



DS03 — *Digital Protocol Vision ...* *How Digital Information Can Transform and Automate Our Processes*

Bill Qubeck

TODAYS SPEAKER



Bill Qubeck





Agenda

- What is a protocol and what are the challenges
- Digital protocol and end user experience
- Tackling a digital protocol project
- Wrap up



Protocol & Challenges

What is a Clinical Protocol?

Clinical Protocol:

A plan that outlines the procedures **to be followed** for the study.

It includes:

Study objectives



Patient population and eligibility criteria



Study design (treatment arms, randomization)



Schedule of Activities (visits, treatments, assessments)



Statistical considerations, etc.



"ICH M11 guideline, Clinical Study Protocol Template and Technical Specifications" and provides detailed guidance on the content and format of clinical study protocols.



Link: <https://www.ema.europa.eu/en/ich-m11-guideline-clinical-study-protocol-template-and-technical-specifications-scientific-guideline>

Let's Take a Look at an Example Protocol

Title Page

TJ301
Solution for Injection
Clinical Trial Protocol

Protocol No.: CTJ301UC201

Date: 16 May 2017
Ver. 1.1
Supersedes: Ver. 1.0
Page 1 of 97

CLINICAL TRIAL PROTOCOL

A Phase II, Randomized, Double-blind, Placebo-controlled Study to Evaluate the Safety and Efficacy of TJ301 (FE 999301) Administered Intravenously in Patients with Active Ulcerative Colitis

Protocol Number: CTJ301UC201

Investigational Medicinal Product: TJ301 (solution for injection), also referred to as FE 999301 and Olamkicept

Indication: Active Ulcerative Colitis

Phase: 2

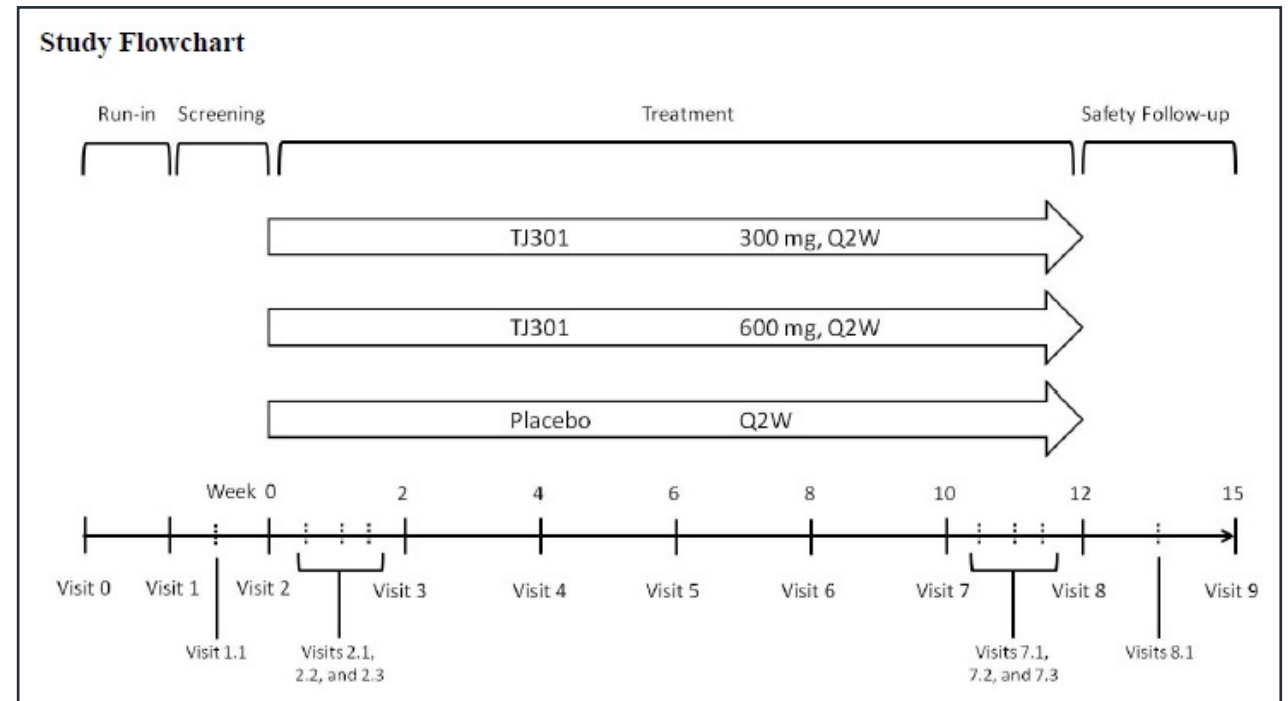
Investigators: Multicenter, international, across Mainland China, Taiwan, Republic of Korea and Australia

