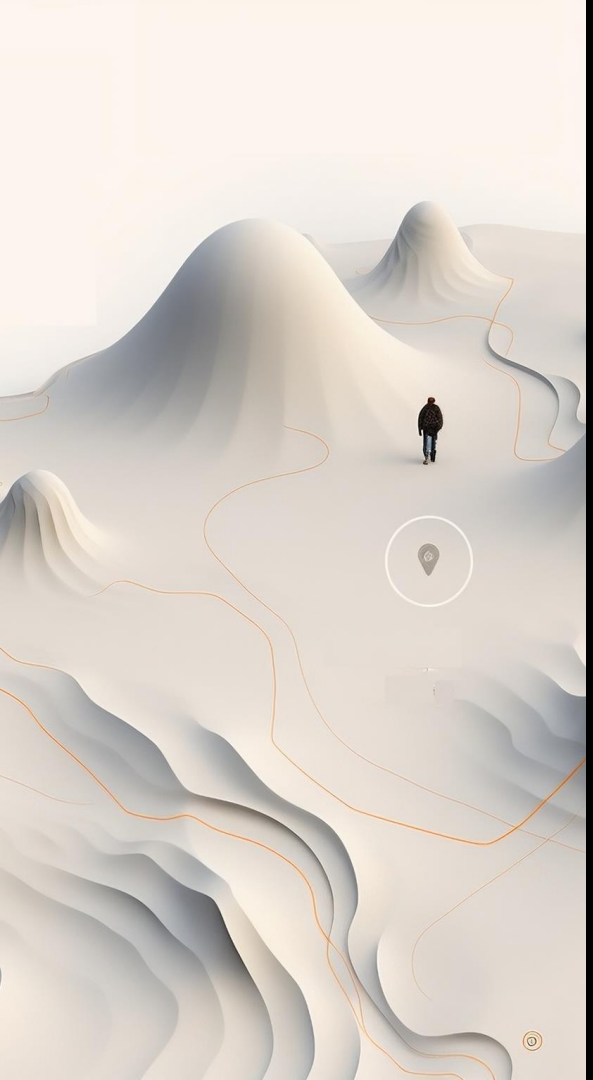

Accelerating and Reducing the Cost of Literature Reviews and Regulatory Dossiers for Rare Diseases with AI

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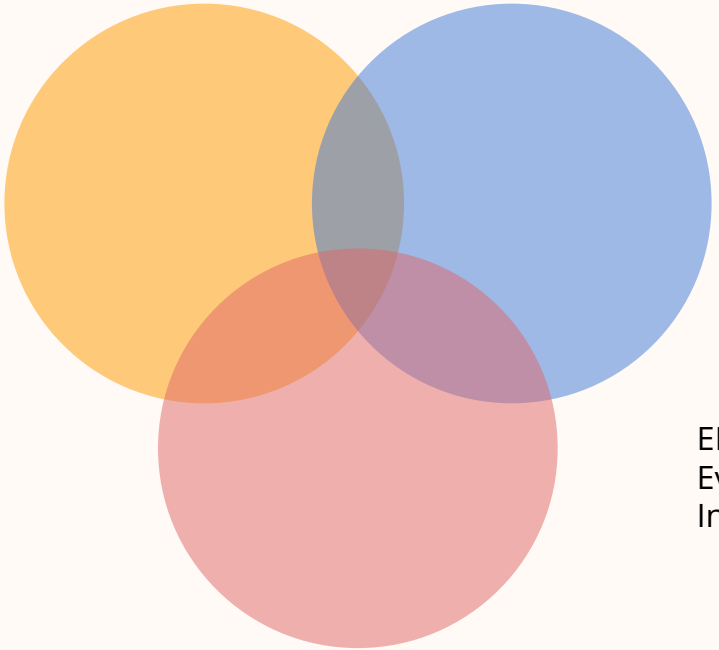
CEO & Founder
Tehistark

