Adoption Story from a Biopharmaceutical Organization

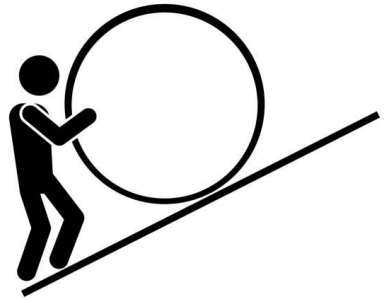
Case Study:
Clinical Content Reuse (CCR) and Document Automation – Key considerations for success

TransCelerate BIOPHARMA INC.

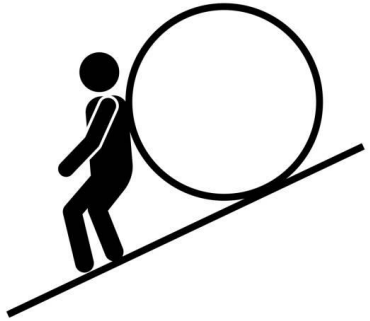
Have we improved clinical trial design and execution?

Process

Consistency



Standardization



Compliance

Industry Challenges

1. Growth in protocol design customizations: 3X the amount of information compared to 10 years ago
    - Approval to FPFV time up by 27%
    - Longer duration of downstream processes eg, EDC build and SDTM creation
    - Phase III trials: 37% increase in total mean endpoints and a 42% increase in total number of procedures from 2016-2021.
2. Increase in the number of PAs = Increase cost burden and drop out rates
    1. Total substantial amendments up by 113%
    2. Average of 4 PAs per study
3. Research sites face increasing burden from protocol complexity
4. Increase in complexity of submission package: how much of the data collected from a clinical trial actually supports the target indication?

Sources:

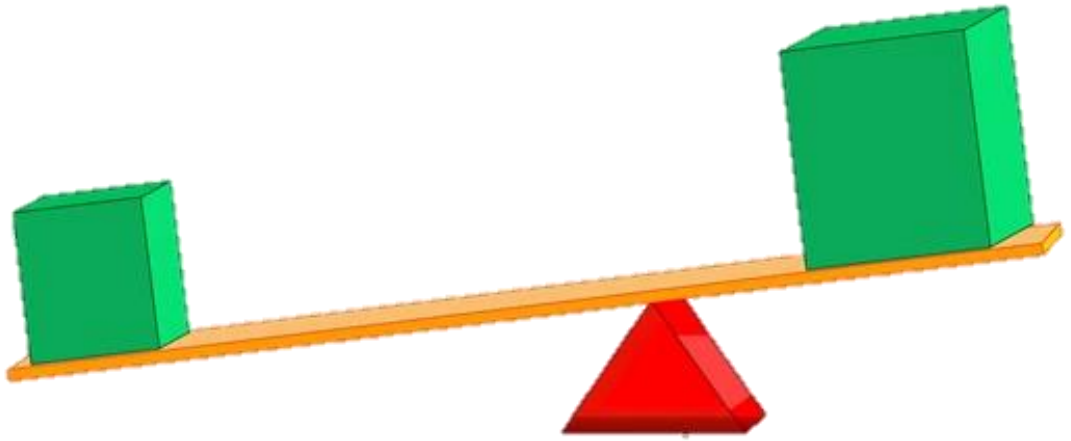
- Getz KA, et al. The Impact of Protocol Amendments on Clinical Trial Performance and Cost. Ther Innov Regul Sci. 2016 Jul;50(4):436-441.
- Getz K, Smith Z, Botto E, Murphy E, Dauchy A. New Benchmarks on Protocol Amendment Practices, Trends and their Impact on Clinical Trial Performance. Ther Innov Regul Sci. 2024 May;58(3):539-548. https://aspe.hhs.gov/reports/examination-clinical-trial-costs-barriers-drug-development-0
- Tufts CSDD Impact Report. Vol 25; 3. May/June 2023
- Quantifying Site Burden to Optimize Protocol Performance https://pubmed.ncbi.nlm.nih.gov/38191957/

Is automation and AI the magical potion that will solve all our industry's problems?

What is the Recipe for Success?

