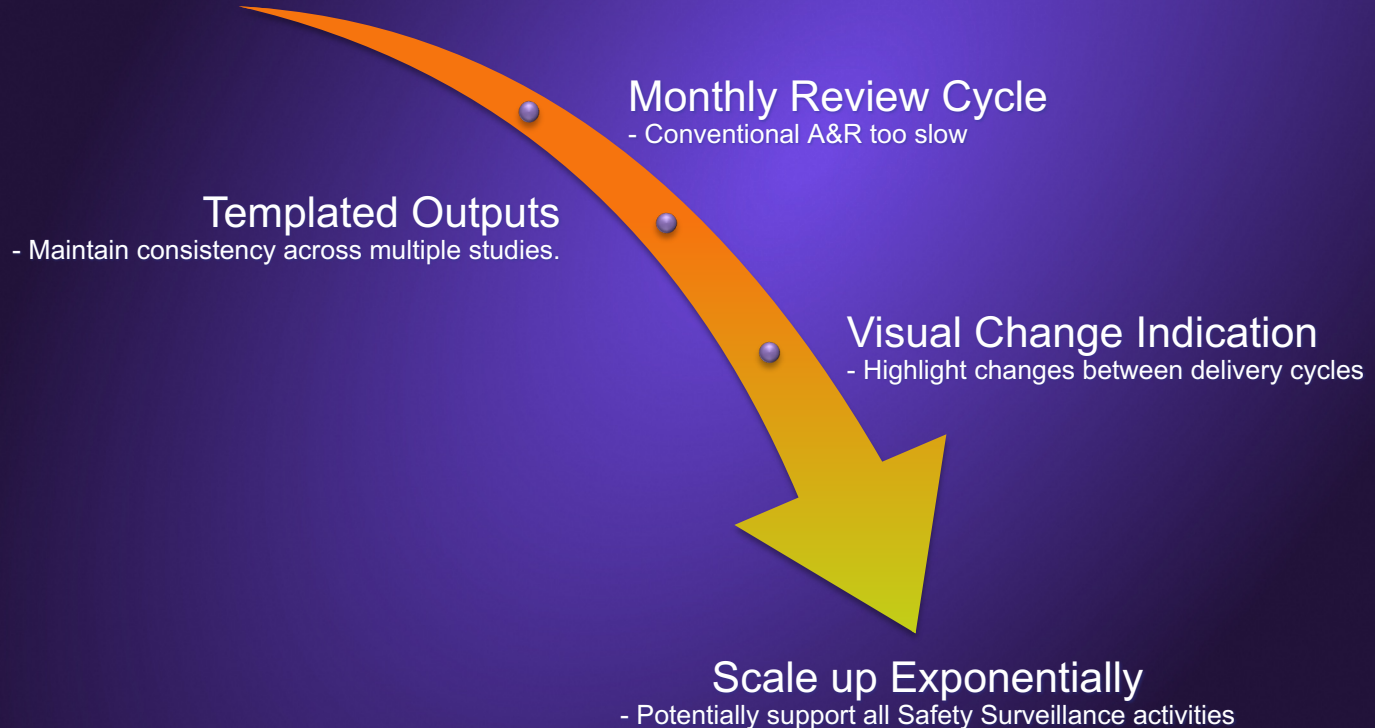
Safety Surveillance and Pharmacovigilance



The Challenge

Optimize Safety Review Process

- To maximize effectiveness safety review



Optimize Safety Review process.

