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ML18

The Best of Both Worlds:
AI and Human-in-the-Loop Processing in TLF Design, Production, and Validation

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Warm Up Questions

- How many of you are working in CRO/Pharma?
- How many of you are stats programmers or data scientists?
- How many of you have a detailed document or place with all the metadata needed for the phase from ADaM to TLFs?

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Our goal is to reduce double programming by 85% in the phase of ADaM to TLFs using a metadata approach

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Why?

In more than 30% of cases, even for standard tables, it is very difficult to replicate the same process.

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How?

Following the same procedures of the software development space with some adaptations.

Specs->Design->Technical Design->Development->Code review->
Unit testing->QA->Feature Release

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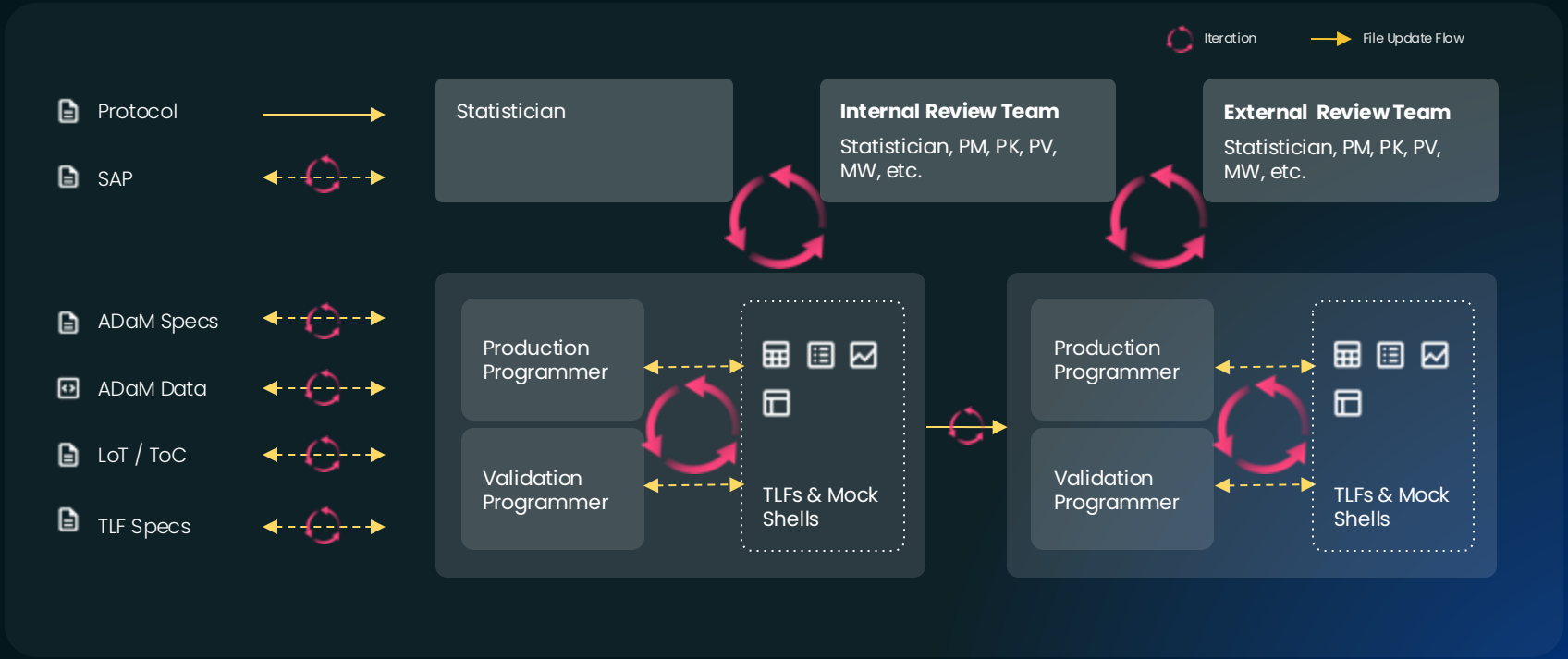
TLF Development and Review: One Deliverable



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What Should the Human-Machine Partnership Look Like?