Widely Used/Typical Recipe in the Industry

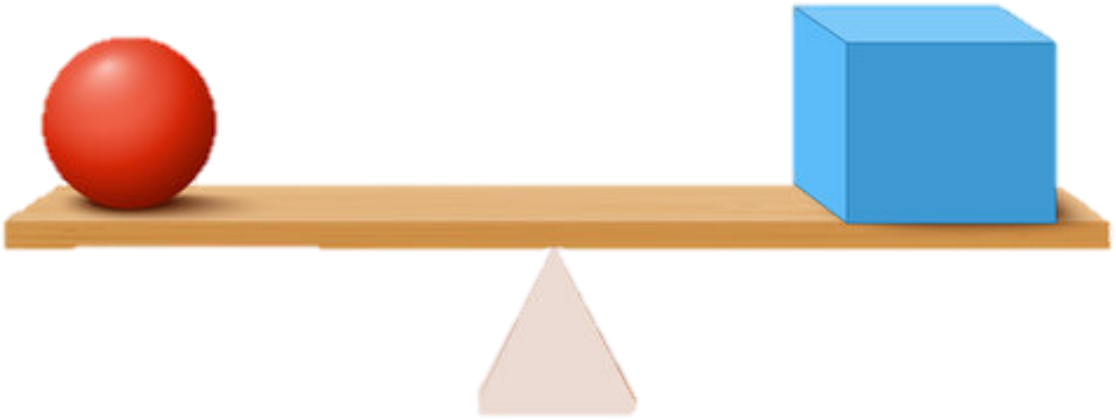
Industry Strategy:
AI/ML (discrete, siloed by document type)



Content/data Standardization

Recipe for Success

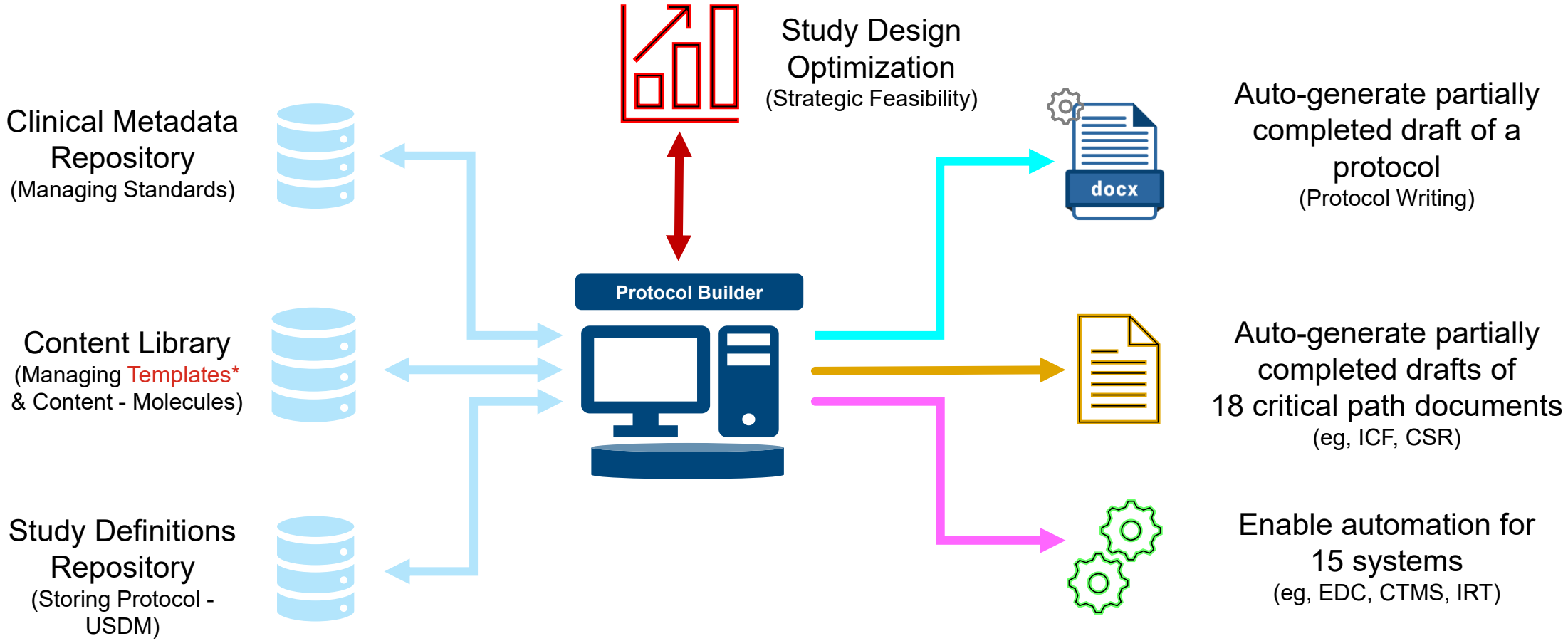
BeOne Strategy: AI/ML (disruptive, CCR connectivity)