Limitations



Regulatory Requirements
- Strict and administratively heavy



Analysis & Reporting
- Process not geared for Safety Surveillance



ADaM as Source
- Infrequent updates



Analysis Outputs
- Not ready in time



Double Programming and Review
- Time consuming



Huge Volume of Data
- Distracting

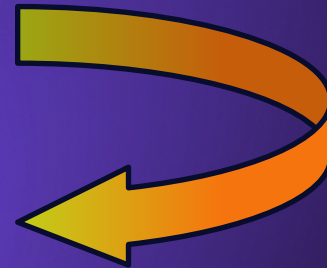
Cultivating the Solution

Monthly Review Cycle

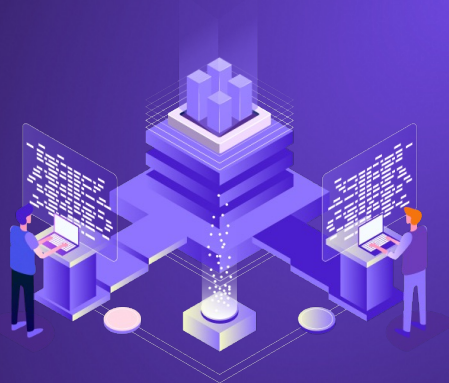
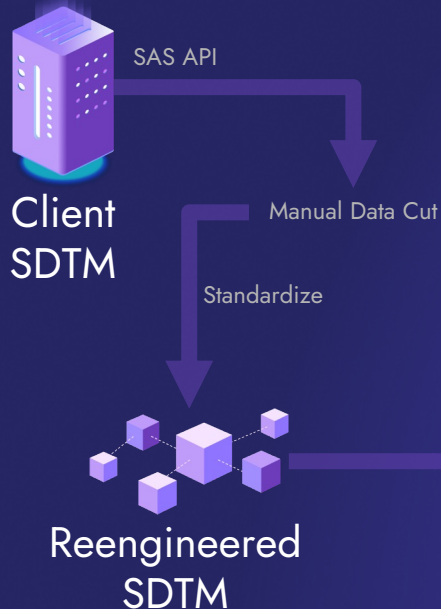
- Conventional A&R too slow

Solution:

- Use SDTM data
- SAS API – No need for transfers



Data Acquisition



Template Outputs

Addressing Limitations

Analysis & Reporting

- Tailored solution independent of A&R

ADaM as Source

- SDTM updated regularly

Analysis Outputs

- Produced as needed



Cultivating the Solution

Templated Outputs

- Maintain consistency across multiple studies



- Individual Study Protocols
- Multiple outcomes
- Baseline flagging: Roll-Over (with De-Novo) vs. Normal
- Multiple data collection methods
- Impact of durations and timing
- Targeted Medical Events
- Etc...