meelis@tehistark.com

Problem: Constraints Compound for Treatment Innovation to Rare Diseases

Limited Data

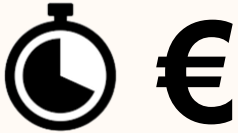
6000 diseases
Variable manifestations



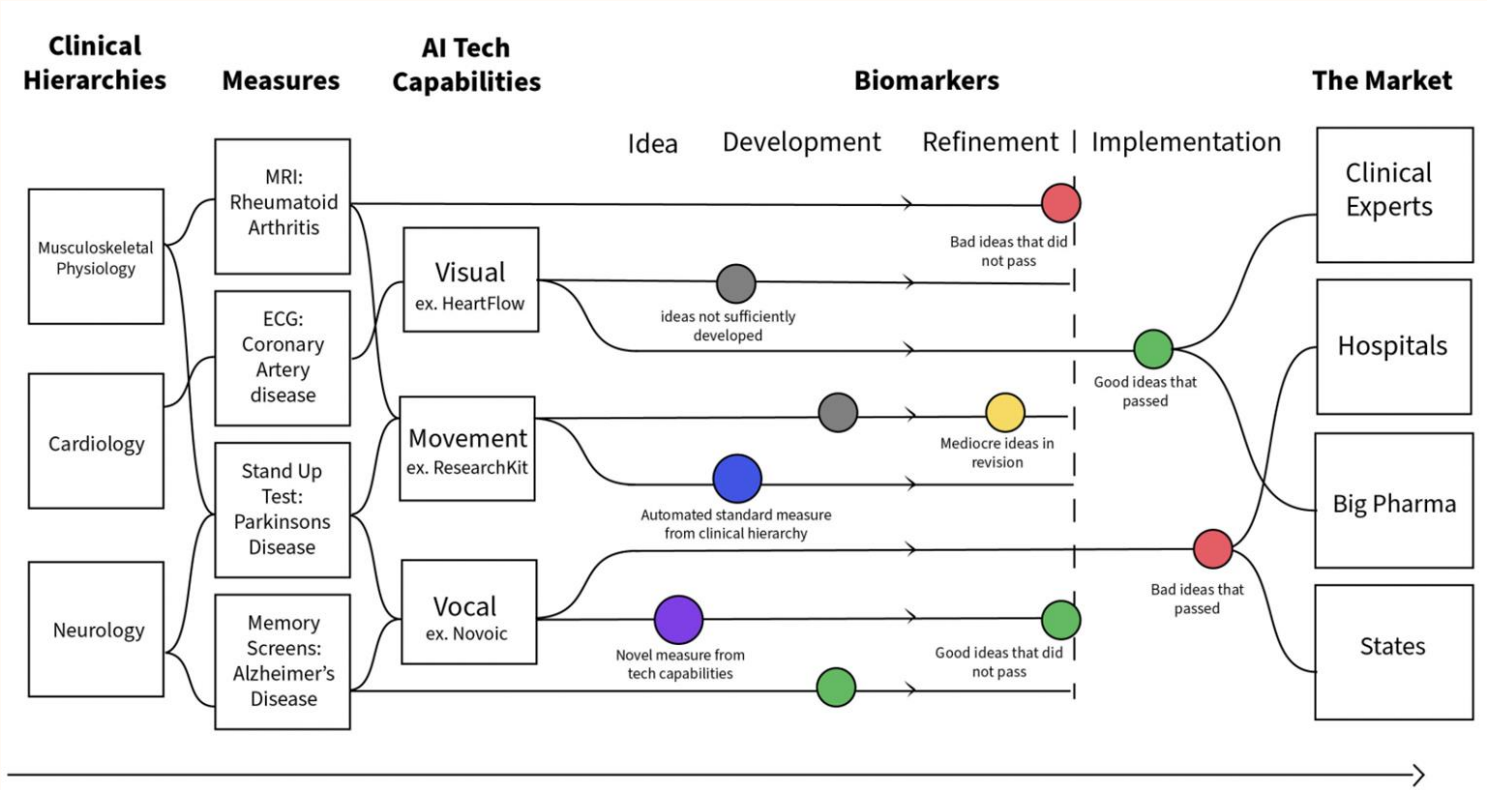
Regulatory Complexity

EMA, national, and global frameworks.
Evolving guidelines
Inconsistencies across jurisdictions.

Resource Constraints



Example: The Uncertain Landscape of Digital Measurement Devices to the Market



Example: Developing Solutions for Myasthenia Gravis (MG)

Completed

1. Write Protocol

Help Build an A.I. Model to Predict Myasthenia Gravis Symptom Patterns and Flares

ClinicalTrials.gov ID NCT04590716

Sponsor doc.ai inc

Information provided by doc.ai inc (Responsible Party)

Last Update Posted 2021-07-29

Drug

Device

Use and impact

Regulatory barrier

2. Collect Data

Front Neurol. 2023 Aug 1:14:1144183. doi: 10.3389/fneur.2023.1144183. eCollection 2023.

A decentralized, prospective, observational study to collect real-world data from patients with myasthenia gravis using smartphones

Sandra Steyaert [1 2], Meelis Lootus [1], Chethan Sarabu [1], Zeenia Framroze [1], Harriet Dickinson [3], Emily Lewis [4], Jean-Christophe Steels [4], Francesca Rinaldo [1]

Affiliations + expand

PMID: 37588667 PMCID: PMC10427188 DOI: 10.3389/fneur.2023.1144183

Abstract

Introduction: We conducted a 3-month, prospective study in a population of patients with Myasthenia Gravis (MG), utilizing a fully decentralized approach for recruitment and monitoring (ClinicalTrials.gov Identifier: NCT04590716). The study objectives were to assess the feasibility of collecting real-world data through a smartphone-based research platform, in order to characterize symptom involvement during MG exacerbations.