Coordinating Investigator: Prof. Dr. Minhu Chen
Chair, Department of Gastroenterology and Hepatology
Vice President
The First Affiliated Hospital, Sun Yat-sen University
58 Zhongshan Road, Guangzhou, China

Expert committee: Prof. Dr. Stefan Schreiber
Institute for Clinical Molecular Biology University Hospital
Schleswig-Holstein
Schittenhelmstrasse 12, 24105 Kiel, Germany

Name and Address of Sponsor: Leading Biopharm Limited

Study Flow Chart



Adapted from FDA's ClinicalTrials.gov website, link:
https://classic.clinicaltrials.gov/ProvidedDocs/52/NCT03235752/Prot_000.pdf

Example Assessments & Inclusion Criteria

Assessments:

There will be 8 visits at the investigational site during the study:

- **Visit 0:** Run-in period: at an optional visit (Visit 0), decision will be made if patients need stable conventional UC treatment to meet the following criteria: with corticosteroids stable for at least 2 weeks prior to Randomization at no more than 20 mg prednisone...
- **Visit 1:** Screening Visit, start of Screening Period (Days -28 to -1 prior to Visit 2)
- **Visit 2:** Randomisation Visit (Baseline), start of 12-week Treatment Period
- **Visits 3-7:** 5 visits during 12-week Treatment Period
- **Visit 8:** End of Treatment (EoT) Visit, completion of 12-week Treatment Period, etc.

Criteria for inclusion / exclusion:

Inclusion Criteria:

A subject will be eligible for inclusion in this study only if all of the following criteria apply:

1. Male and female patients 18-70 (inclusive) years of age.
2. Active UC confirmed by colonoscopy with biopsy or flexible sigmoidoscopy with biopsy at Screening, with extending > 15-cm past the anal verge from endoscopy.
3. Active UC with a full Mayo score ≥ 5 and a rectal bleeding subscore ≥ 1 at screening.
4. During Day -35 to Day -6 prior to Randomisation, an endoscopy subscore ≥ 2 .
5. Etc.

Adapted from FDA's ClinicalTrials.gov website, link:
https://classic.clinicaltrials.gov/ProvidedDocs/52/NCT03235752/Prot_000.pdf

Clinical Study Schedule of Activities (SoA)

Protocol Attachment LZTZ.1
Schedule of Events for Protocol H2Q-MC-LZZT(c)

	VISIT	1	2	3	4	5		7	8
ACTIVITY	WEEK	-2	-3	0	2	4		6	8
Informed consent		X							
Patient number assigned		X							
Hachinski ≤ 4		X							
MMSE 10-23		X							
Physical examination		X							
Medical History		X							
Habits		X							
Chest x-ray		X							
Apo E genotyping					X				
Patient randomized				X					
Vital signs/Temperature		X	X	X	X	X		X	X
Ambulatory ECG placed			X						
Ambulatory ECG removed				X					
ECG		X			X	X		X	X

- The Encounters/Visits (any planned event corresponding to clinical data collection) are represented along the horizontal axis (example: see Visit 3)
- The Activities (the planned activities expected to occur at the event) are represented vertically (for an example see Vital Signs/Temperature)
- ... with the required Activities at each Encounter shown by a cross (X) in the matrix.