Considerations

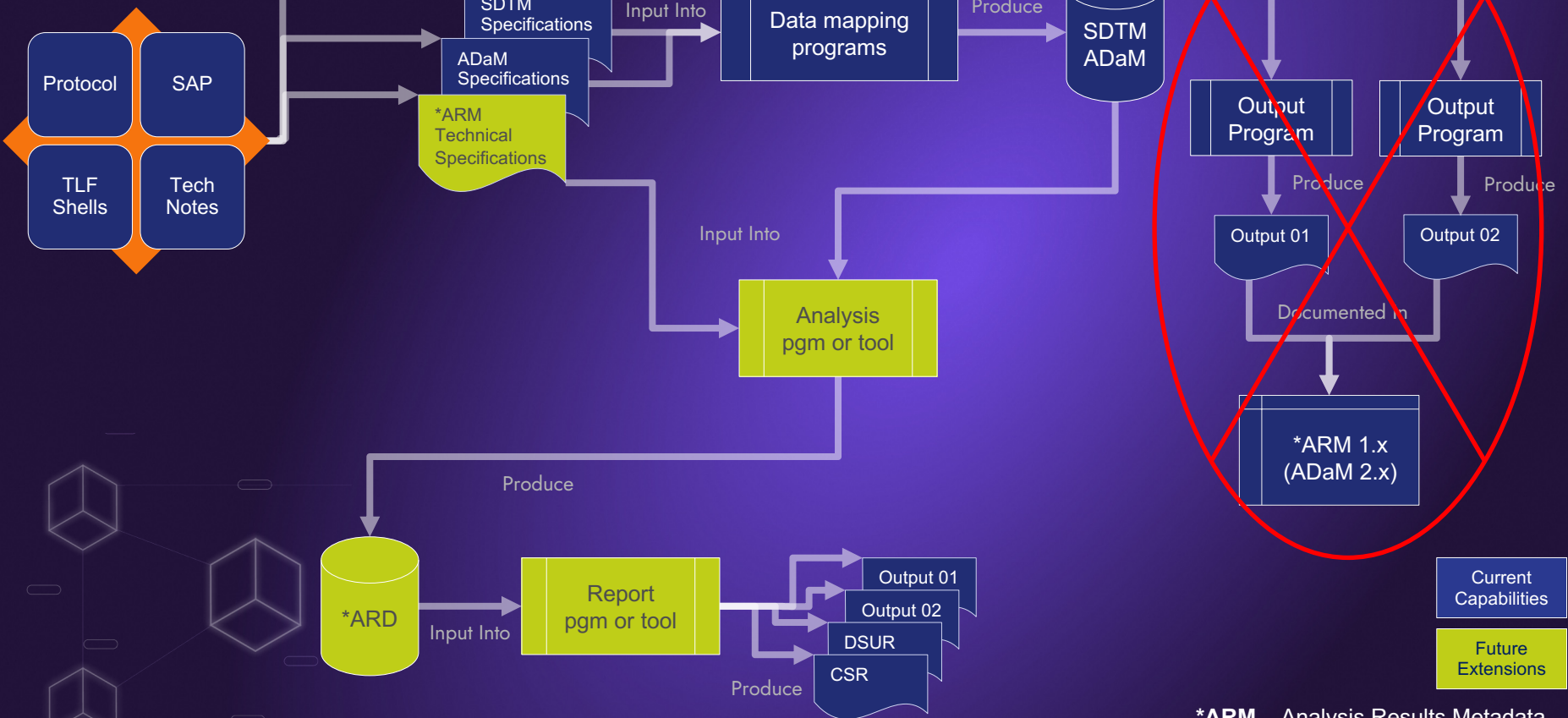
Approach

- CDISC: Analysis Reporting Standard (**ARS**)
- (*Reengineered*)

- **ARS** adds extra layer of standardization
- Compact and comparable results
- Groundwork for automation

Outcome

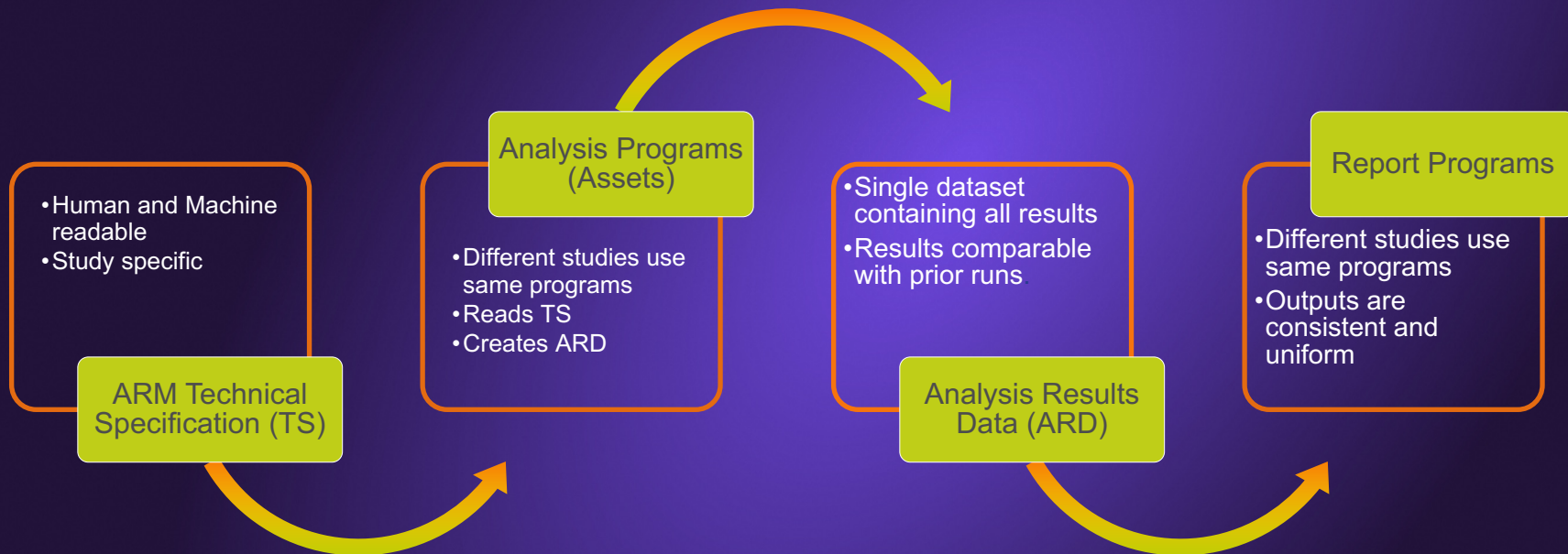
CDISC ARS



Current Capabilities

Future Extensions

Application of ARS and ARD for Safety Surveillance



Outcomes:

- Able to deploy to many studies much easier
- Keeps maintenance centralized
- Lays the groundwork for automation

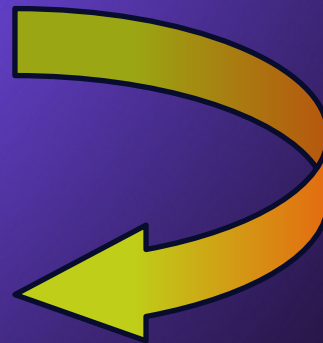
Solving the Double Programming Problem

What we had to work with:

- Frequent reruns with very little updates.
- SDTM source data – Structure would stay the same
- Input data – transformed for conformance before reporting.
- Ample lead time – short subsequent turnaround.
- Outputs meant for internal Safety Review.
- Many studies – same output.