Content/data Standardization + Development Data Flow + Building Repository

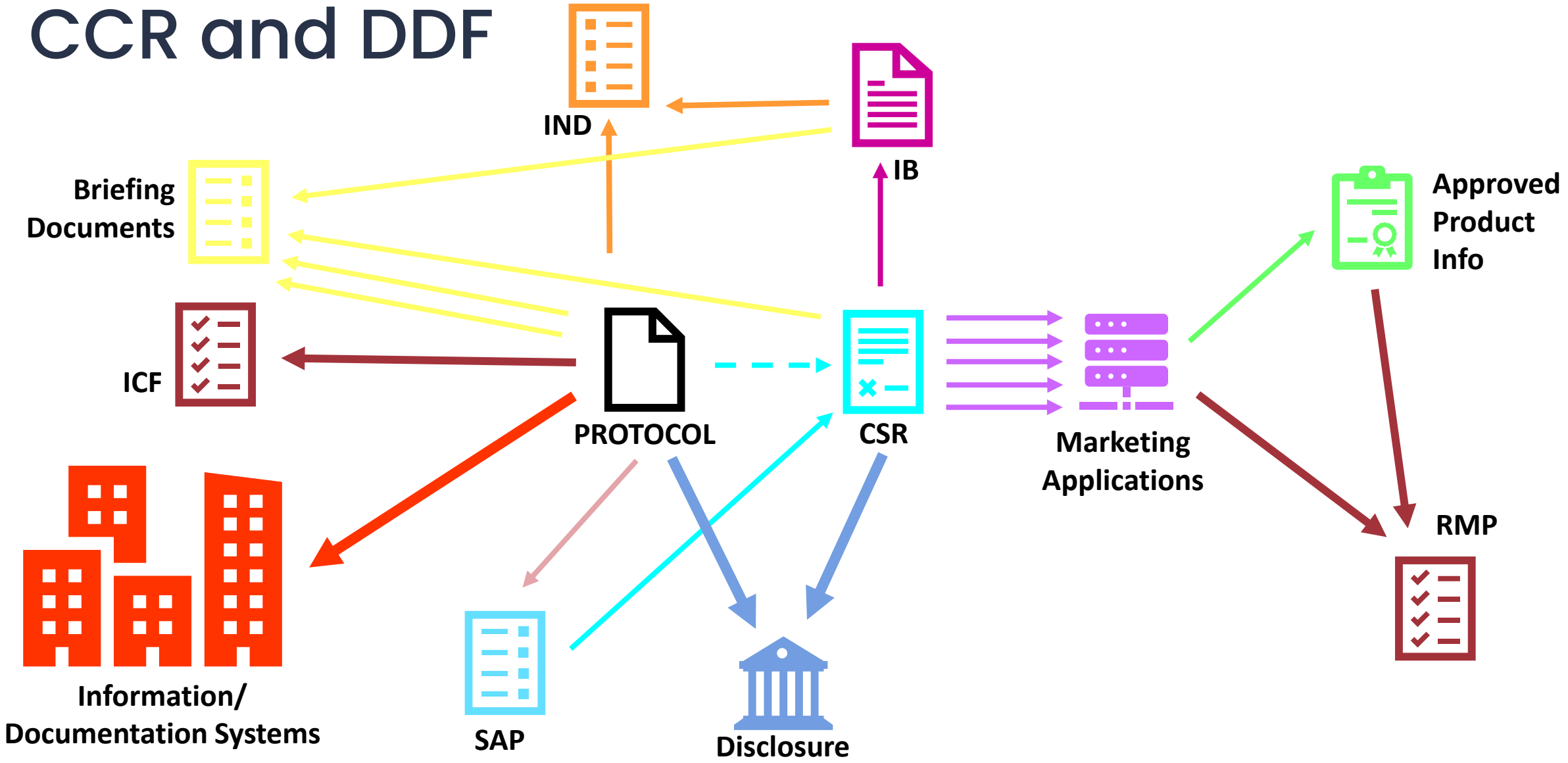
BeOne adoption: Looking ahead to ~18 documents and multiple systems

Protocol Builder Vision



*Template_Protocol based on TransCelerate Common Protocol Template (CPT)

CCR and DDF



Networking effect	Productivity improvement (time & resource)	Better quality (consistency)