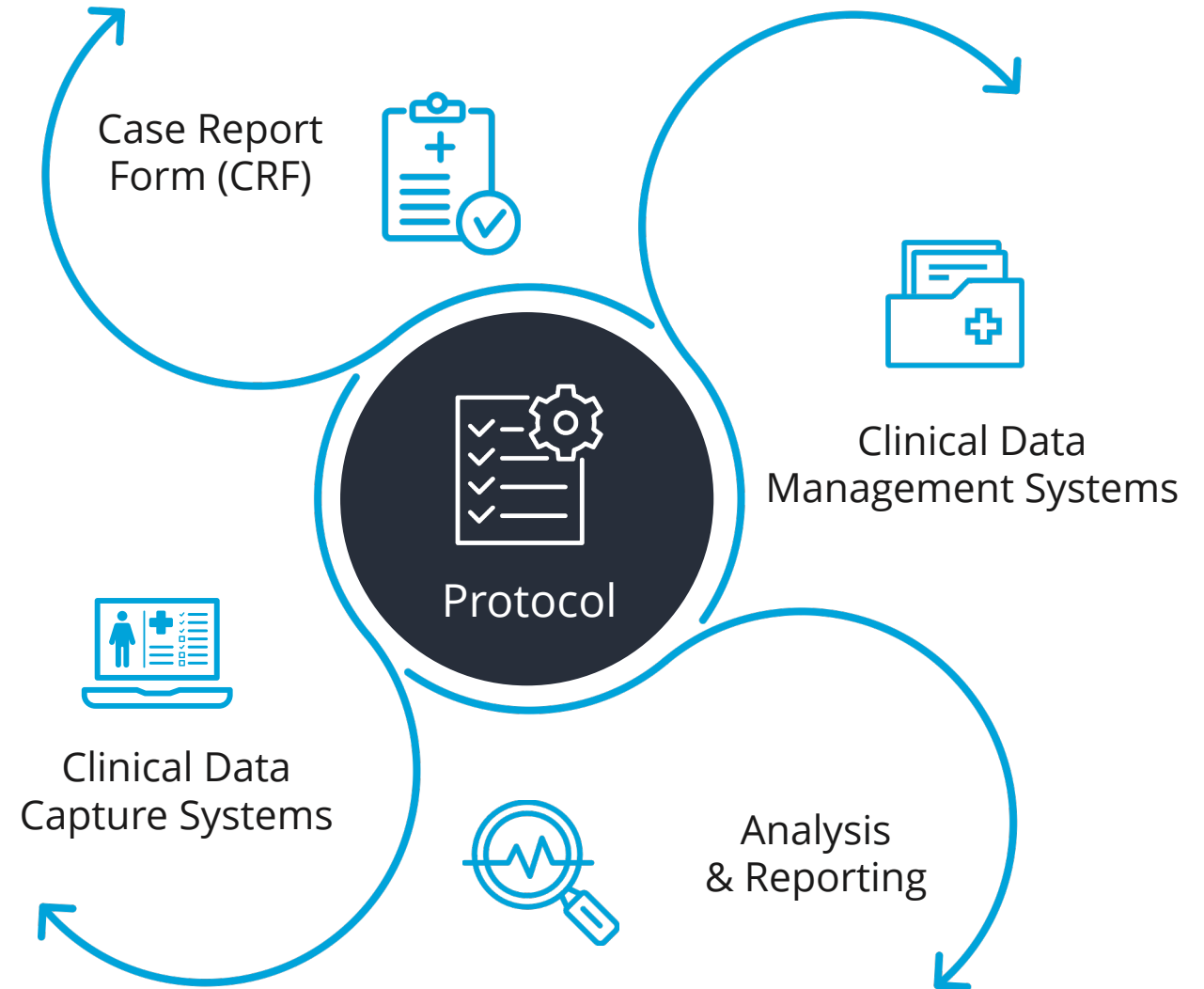
Adapted from HL7's Vulcan website, link:
<https://build.fhir.org/ig/HL7/Vulcan-schedule-ig/basic-structure.html>

Is the Protocol the Center of Your Universe?