Since it ticked a lot of Validated Computer System boxes:

– Let's CSV the Programs...



Solving the Double Programming Problem Continued...

Why CSV? Considerations:

Double Programming

- Requires minimum 2x people
- Rerun = Revalidate
- Programs in different locations
- Quick start / takes time later
- Less complex
- Less documentation
- Suited to frequent changes

Computer Systems Validation (CSV)

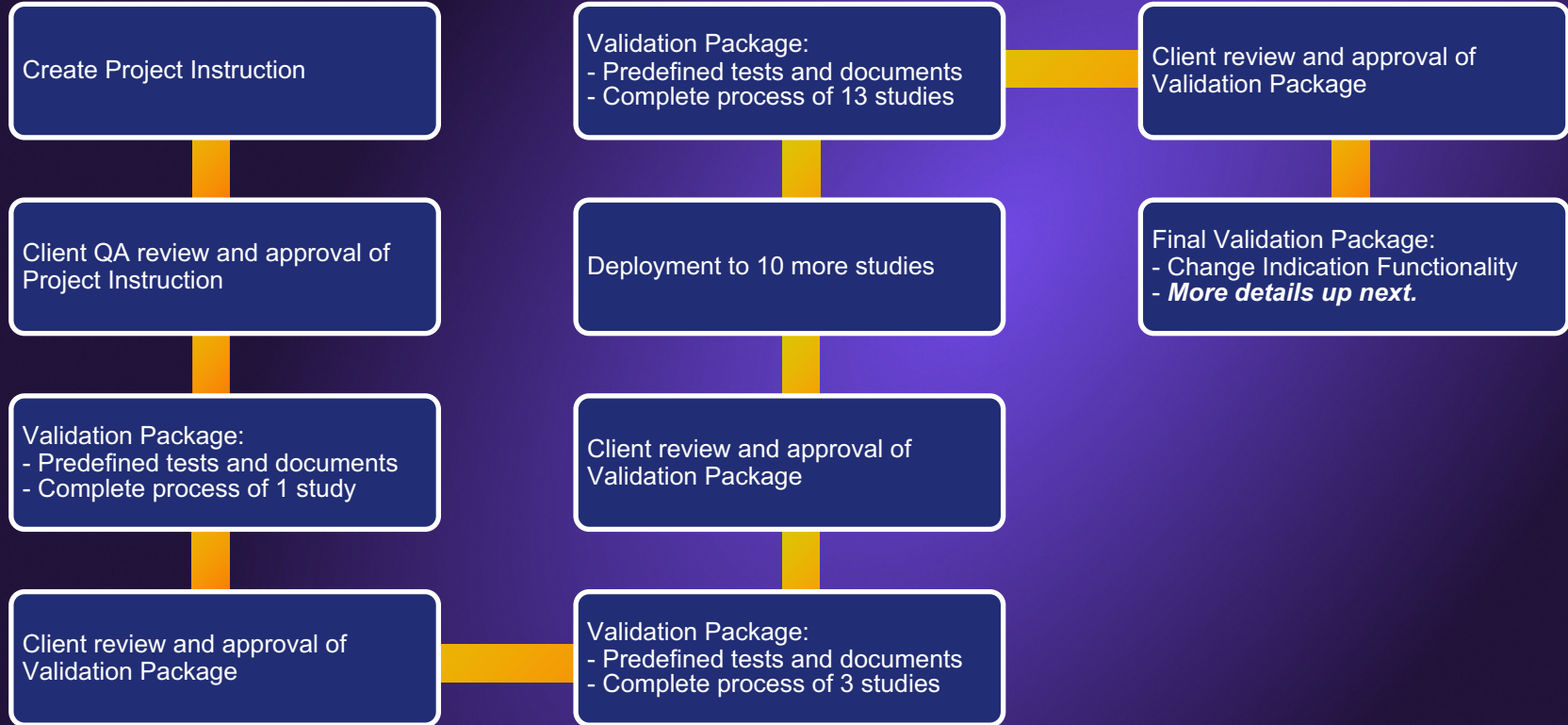
- Requires minimum 1x person
- Rerun = Done
- Programs centralized
- Slow start / takes no time later
- More complex
- Documentation Heavy!
- Suitable when little to no changes expected



CSV approach:
Solves the double programming problem!