3. Use Data for Decisions, Planning

Digit Biomark. 2023 Jul 28;7(1):63-73. doi: 10.1159/000531224. eCollection 2023 Jan-Dec.

Development and Assessment of an Artificial Intelligence-Based Tool for Ptosis Measurement in Adult Myasthenia Gravis Patients Using Selfie Video Clips Recorded on Smartphones

Meelis Lootus [1], Lulu Beatson [1], Lucas Atwood [1], Theo Bourdais [1], Sandra Steyaert [2], Chethan Sarabu [1], Zeenia Framroze [1], Harriet Dickinson [3], Jean-Christophe Steels [4], Emily Lewis [4], Nirav R Shah [5], Francesca Rinaldo [1]

Affiliations + expand

PMID: 37545566 PMCID: PMC10399113 DOI: 10.1159/000531224

Abstract

Introduction: Myasthenia gravis (MG) is a rare autoimmune disease characterized by muscle weakness and fatigue. Ptosis (eyelid drooping) occurs due to fatigue of the muscles for eyelid elevation and is one symptom widely used by patients and healthcare providers to track progression of the disease. Margin reflex distance 1 (MRD1) is an accepted clinical measure of ptosis and is typically assessed using a hand-held ruler. In this work, we develop an AI model that enables automated measurement of MRD1 in self-recorded video clips collected using patient smartphones.

Solution: AutoDossier to make High Quality Dossiers Fast

WHAT IS AUTODOSSIER AND HOW DOES IT WORK?

Step 1: Upload your data

Upload to secure platform. No organisation required.

Step 2: Go for coffee

AI completes a first draft (or several different versions) fully autonomously, for you to iterate on.

Step 3: Review and iterate

Return to a completed first draft - much faster than starting from scratch - with source data shown. Iterate faster and better with AI assistance.

Solution: AutoDossier to make High Quality Dossiers Fast

WHAT DOCUMENTS CAN YOU CREATE ON AUTODOSSIER?