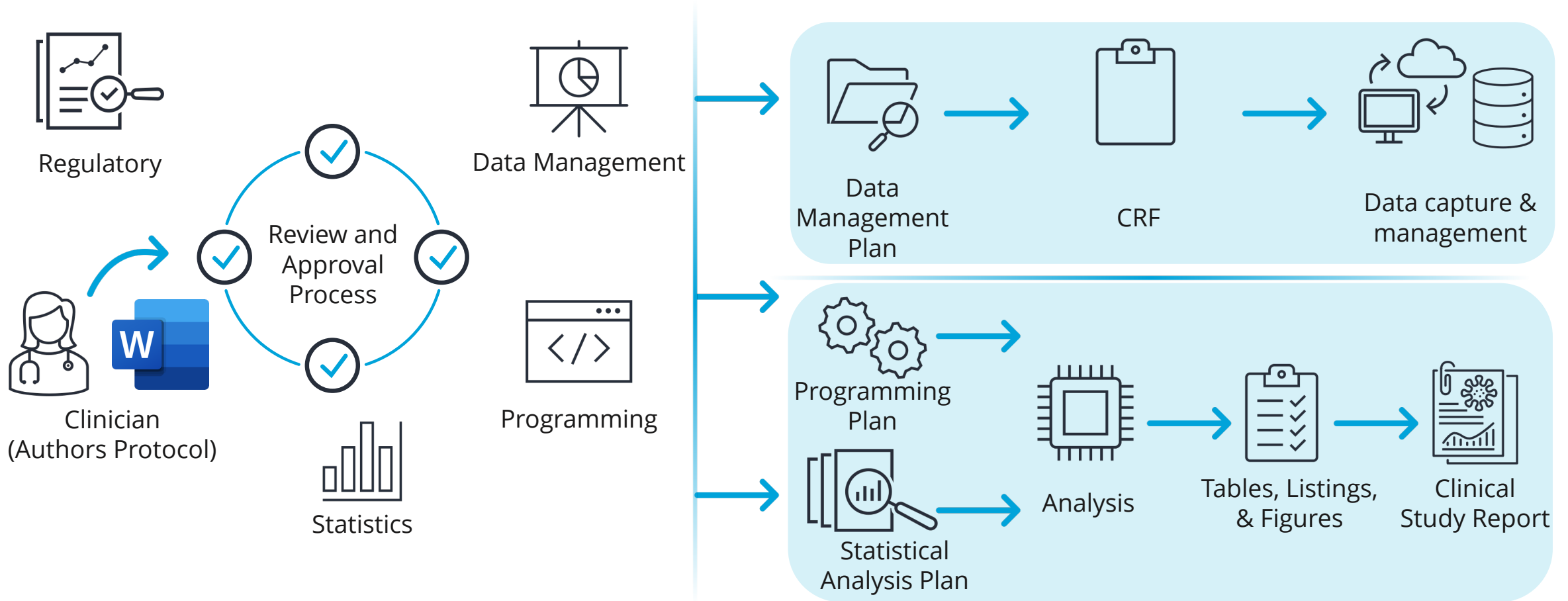
Does it **drive** your study operations?

Or...

...is it an **'island'** and disconnected?