The CSV Process:



Helping Reviewers: Visual Change Indication



Huge Volume of Data

Create visual cues to aid reviewers.

- New records – **Green**
- Changed records affecting table counts - **Yellow**
- Changed records not affecting table counts - **Orange**
- Deleted records – **Red, separate presentation**



Visual Change Indication: Listing Example

Columns with Differences	AESPID - AE Sponsor ID	AETERM - Reported Term	AEDECOD - MedDRA Preferred Term	AESOC - M System C Class
New Record	5	CAR ACCIDENT	Road traffic accident	Injury, poisoning procedural complications
New Record	6	BRUISES BILATERALLY OVER THE THORACIC RIB CAGE	Bone contusion	Injury, poisoning procedural complications
New Record	7	POST CAR ACCIDENT PAIN	Post-traumatic pain	Injury, poisoning procedural complications
New Record	8	BRUISES BILATERALLY ON BOTH LOWER LEGS	Contusion	Injury, poisoning procedural complications
New Record	12	MINOR REDUCTION IN SENSITIVITY IN VISUAL FIELD	Visual acuity reduced	Eye disorders
New Record	2	GLAUCOME		

New records since last run.

Visual Change Indication: Listing Example

Columns with Differences	AESPID - AE Sponsor ID	AETERM - Reported Term	AEDECOD - MedDRA Preferred Term	AESOC - MedDRA System Organ Class
AEDECOD - MedDRA Preferred Term	1	LEAKY GUT SYNDROME - RECENT DIAGNOSIS	Intestinal barrier dysfunction	Gastrointestinal disorders
AEDECOD - MedDRA Preferred Term; AESOC - MedDRA System Organ Class	14	SWELLING IN SINUSES	Sinus congestion	Respiratory, thoracic and mediastinal disorders
AETERM - Reported Term; AEDECOD - MedDRA Preferred Term; AESOC - MedDRA System Organ Class; Derived TEAE with Increased Intraocular Pressure Flag; Record Excluded	4	OPHTHALMOLOGY FINDING, ENLARGED CUP TO DISC RATIO	Optic nerve cup/disc ratio increased	Investigations
AEDECOD - MedDRA Preferred Term; AESOC - MedDRA System Organ Class	7	NEOPLASM OF UNCERTAIN BEHAVIOR- LEFT LATERAL UPPER BACK - MELANOCYTIC PROLIFERATION - BENIGN	Melanocytic naevus	Neoplasms benign and unspecified (incl. cysts and polyps)
AEREFID - AE Reference ID; AETERM - Reported Term; AEDECOD - MedDRA Preferred Term; Adverse Event of Special Interest; Derived TEAE with Increased Intraocular Pressure Flag	1	ABNORMAL OPHTHALMOLOGICAL EXAM INCREASED CUP/DISK RATIO GREATER THAN NORMAL OF .70	Optic nerve cup/disc ratio increased	Investigations
AEDECOD - MedDRA Preferred Term	1	POST-EXERCISE FATIGUE	Fatigue	General disorders and administrative site conditions
AEDECOD - MedDRA Preferred Term	6	POST-EXERCISE FATIGUE	Fatigue	General disorders and administrative site conditions

Changed records that are affecting associated Table output.

Visual Change Indication: Listing Example

Columns with Differences	AESPID - AE Sponsor ID	AETERM - Reported Term	AEDECOD - MedDRA Preferred Term	AESOC - System Class
AEACN - Action Taken	1	SYMPTOMATIC INDIGESTION	Dyspepsia	Gastrointestinal disorders
AEACNOTH - Action Taken, Other	1	CATARACT OF THE RIGHT EYE	Cataract	Eye disorders
AEENDTC - End Date of AE; AEENDY - Study Day of AE End	1	GASTROESOPHAGEAL REFLUX	Gastroesophageal reflux disease	Gastrointestinal disorders
AETERM - Reported Term	2	MILD EXACERBATION OF ARRHYTHMIA (NON-THREATENING ADDITIONAL STIMULATIONS)	Arrhythmia	Cardiac disorders
AEACNOTH - Action Taken, Other	3	DIZZINESS	Dizziness	Nervous system disorders
AESTDTC - Start Date of AE; AESTDY - Study Day of AE Start	1	MILD LEUCOPENIA	Leukopenia	Blood and lymphatic system disorders
AESTDTC - Start Date of AE; AEENDTC - End Date of AE; AESTDY - Study Day of AE Start; AEENDY - Study Day of AE End	6	WORSENING TASTE DISORDER WITH METALLIC TASTE SENSATION	Dysgeusia	Nervous system disorders
AEOUT - Outcome	1	INSOMNIA	Insomnia	Psychiatric disorders