Literature Reviews: Rapid, Targeted, Systematic

Search
Screen
Extract
Synthesize

IND & CTA

CMC
Toxicology
Pharmacology
Pharmacokinetics

HTA

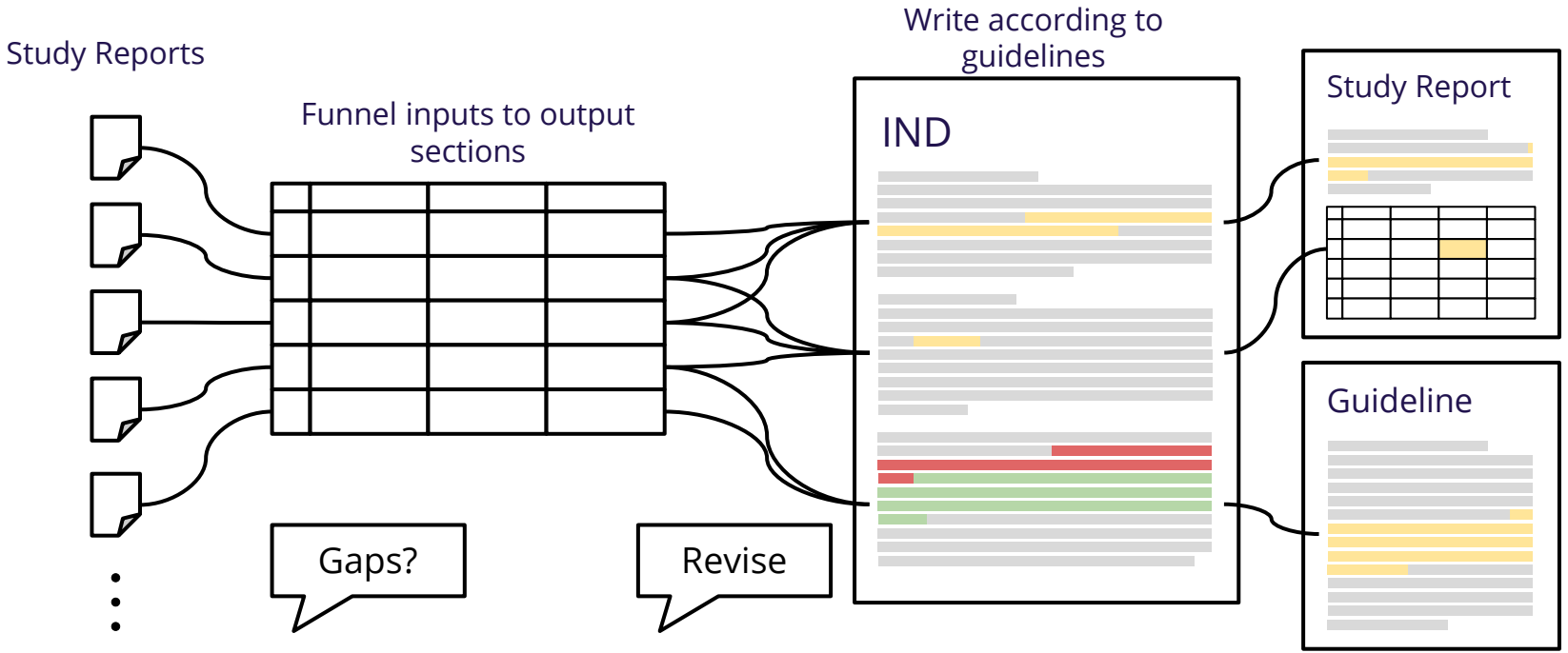
Clinical
Economic

AutoDossier: How do we use AI

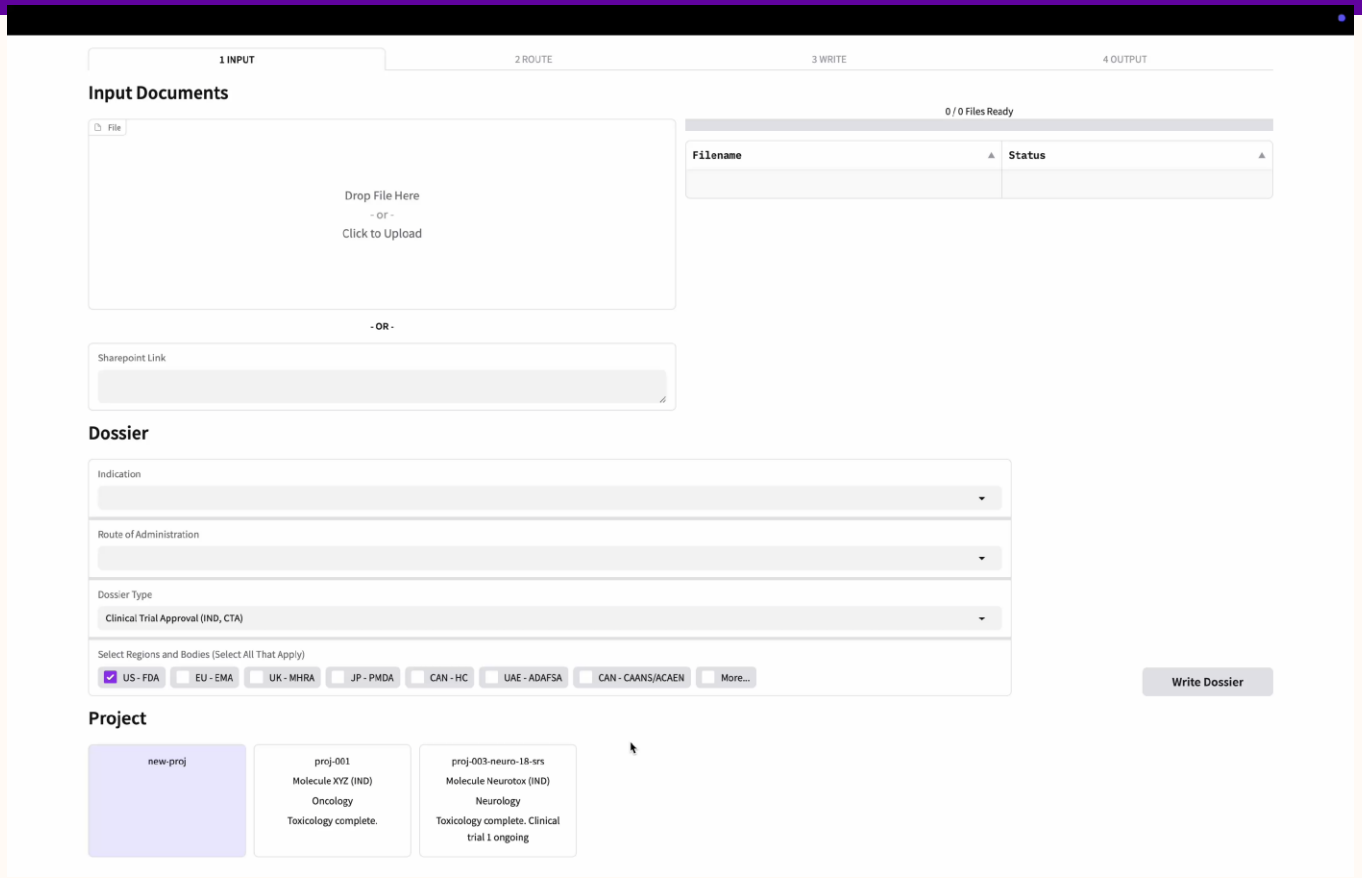
MVP pilot-ready!
(Secure Usable Cloud Platform)

Draft the IND in minutes, by optimally combining AI and human input.