Humans

- **Endpoint definition,** characterization
- Study conceptualization and design
- **Review, coalesce, interpret**
- Drive **continuous process improvement** for AI algorithms

Verify AI

- **Parse and understand** multiple document types
- **Automate review** with NLP, NER, RAG
- **Generate TLFs automatically** with HITL
- **Continually self-improve** AI models and algorithms

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How can we leverage/reuse the metadata acquired in one trial many times over?

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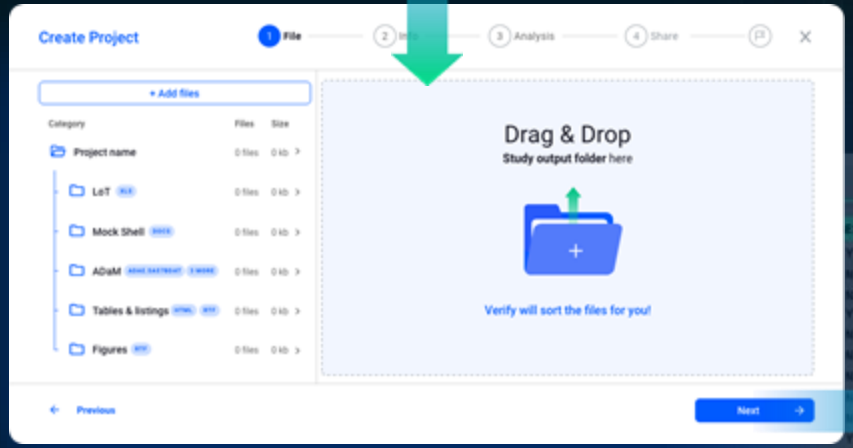
Verify's Dynamic Core

AI-Enabled Parsing and Results Metadata Extraction

Drag & Drop

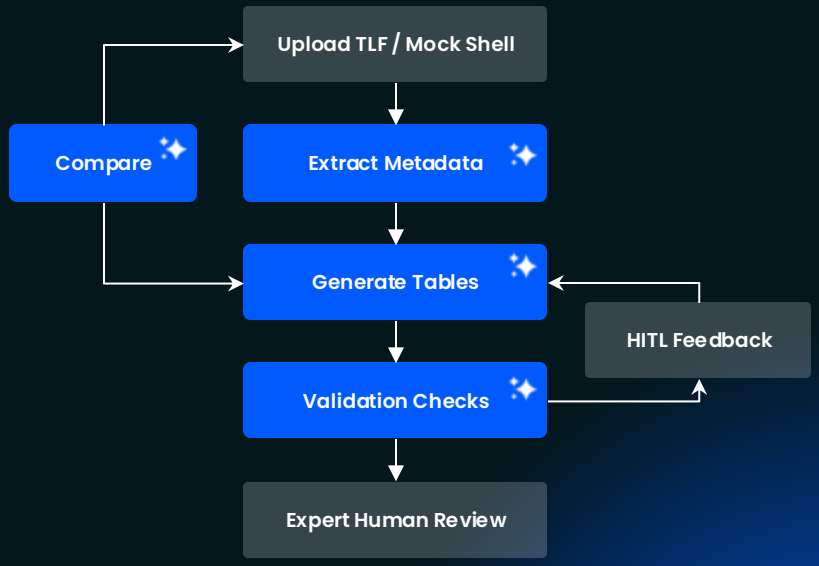


Parse & Ingest

Best of Both Worlds

AI-Enabled Output Generation with HITL Feedback

1. Verify **parses TLFs, extracts and links** data and results metadata
2. Verify **checks** your outputs (format, arithmetic, within-table, cross-table)
3. Verify identifies **linkages** between **ADaM** and **tables***
4. Verify incorporates **SME feedback** via the Metadata Curator
5. Verify **continually improves accuracy**



User

Verify AI (NER + LLM)

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Best of Both Worlds Use Case

AI-Enabled Output Generation with HITL Feedback

Programmer-Generated Table

N=5

Table 14.3.2.5.2
BE-0552543 Protocol A1234567
Treatment-Emergent Adverse Events by System Organ Class (Treatment Related, Immunogenicity Sub-study Analysis Set)

	Placebo (N=9)	BE-0552543 100mg QD (N=5)	BE-0552543 200mg QD (N=11)
Number of Subjects Evaluable for AEs			
Number (%) of Subjects: by SYSTEM ORGAN CLASS	n (%)	n (%)	n (%)