Value of Clinical Content Reuse (CCR): Documents and Systems

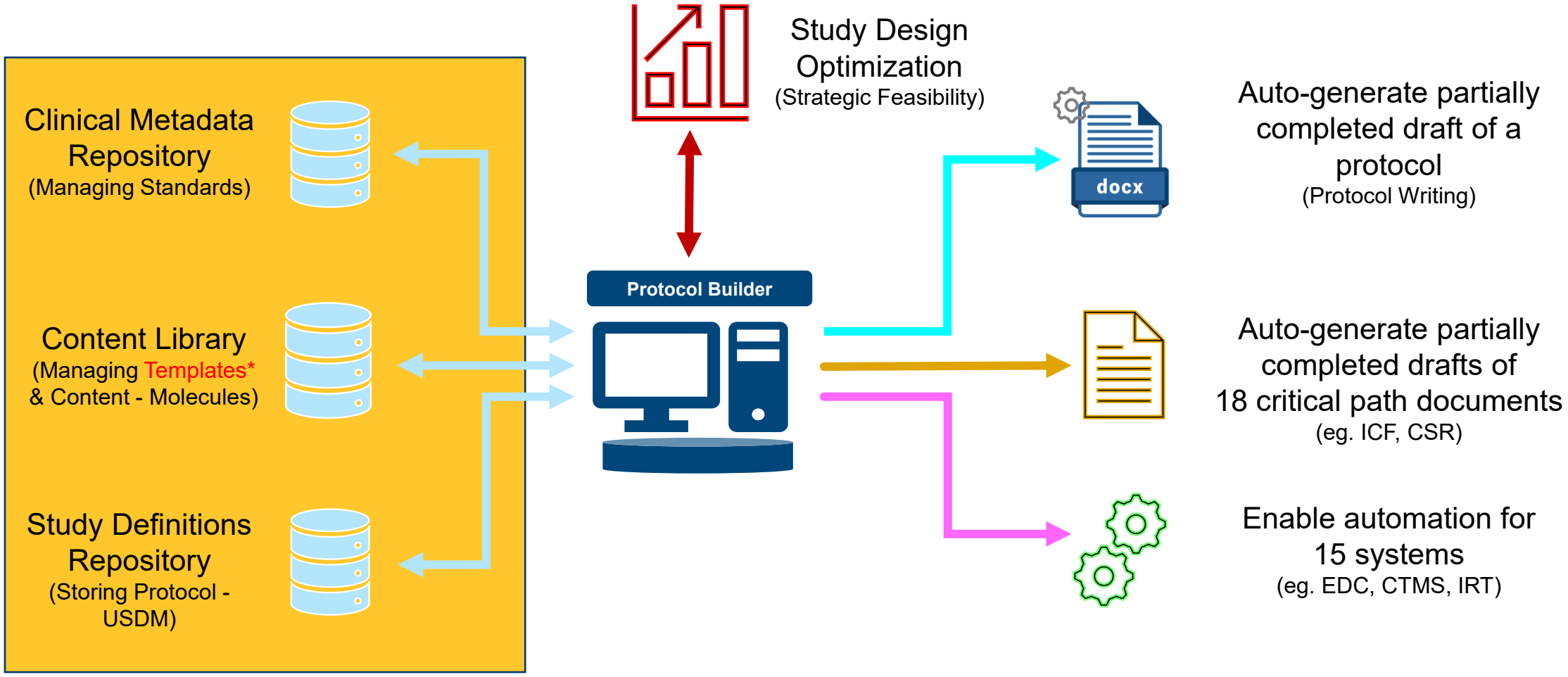
Document Type
IB/IB updated
Original protocol, protocol amendment
CSR (all types)
Module 2 and other documents to support IND, NDA, BLA
ADR, safety reports
Briefing documents
Pediatric documents
RMP

Information/Documentation Systems
Electronic documentation systems
CTMS, IRT
EDC
Safety reporting system
CT.gov, Sponsor → Science → Clinical-Trials
Learning systems
Finance platforms