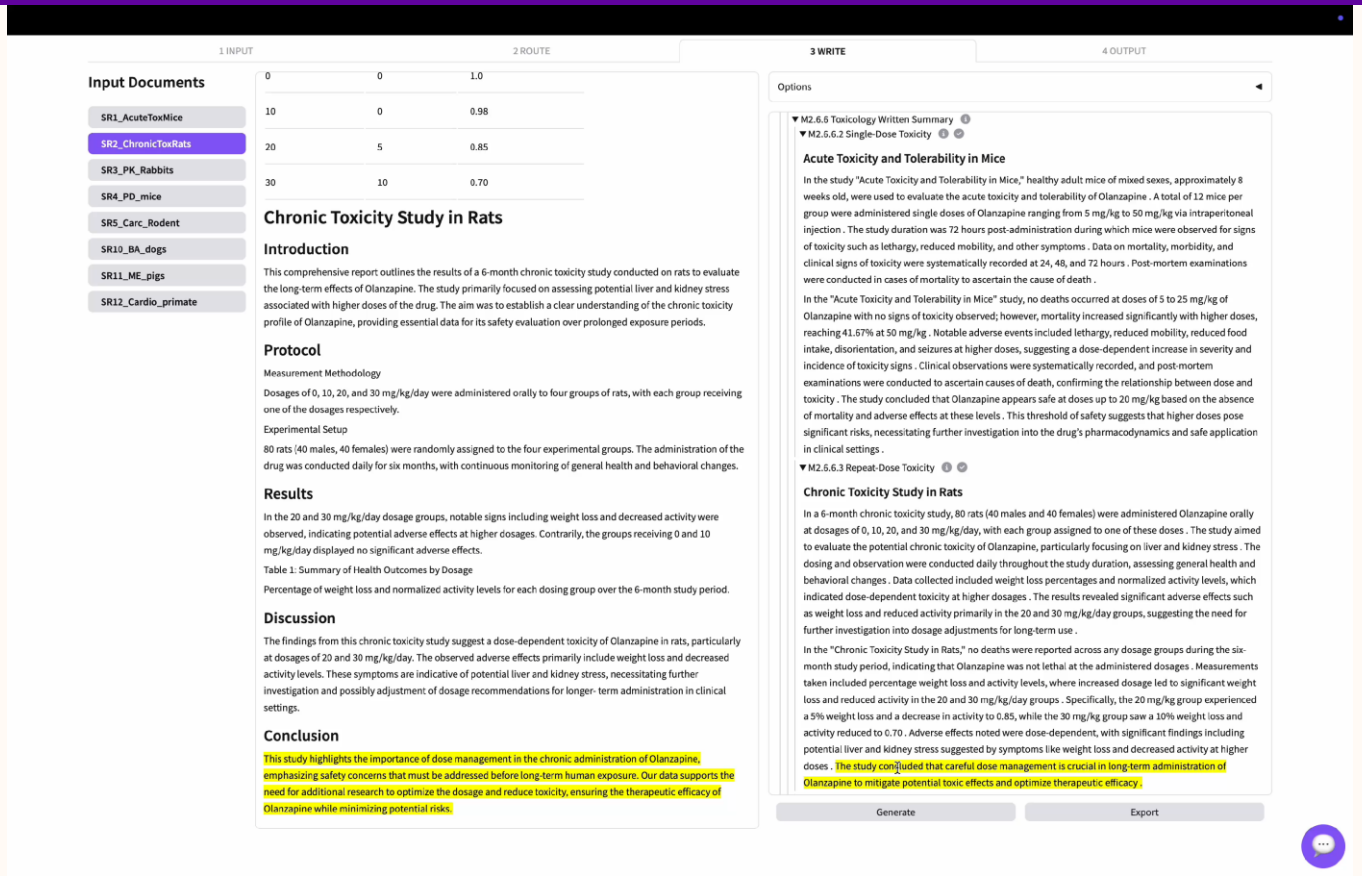
1. Upload inputs **2. Route, find gaps** **3. Auto-draft** **4. Verify & Revise**