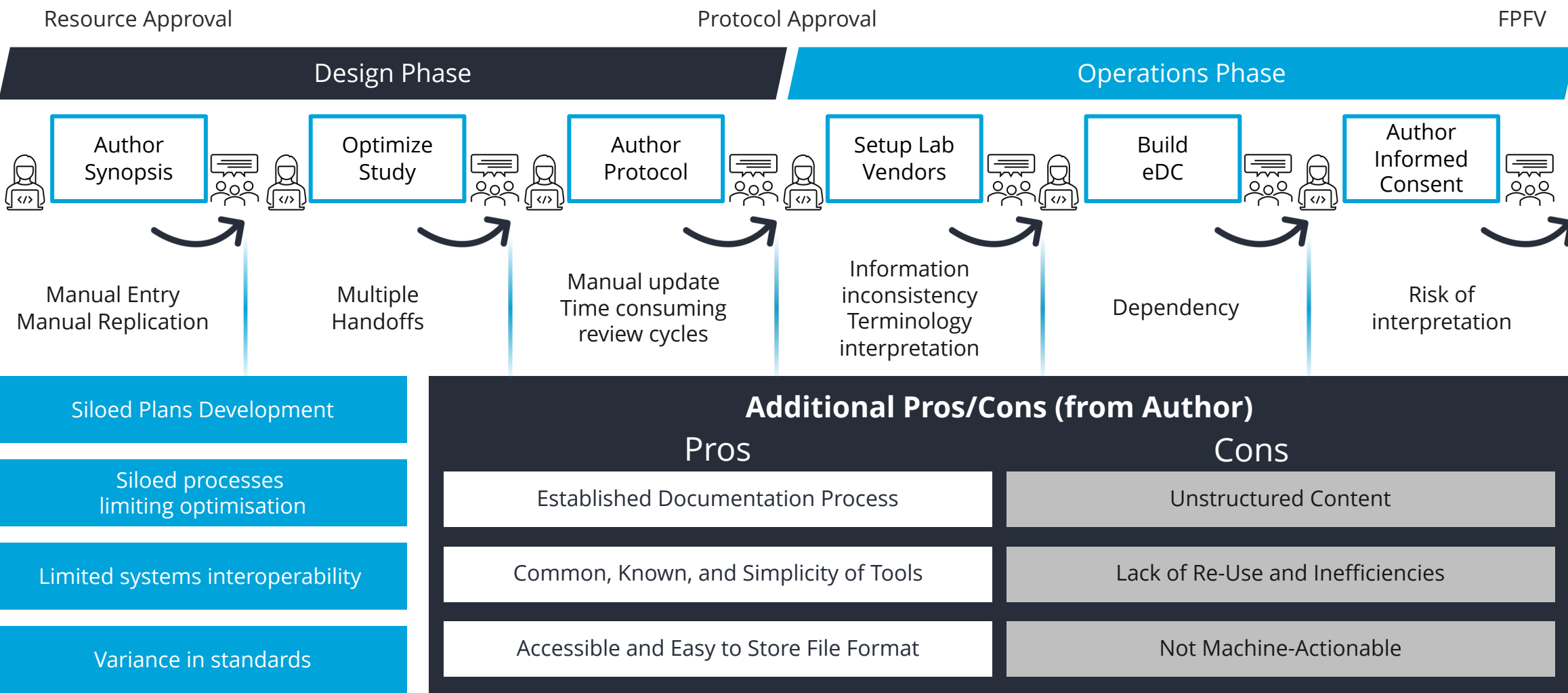


Protocol Development to Clinical Study Report



The protocol is the 'source' from which downstream processes and systems initiate from, however, it is not 'machine-actionable' and manual intervention is required across the entire process.