Understanding the volume and complexity

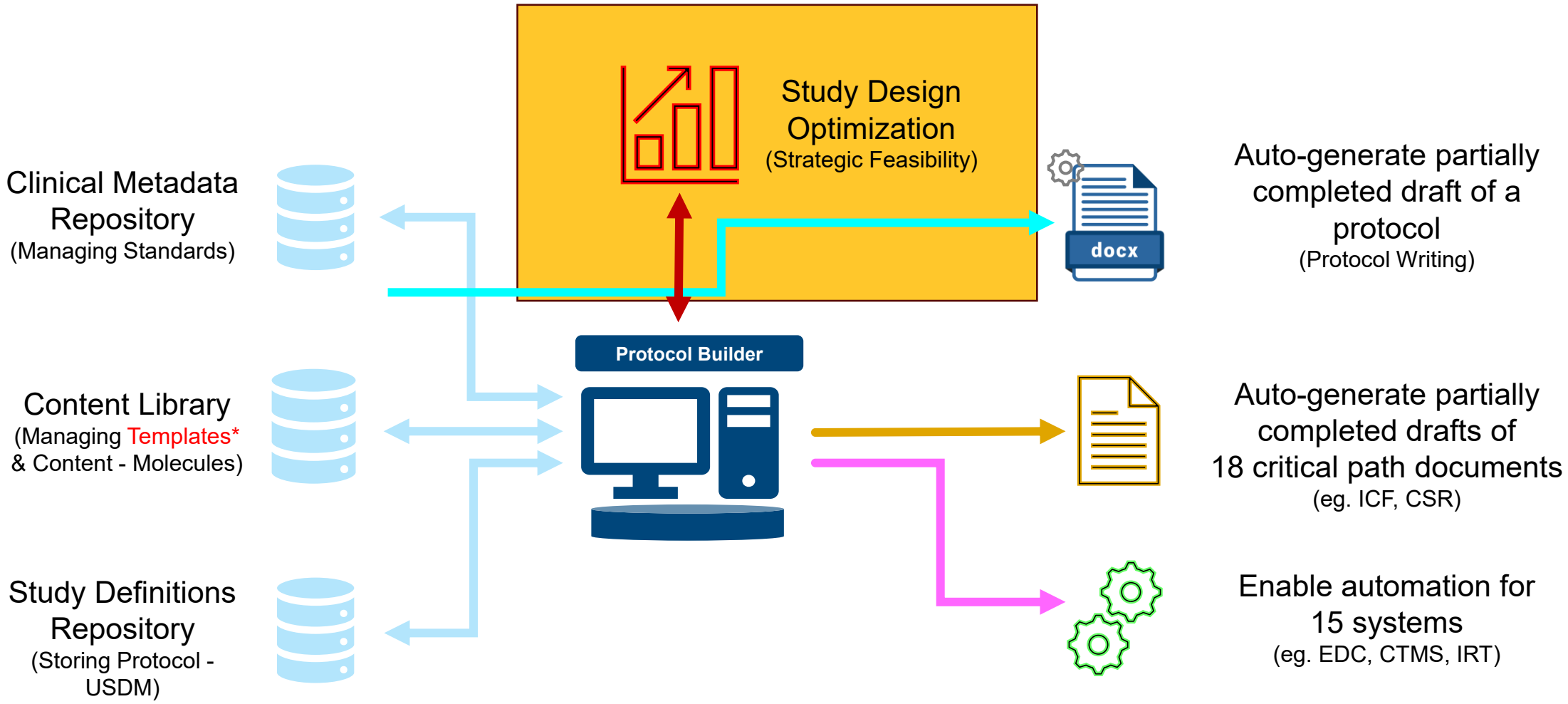
Exponential Value of CCR = (~18 critical document types) x (~15 key systems) x (No. of Users)

Protocol Builder Vision



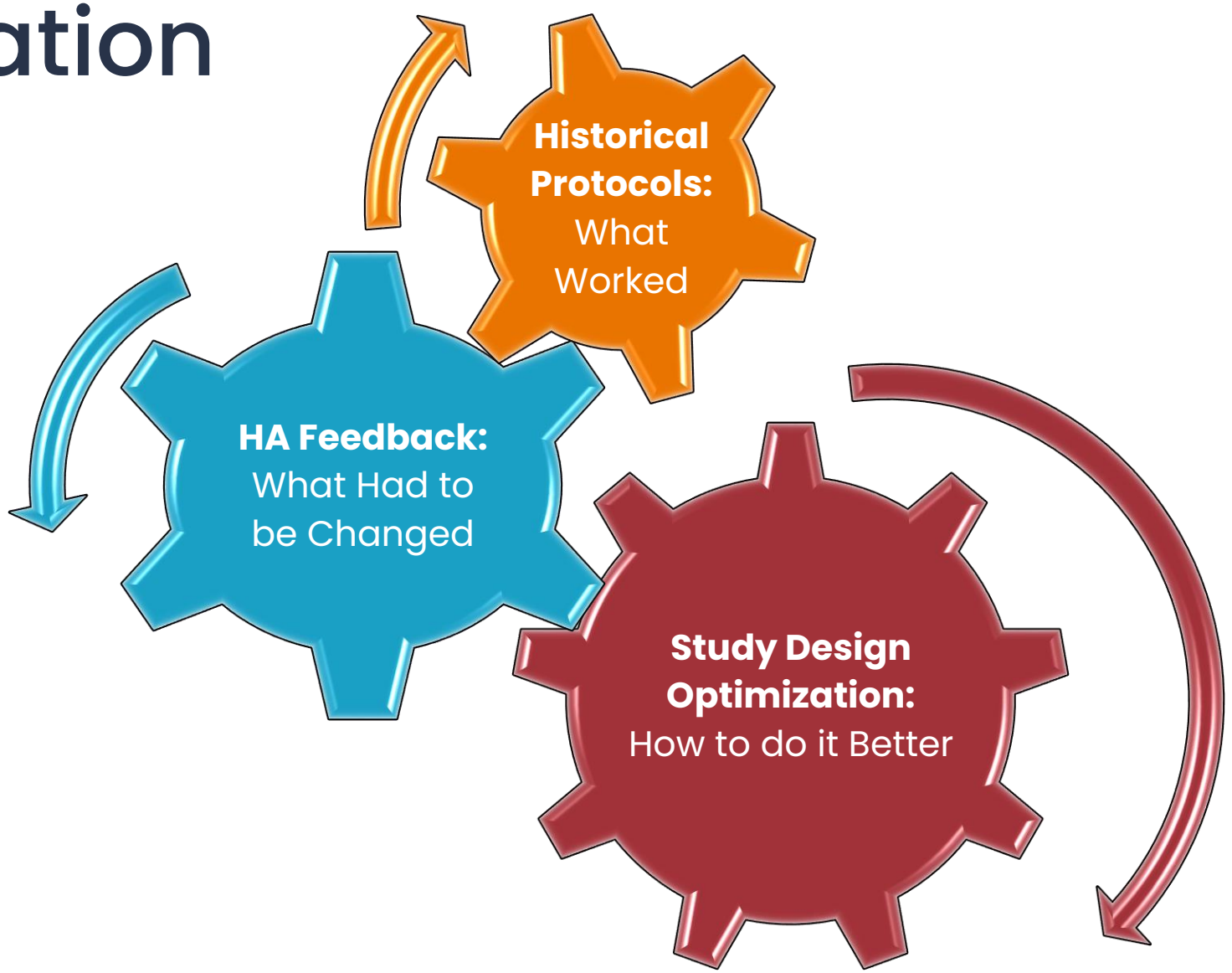
*Template_Protocol based on TransCelerate Common Protocol Template (CPT)