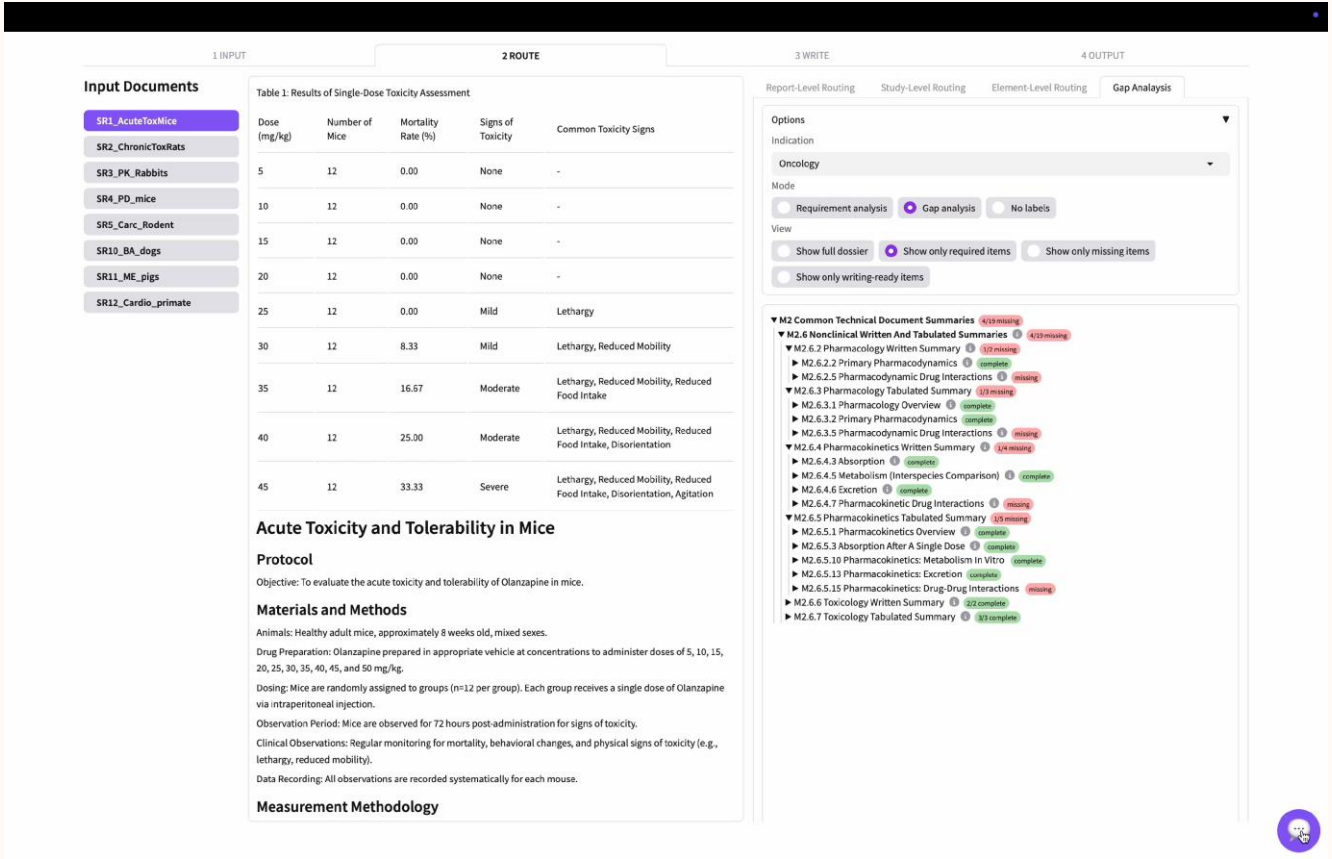
Demo 1: Writing an IND



Demo 2: Gap Analysis



Demo 3: Updating an IND



AutoDossier: Benefits

WHAT ARE THE BENEFITS OF AUTODOSSIER?

Higher quality, more transparent work

Ground your applications in the optimal content. Draft with the help of AI. It takes less time to review than to generate from scratch.

Less Expert time spent on Admin Work

Let AI do the heavy lifting on repetitive work, and ask its second opinion on narration, or work out the most fitting narrative with its assistance.

Faster to Market

Thanks to time saved with AI-based document organisation and narrative suggestions, you are able to cut months off project timelines.

Product (2/2): AutoSLR (Systematic Lit Review)

MVP pilot-ready!
(Secure Usable Cloud Platform)

Ground the therapeutic program in clinical and market context better, cheaper, faster

1 Study Setup

- Sculpt your **research question**
- Craft or upload methodology
- **Article Harvester**
  - Directly from databases