Compare & Decide: Update TLF title or subset

Verify-Generated Table

N=6

Generated by Verify

Table 14.3.2.5.2
BE-0552543 Protocol A1234567
Treatment-Emergent Adverse Events by System Organ Class (Treatment Related, Immunogenicity Sub-study Analysis Set)

	Placebo (N=9)	BE-0552543 100mg QD (N=6)	BE-0552543 200mg QD (N=11)
Number of Subjects Evaluable for AEs			
Number (%) of Subjects: by SYSTEM ORGAN CLASS	n (%)	n (%)	n (%)

ADAM Dataset

N=6

Unique Subject Identifier	Full Analysis Set Population Flag	Safety Population Flag	Per-Protocol Population Flag	Completers Population Flag	Randomized Population Flag	Immunogenicity Substudy Analysis Flag	Description of Planned Arm	Planned Arm Code	Description of Actual Arm	Actual Arm Code
USUBJ.	FASFL	SAFFL	PPROTFL	COMPLFL	RANDFL	ISSFL	ARM	ARMCD	ACTARM	ACTARMCD
A1234567 1001 10015001	Y	Y	Y	Y	Y	Y	BE-0552543 100mg QD	D	BE-0552543 100mg QD	D
A1234567 1001 10015002	N	N	N	N	N	N	SCREEN FAILURE	SCRNFAIL	SCREEN FAILURE	SCRNFAIL
A1234567 1001 10015003	Y	Y	Y	Y	Y	N	Placebo	A	Placebo	A
A1234567 1001 10015004	Y	Y	Y	Y	Y	Y	BE-0552543 100mg QD	D	BE-0552543 100mg QD	D
A1234567 1001 10015005	Y	Y	Y	Y	Y	Y	BE-0552543 100mg QD	D	BE-0552543 100mg QD	D
A1234567 1001 10015006	Y	Y	Y	Y	Y	Y	BE-0552543 100mg QD	A	BE-0552543 100mg QD	A
A1234567 1001 10015007	Y	Y	Y	Y	Y	Y	BE-0552543 100mg QD	D	BE-0552543 100mg QD	D
A1234567 1001 10015008	Y	Y	Y	Y	Y	Y	BE-0552543 100mg QD	D	BE-0552543 100mg QD	D
A1234567 1001 10015009	Y	Y	Y	Y	Y	Y	BE-0552543 100mg QD	D	BE-0552543 100mg QD	D

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Verify

Projects

Help and Support

14.1.1.13

100

Table 14.1.1.13

Treatment-Emergent Adverse Events and Preferred Term Leading to Discontinuation of Study Drug Treatment Related - Safety Population by System Organ Clas

	Drug A (N=119)				Drug B (N=109)			
	Mild	Mod.	Sev.	Total	Mild	Mod.	Sev.	Total
Any TEAEs	1 (0.8%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	2 (2.0%)	2 (2.0%
Infection	1 (0.8%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	2 (2.0%)	2 (2.0
Bronchitis viral	1 (0.8%)	0 (0.0%)	0 (0.0%)	1 (0.8%)	0 (0.0%)	0 (0.0%)	2 (2.0%)	2 (2.0

N = number of subjects in the specified group, or the total sample. This value is the denominator for the percentage calculatio
Subjects are only counted once per event in each row.
BEACONCURE CONFIDENTIAL SDTM Creation: 08OCT2021 (00:55) Source Data: adae Table Generation: 09OCT2021

Metadata Alignment

Review the current alignment between **table entity and** ADaM column and values. Revise if necessary.

Table Entity	ADaM Column	ADaM Value(s)
Title		
Treatment-Emergent	TRTEMFL	Y
Leading to Discont...	AEACN	DRUG WI...
Treatment Related	AEREL	RELATED
Safety Population	SAFFL	Y
Column/Row Headers		
Major (Treatment)	TRTA	
Minor (Severity)	AESEV	

Cancel

Save

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Automate Reuse of Context-Rich Results Metadata

- **Human-in-the-loop (HITL) feedback**
  - Modify metadata alignment between table entities and ADaM
  - Alignment saved and applied to subsequent checks and analyses
- **Compatibility with CDISC ARS** framework
- Basis for **automated output generation**
- **Activity Log** automatically records changes