Protocol Builder Vision

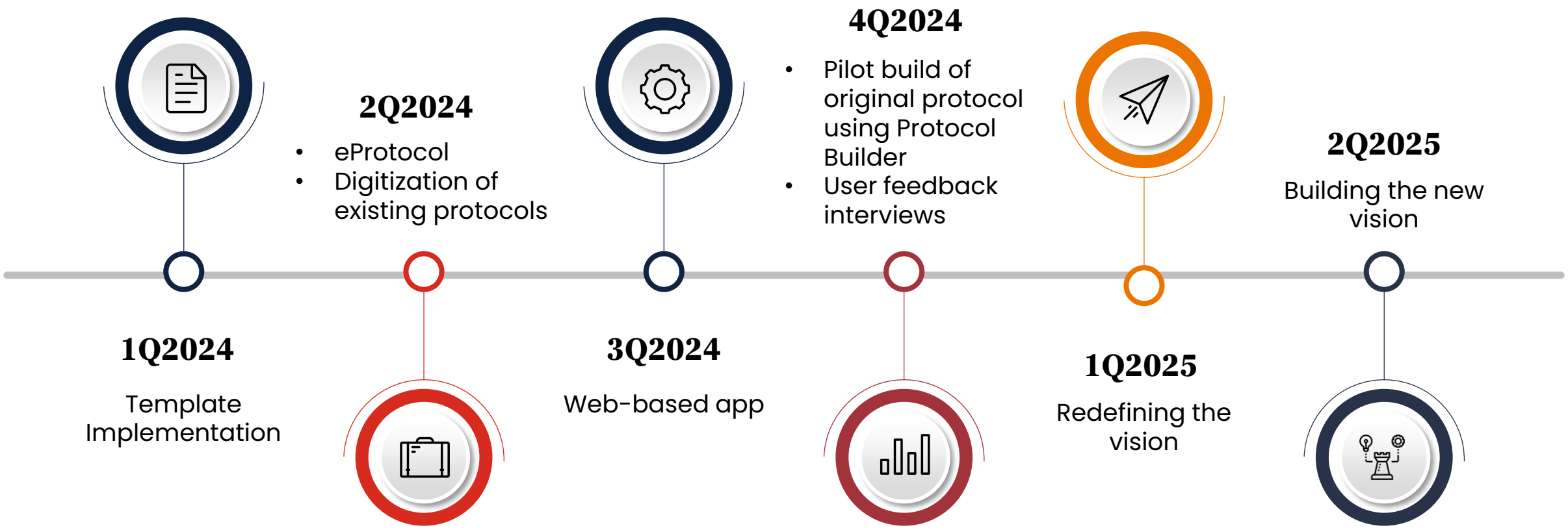


*Template_Protocol based on TransCelerate Common Protocol Template (CPT)

Optimization



Roadmap – Destination 1: Building a Protocol



Modifying the Vision – Looking through the User Lens

Is the platform easy to use?	• Web-based app • MS Word-based environment
How does it facilitate the process?	• What features allow the user to significantly decrease time? • What features are nice to have but not real value added
What is needed for successful change management?	• What does minimum viable product (MVP) mean to the user? • Focus on completion of parts vs. overall benefit picture

Modifying the Vision – Parallel Paths to Achieve More

SoA Builder

Clinical
Metadata
Content
Library
Study
Definitions
***Repositories**

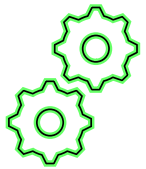
Per SOP

Draft
Protocol

Final Approved
Protocol

ePROTOCOL Suite – Microsoft Word Add-in

3 key business needs -- AI assist, manage content library, and template compliance checks



Enable automation for downstream systems
(eg. EDC, CTMS, IRT)