Challenges*





Digital Protocols and benefits

Digital Protocol Approach



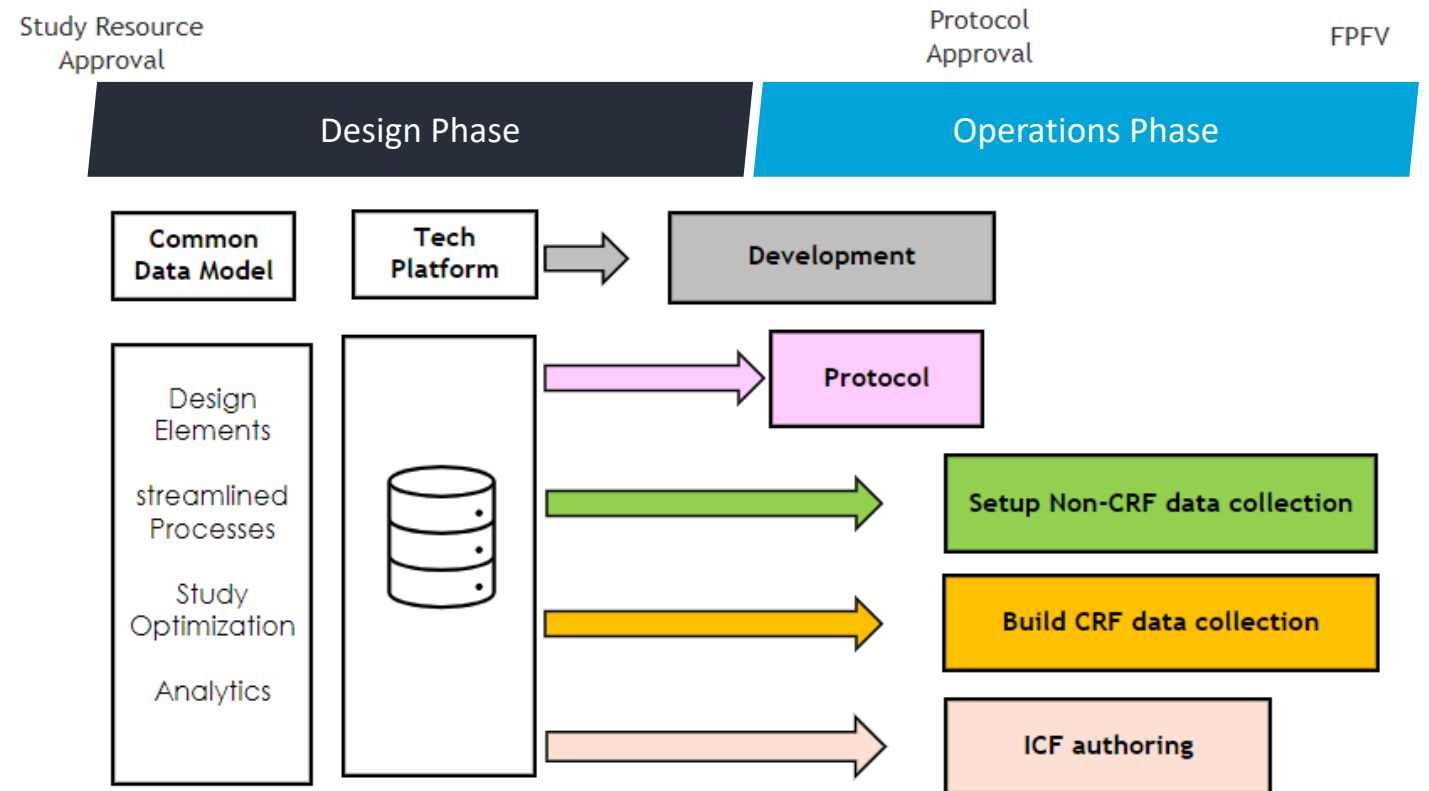
Single source
of design truth



Executable
study concept model



Automated clinical
operations processes



Benefits



STUDY OPTIMISATION

Time savings & reusability

- Centralized review around a unique document for protocol and study optimisation
- Reduce the amount of manual formatting
- Optimise change review cycle time



PROCESS FLOW

Contents Lineage

- End to end traceability
- Automated flow of content to key clinical documents
- Automation to clinical & operational systems (i.e. EDC)