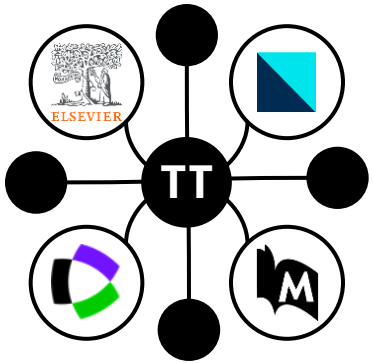
2 PRISMA Machine

- Duplicate removal
- Relevance screening
- Quality screening

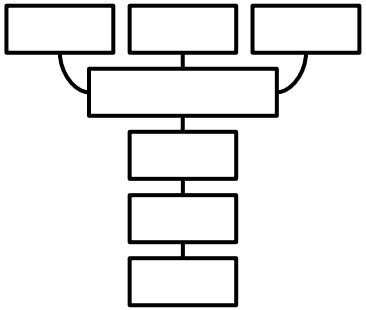
3 Extract-Analyse-Write

- Extract relevant data
- Analyse and iterate
- Write the SLR draft

Data sources

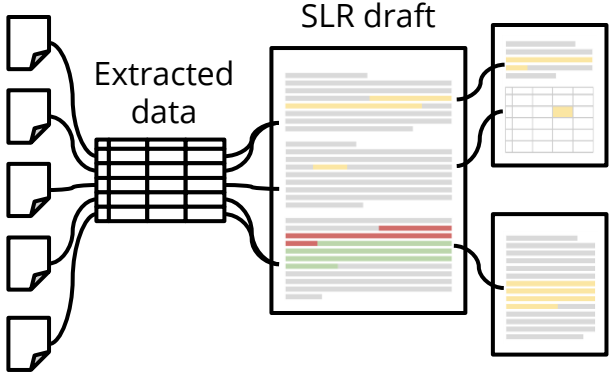


Downloaded articles

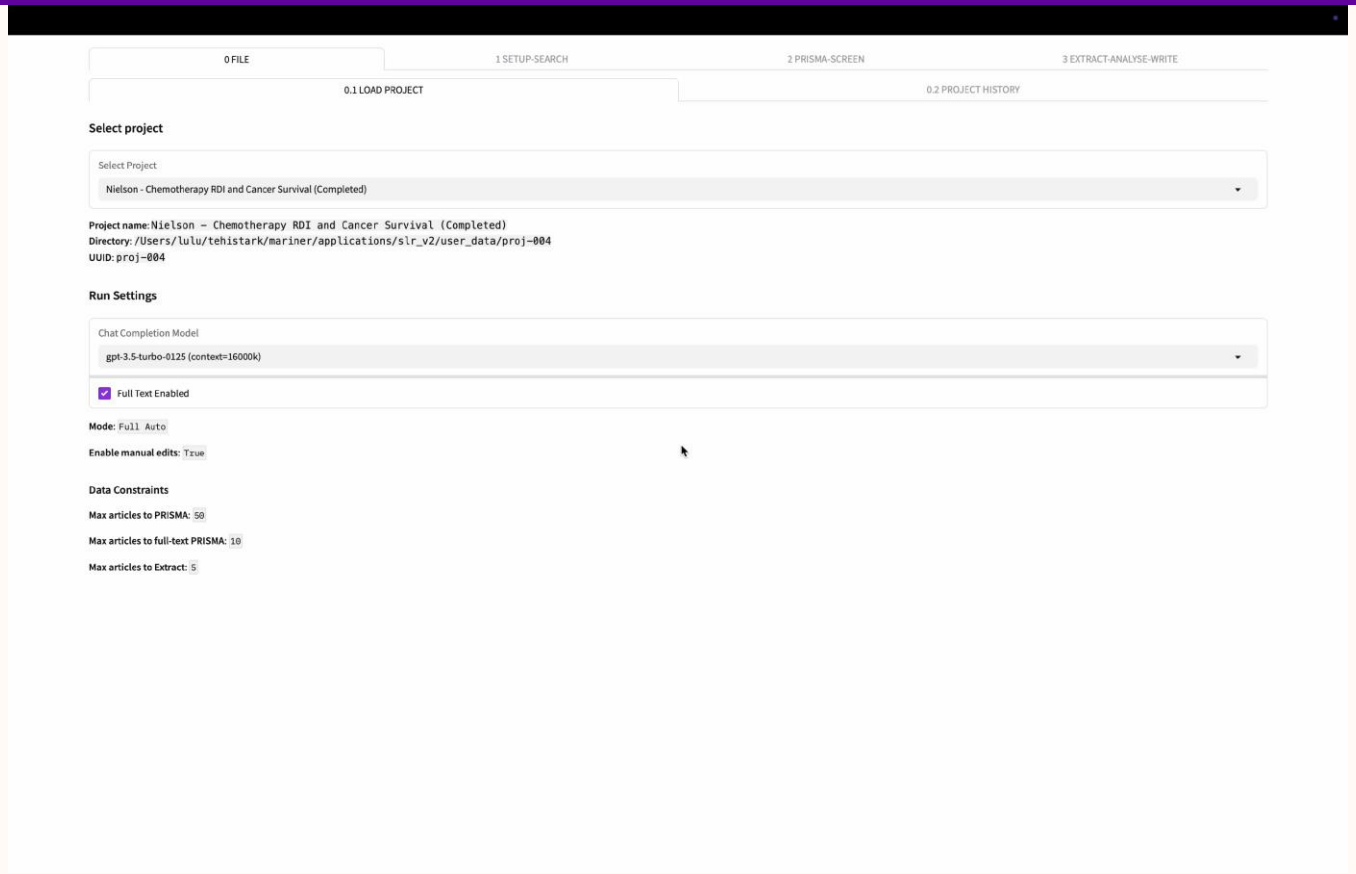


Included articles

Included articles



Demo 4: AutoSLR



Performance & Utility

	Step 1: Protocol Development	**Step 2**: Search articles	**Step 3**: Screen articles	**Step 4**: Extract to tables	**Efficiency Metrics**
Full-Auto	INCLUSION • Population: Studies must include patients diagnosed with secondary progressive multiple sclerosis (**SPMS**). • Intervention: Studies must investigate the effects of Siponimod as a treatment. • Outcome: Studies must report on clinical efficacy and/or safety outcomes of Siponimod treatment. EXCLUSION • Non-human studies: Exclude studies that are not conducted on human subjects. • Non-SPMS population: Exclude studies that do not focus on patients with secondary progressive multiple sclerosis. • Other Interventions: Exclude studies that do not focus specifically on Siponimod as the intervention.	**The query**: 75-term query fully autonomously written by AI, optimised research question and protocol: 18 P-terms, 15 I-terms, 11 C-terms, 17 O-terms, 14 S-terms. **Sources:** PubMed **Records returned: 85**	Records identified: **85** Input to TA: 85 Included by TA: 31 FT-s auto-obtained: 13 FT-included: **12 (disjoint with manual)** Out of the included articles, 1 is a protocol (the inclusion exclusion criteria did not ask these to be exclude, 1 is in German - but the extraction still worked.	Data Extraction Accuracy (Full Auto): • 60% perfect match • 33% partial match • 7% requiring review • Zero hallucinations	85 records → 12 studies 5 minutes
Part-Auto	INCLUSION • Adult: The study population includes adults aged 18 years and older. • SPMS: Patients are diagnosed with secondary progressive multiple sclerosis (**SPMS**). • Intervention: The study must investigate at least one of the following interventions: *(list of 25 treatments including Siponimod)* • Comparator: *(conditions on placebo, in 50 words)* • Outcomes: The study must report any efficacy, health-related quality of life (HRQoL) or safety outcomes, including: *(plus 115 words more)* • Study Design: The study design one of the following allowed types: (+70) • English: The abstract or full text is in English. EXCLUSION • Mixed Population: The study reports eligible outcomes in a mixed population, without separately reporting data for the population of interest (unless more than 80% of study population are adults with SPMS) • Non-human: The study has non-human subjects.	