Auto-generate partially completed drafts of critical path documents
(eg. Contracts, ICF, CSR)

Study Startup Activities

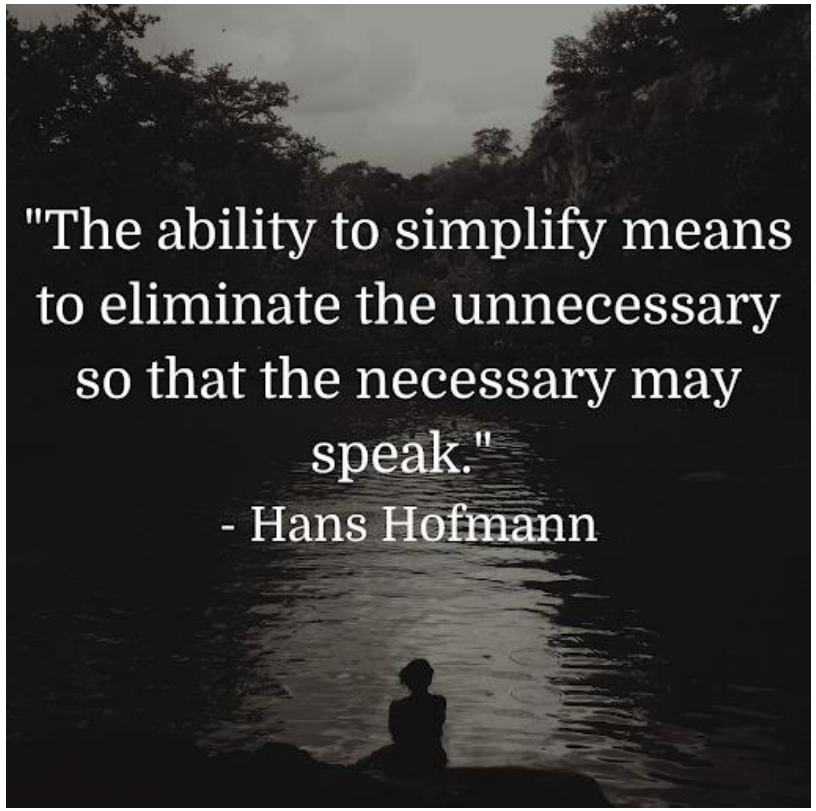
*Repositories – Clinical Metadata Repository managing standards, content library managing templates and content reuse, study definitions storing Protocol Information (TransCelerate/CDISC USDM)

Recipe for Success

- 1 cup AI
- 1 cup Automation
- ¾ cup CCR
- ?
- ?

Strategic Writing

- Strategic Writing is about writing for your Audience
- Write with the reviewer in mind; not just their background but how and why they review
- Documents must be:
  - ✓ Usable: They must be able to easily find what they are looking for
  - ✓ Readable: Electronic reviewing lends itself to skim reading



Source: Cuppan and Bernhardt Writing for the Biopharmaceutical Regulatory Reader https://a.co/fqDdDpp

Strategic Writing

Before

78 patients were included in the Efficacy Analysis set for Primary Analysis. Results of Study [redacted] showed that in patients with [redacted], treatment with [redacted] resulted in high response rate, deep response, and rapid response. In the Efficacy Analysis Set for Primary Analysis excluding 18 patients (N=60) (Table 3):

- The ORR assessed by IRC was high (76.7%), with p value of < 0.0001 to reject the null hypothesis of ORR of 40%.
  - Subgroup analyses showed that benefit in ORR per IRC assessment was generally observed across all predefined subgroups, including subgroups that have traditionally responded poorly to therapy (eg, those with cytogenic abnormalities).
- The complete response rate was 20.0%.
  - Among the patients with CR/CRi as assessed by IRC, 50.0% and 50.0% of patients had best blood and bone marrow MRD negativity (< 10^{-4}), respectively.
- Responses occurred rapidly, as evidenced by the medial TTR of 3.70 months.
- DOR, PFS and OS were not mature as of the data cutoff date.
  - The median DOR by IRC was not reached; the event-free rate at 6 months was 87.1%.
  - The median PFS by IRC was not reached; PFS at 6 months was 87.3%.
  - The median OS was not reached; OS at 6 months was 95.0%.
- Efficacy results in the Efficacy Analysis Set for Primary Analysis (N=78) were consistent with those in Efficacy Analysis Set for Primary Analysis excluding 18 patients.
- Efficacy results as assessed by the investigator, including ORR, DOR, TTR, PFS, and OS, were similar to the IRC assessment.