Changed records not affecting associated Table output.

Visual Change Indication: Listing Example

Columns with Differences	AESPID - AE Sponsor ID	AETERM - Reported Term	AEDECOD - MedDRA Preferred Term	AESOC - MedDRA System Organ Class
	1	HEADACHE	Headache	Nervous system disorders
	2	CHANGE IN SENSE OF SMELL	Parosmia	Nervous system disorders
	3	NASAL CONGESTION	Nasal congestion	Respiratory, thoracic and mediastinal disorders
	4	ACUTE VIRAL SYNDROME	Viral infection	Infections and infestations
	1	BILATERAL LEG EDEMA	Oedema peripheral	General disorders and administration site conditions

Normal records – for reference.

Visual Change Indication: Table Example

System Organ Class Preferred Term	BLINDED (N=529)			
	Mild n (%) [e]	Moderate n (%) [e]	Severe n (%) [e]	Total n (%) [e]
Gastrointestinal disorders (CONT.)				
Epigastric discomfort	1 (< 1.0) [1]	0 (0) [0]	0 (0) [0]	1 (< 1.0) [1]
Faecaloma	0 (0) [0]	1 (< 1.0) [1]	0 (0) [0]	1 (< 1.0) [1]
Hyperaesthesia teeth	1 (< 1.0) [1]	0 (0) [0]	0 (0) [0]	1 (< 1.0) [1]
Intestinal barrier dysfunction	1 (< 1.0) [1]	0 (0) [0]	0 (0) [0]	1 (< 1.0) [1]
Lip swelling	1 (< 1.0) [1]	0 (0) [0]	0 (0) [0]	1 (< 1.0) [1]

New event – Row is highlighted.

Visual Change Indication: Table Example

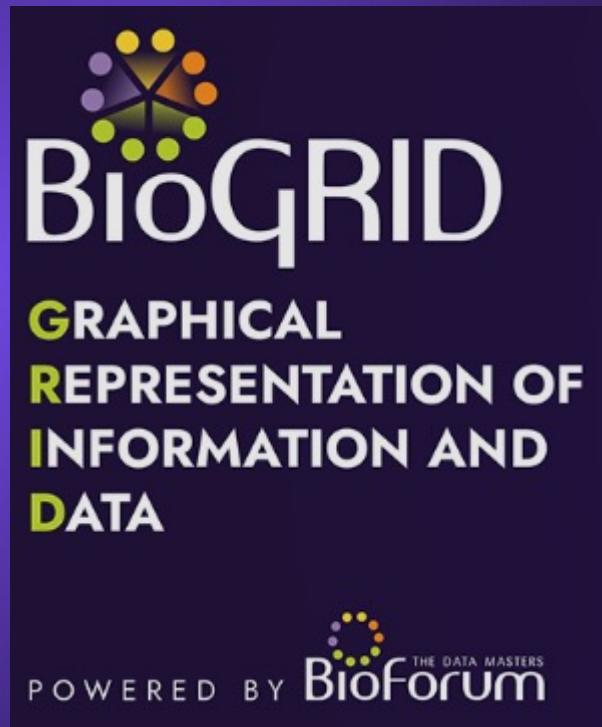
System Organ Class Preferred Term	BLINDED (N=529)			
	Mild n (%) [e]	Moderate n (%) [e]	Severe n (%) [e]	Total n (%) [e]
Nervous system disorders (CONT.)				
Sciatica	0 (0) [0]	1 (< 1.0) [1]	0 (0) [0]	1 (< 1.0) [1]
Sinus headache	1 (< 1.0) [1]	0 (0) [0]	0 (0) [0]	1 (< 1.0) [1]
Transient global amnesia	0 (0) [0]	0 (0) [0]	1 (< 1.0) [1]	1 (< 1.0) [1]
Transient ischaemic attack	0 (0) [0]	1 (< 1.0) [2]	0 (0) [0]	1 (< 1.0) [2]
Gastrointestinal disorders				
Total	87 (16.4) [172]	53 (10.0) [84]	8 (1.5) [9]	148 (28.0) [265]
Nausea	61 (11.5) [70]	26 (4.9) [29]	2 (< 1.0) [2]	89 (16.8) [101]

Changed events – updated values are highlighted.