**The query**: 69 part composite query written by the original study team: 6 I&P-terms, 32 S-terms, 30 I&C-terms. **Sources**: PubMed **Records returned**: 2715	Records identified: **2715** Input to TA: 336 TA-included: 36 FT-s obtained: 25 FT-included: **17** **TA Recall = 0.92** **FT recall = 0.90**	Hybrid Performance: • 58% perfect match • 35% partial match • 8% poor match • Zero hallucinations	2,715 records → 13 studies 1 week
Manual		**The query**: Same as last row. **Sources**: PubMed + other **Records returned**: 3478 total (2726 from PubMed)	Records identified: **3478** Input to TA: 3212 TA-included: 341 FT-s obtained: 341 FT-included: 97 (23 studies)	The AI discovered (1) page 55 NCT number wrong for ASCEND trial, (2) two cells that were missing from the original dossier draft IMPACT study on page 58.	3,478 records → 23 studies 8 weeks

Value

- First draft rapidly (5 minutes)
- Make better decisions for the rest
- Speed up the rest

Potential for Rare Diseases

- Patient Interviews
  - Automate interviews
- Data analysis
  - Rapid reviews and other reasoning across the 6000 diseases
- Regulatory documents
  - Produce them faster, at lower cost

Other?

Who are we at Tehistark

Dr. Meelis Lootus

CEO and Founder

PhD ML, University of Oxford VGG

- 13 years in AI + clinical research
- 5 start-ups, 2 acquisitions
- Senior ML Engineer @ doc.ai
- Director of AI Engineering @ Sharecare Inc

Dr. Lynn Gold

Chief Regulatory Advisor

PhD Organic Chemistry

- 35 years of leadership in the pharma industry
- 70 IND, 27 NDA, 6 ANDA, 2 BLA and 1 PMA
- VP Reg Affairs Impel Pharma

Lulu Beatson

Founding Engineer

BA Maths, University of Cambridge

- Co-authored papers on ML for digital biomarkers
- Developing ML pipelines
- Data & AI Engineer @ doc.ai
- Software Engineer @ RegGenome

Dr. Derek Driggs

Machine Learning Engineer

PhD ML, University of Cambridge

- Training AI systems to predict financial markets
- Published in top ML journals incl. Nature Machine Intelligence (example SLR - Nature, cited by 783)

Kerry Hu

Research Assistant

MSci Neuro + MD student

- Validation Studies for in-house neurotechnology device @ HealthTech Connex
- Digital Biomarker Regulations Researcher at IEEE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