Strategic Writing

- **Make good use of cross-reference to intext tables**
- **Provide key messages**
- **Highlight the important numbers**

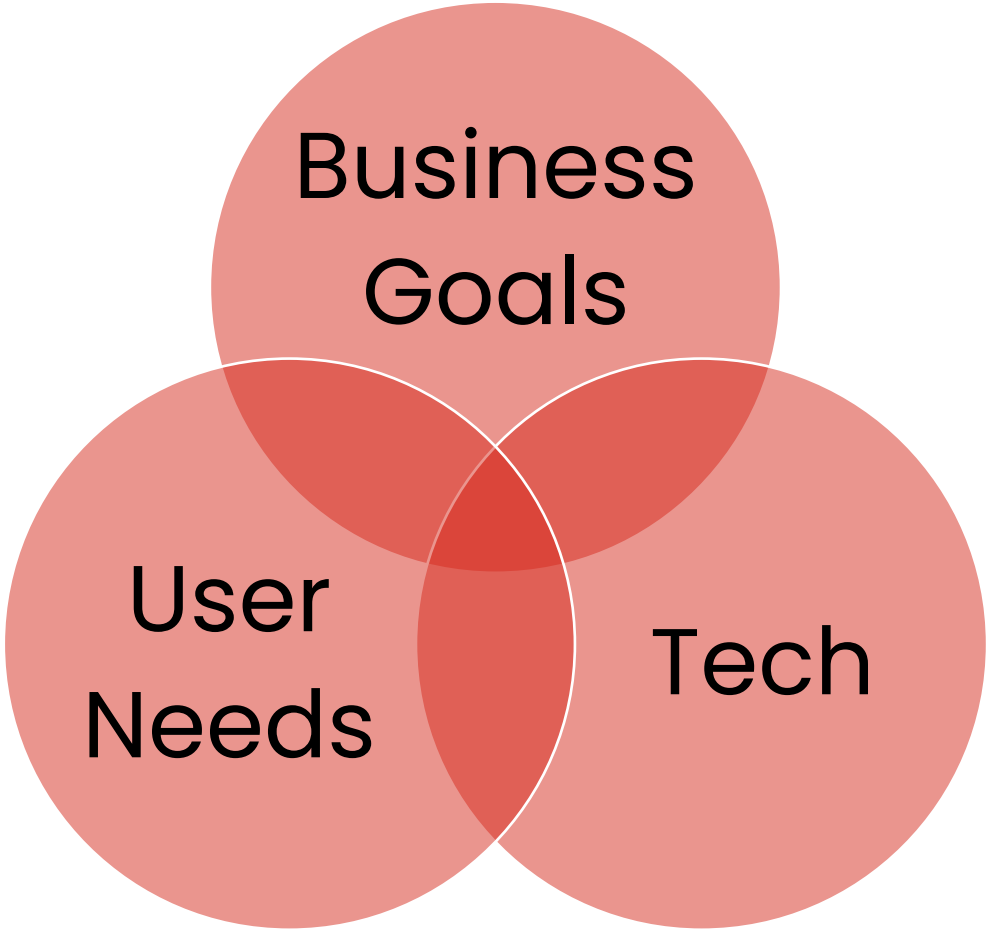
After

Efficacy analyses showed that treatment with [redacted] resulted in high response rates with rapid and deep responses in patients with [redacted] who have failed treatment with [redacted] as evidenced by high ORR, high complete response rate, high best undetectable MRD rate and short time to response in both Efficacy Analysis Set and Efficacy Analysis Set excluding 18 patients (Table 3 and Table 15).

DOR, PFS and OS were not mature as of the data cutoff date, with median DOR, PFS, and OS not being reached. For DOR, event-free rate at 6 months was high (Table 3).

Efficacy results in the Efficacy Analysis Set (N = 100) were consistent with those in Efficacy Analysis Set excluding 18 patients (N = 82).

Technology vs Business Needs



BeOne Roadmap – Parallel Paths to the Pinnacle

2026 and beyond

2Q2025

- Building the new vision: SOA Builder & eProtocol Suite
- OneTemplate Updates (protocol, IB, CSR)
- Strategic Writing Implementation

3Q2025

- Integration of content libraries
- Full implementation of SOA Builder

4Q2025

- Streamline dataset preparation
- Integrate into study startup activities (CRF/EDC) and budget estimation tools

- AI implementation to support document generation
- Semi-automate ICF generation

- Automate data disclosure process
- Building the next vision: Study Designer utilizing Data and AI

Continue DDF and CCR into downstream documents eg, M2

People, Process, Technology: Together to the Summit

Approval and Market

The People:

- ✓ Clinical Development
- ✓ Clinical Operations
- ✓ Statistics
- ✓ Safety
- ✓ Regulatory
- ✓ Clinical Pharmacology and Biomarkers

The Process:

- ✓ Clear roles and responsibilities
- ✓ Writing and reviewing best practices
- ✓ Standard timelines and steps

The Technology:

- ✓ SoA Builder
- ✓ eProtocol Suite
- ✓ CCR/DDF
- ✓ AI/LLM