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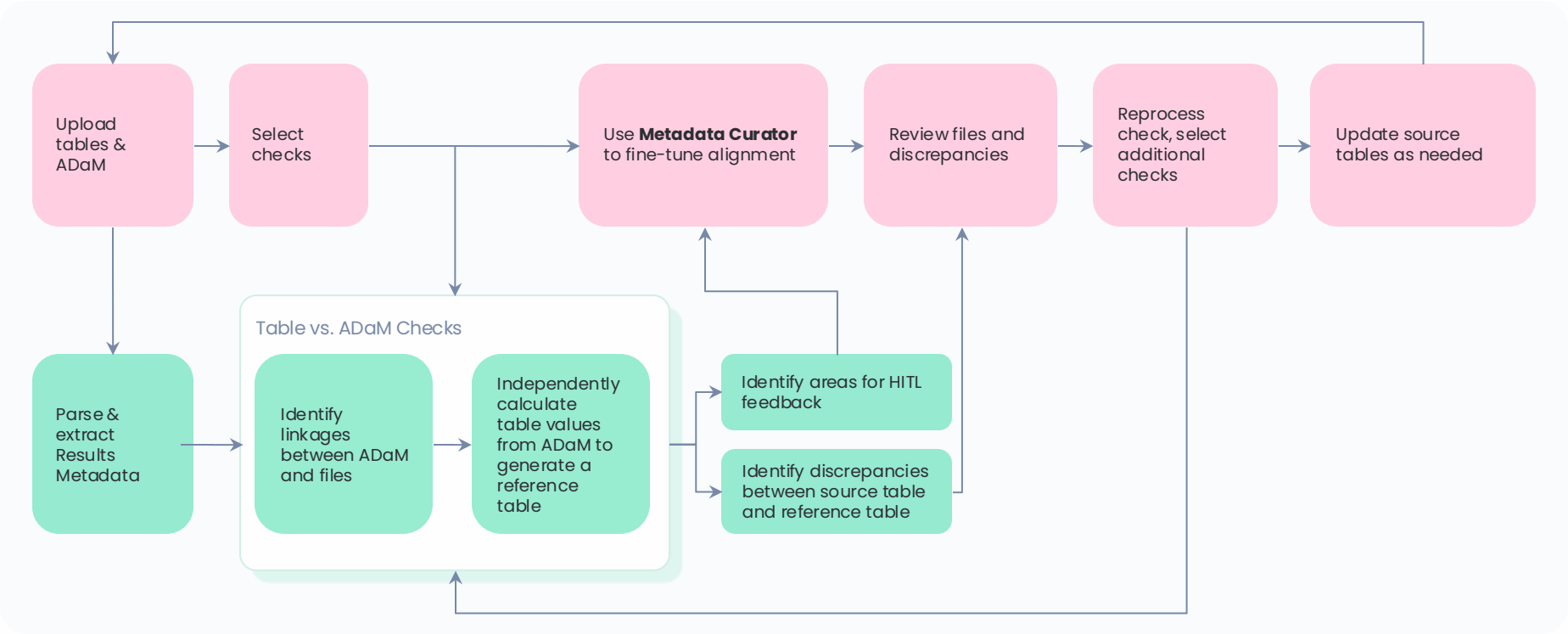
Metadata Curator Process Map:
Current User and Verify Flow

User flow (Statistical Programmer)

Verify flow - AI-enabled table generation and checks



Evolution of Clinical Research Analytics: Human-AI Integration

AI Processing Pipeline

- Document parsing
- Entity extraction
- Relationship mapping
- Automated validation checks
- Discrepancy identification

Human Review Interface

- Clear presentation of AI-identified elements
- Intuitive tools for reviewing and modifying metadata
- Feedback capture mechanisms
- Activity logging for audit trails

Learning Loop

- Capture of human decisions and corrections
- Integration of feedback into training data
- Continuous model improvement
- Performance monitoring and metrics

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Verify Benefits and Outcomes

Speed

- Shorter Review Cycles
- Reduced Review Effort
- Enhanced Accuracy

Efficiency

- Reduced Spreadsheet Maintenance
- Fewer Email Chains
- Scalable Growth

Visibility

- Centralized Management
- Enhanced Executive Oversight
- Transparent Audit Trail

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Thank You!

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