What's next?

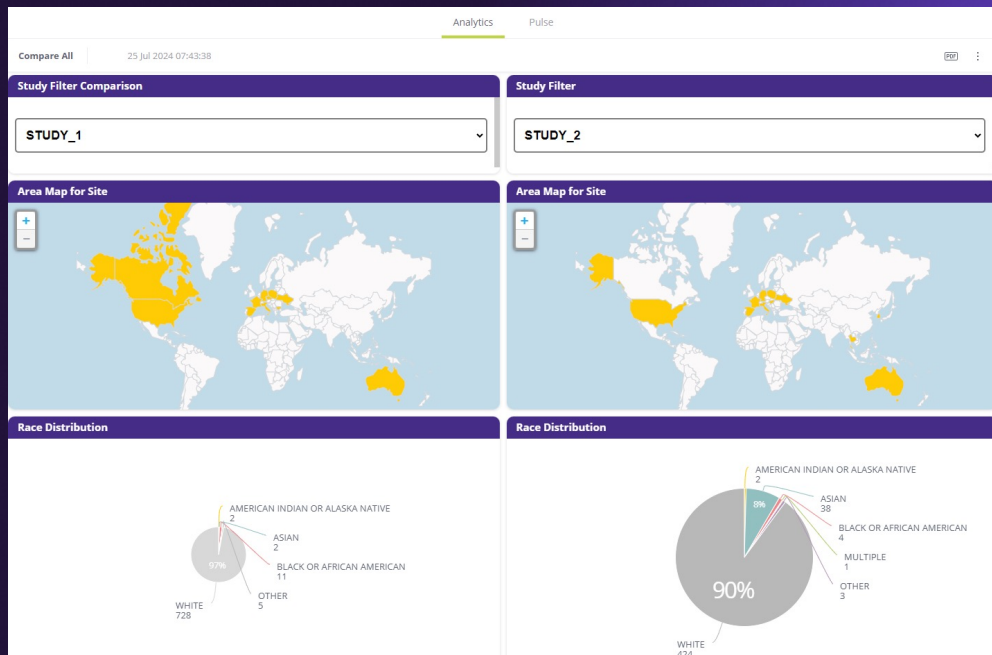
Future plans include:

- Expanding to BioGRID (an in-house development)
- Even faster
- Dynamic data review capabilities.
- Graphical representation of data linked directly to source.



What's next?

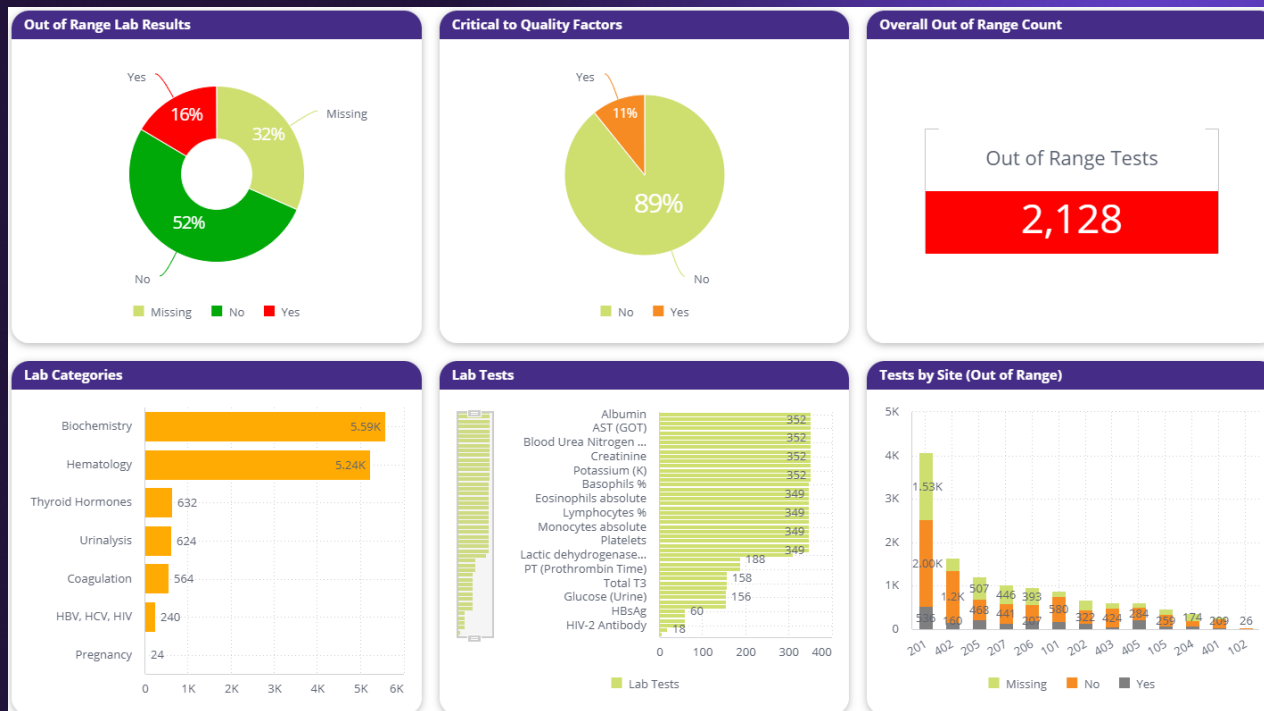
Some early examples:



Cross Study – Comparison

What's next?

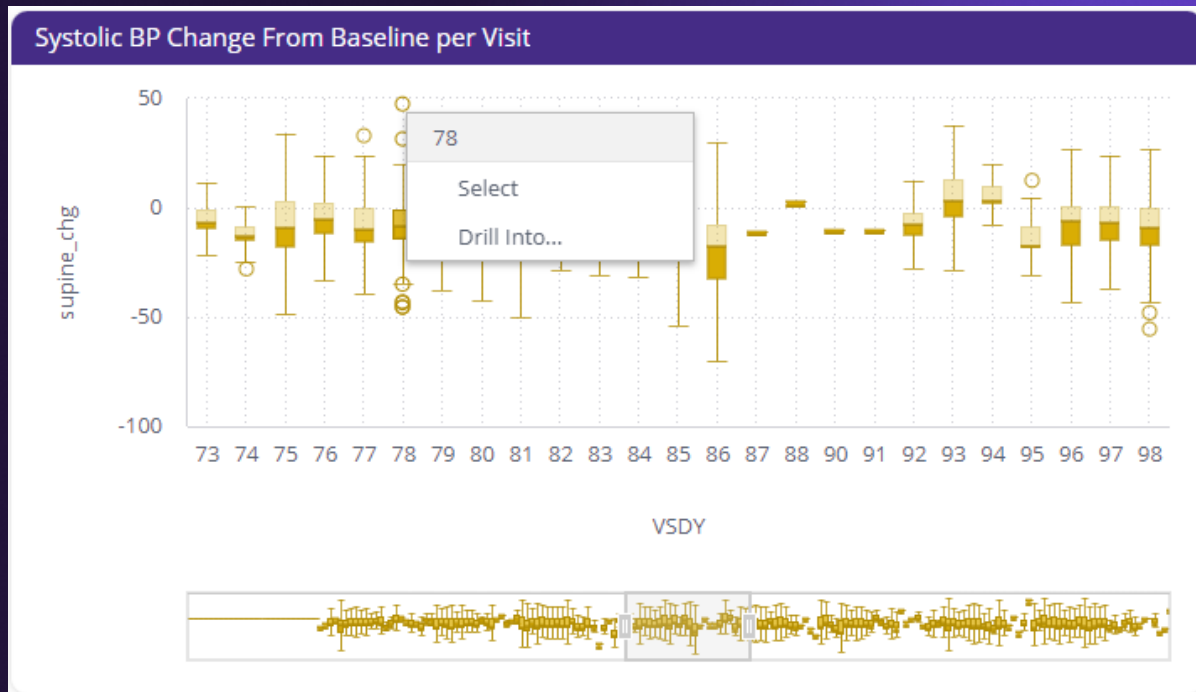
Some early examples:



Big picture overview.

What's next?

Some early examples:



The ability to drill right down into detail at a patient level. And lots more!

Keep watching this space!

THANK YOU!