START UP

Quality and Consistency

- CRF design integration
- Automation of translation of visit schedule, treatments, arms, ...
- Digital Integration of contents



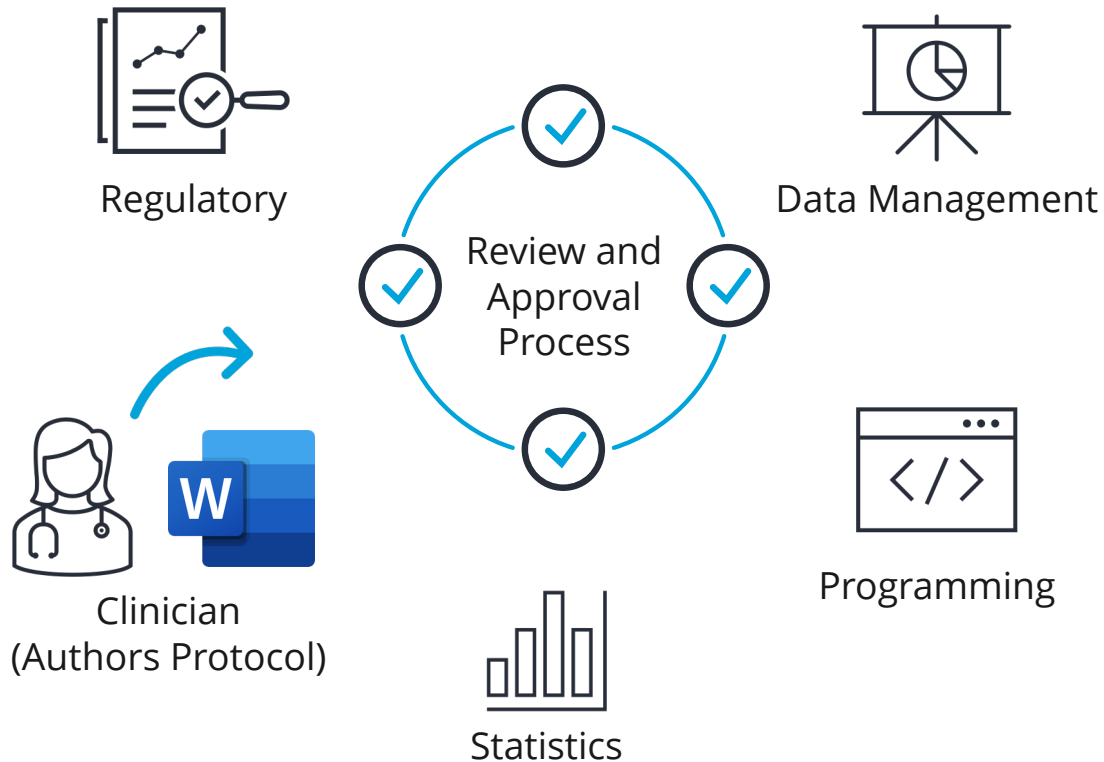
CONDUCT & CLOSE OUT

Quality and Delivery

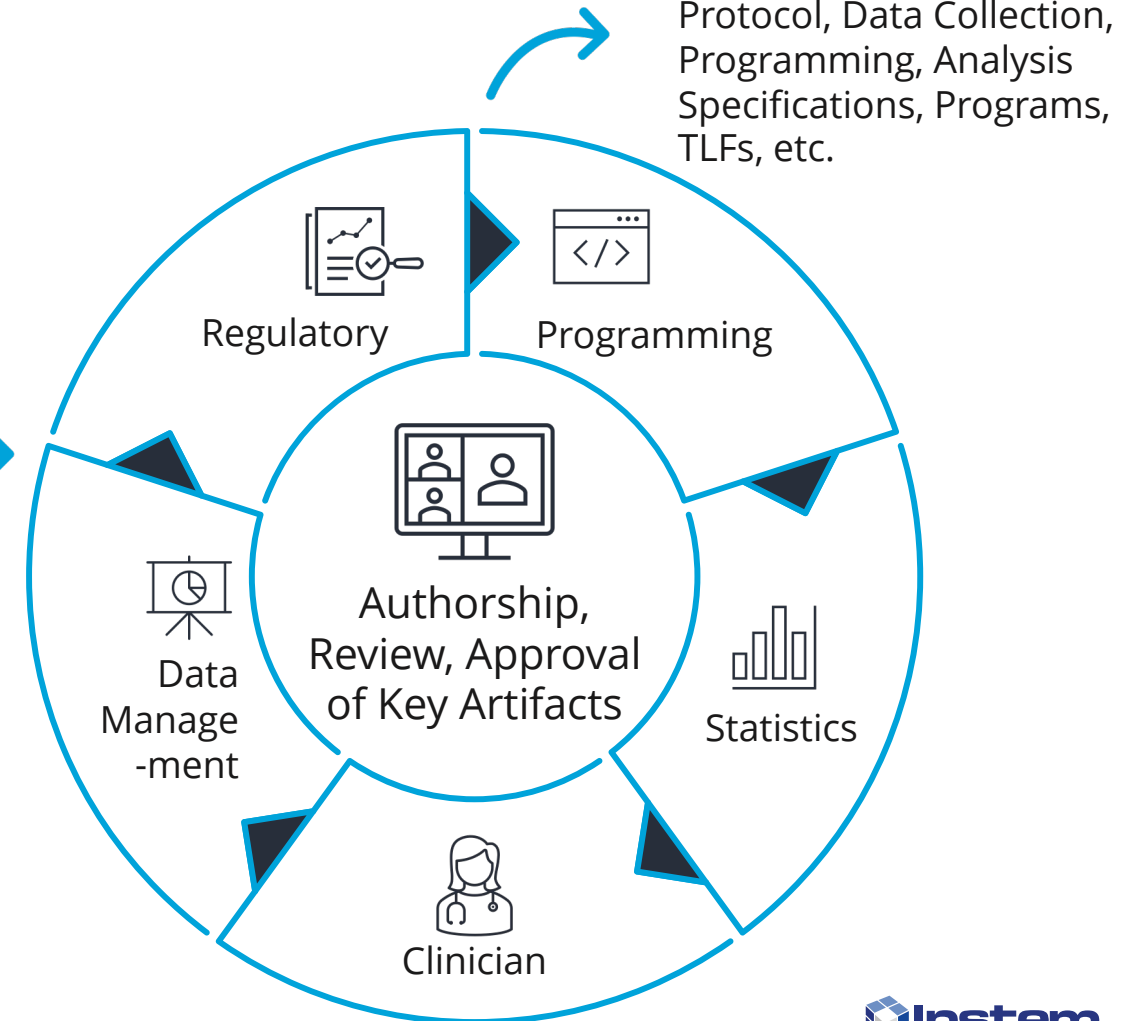
- Reduced efforts for amendments
- Reduced cycle time for update
- Documentation update consistency (SAP, data transfer specs, ...)

Process Transformation

Current Process:



Future Process:



Definition Transformation

	VISIT	1
Activity	WEEK	-2
Informed consent		X
Patient number assigned		X
Hachinski ≤ 4		X
Physical examination		X
Medical History		X
Habits		X
Chest x-ray		X
Apo E genotyping		
Patient randomized		
Vital signs/Temperature		X



Site Number

Subject Number

Form VS - Vital Signs HorizontalGeneric		
1.1	Were vital signs performed?	☐ No ☒ Yes
		VSPERF
1.2	Date (DD-MMM-YYYY)	
		VSDAT
2 Vital Signs Details		
2.1	Systolic Blood Pressure	
		SYSBP_VSORRES
2.2	Systolic Blood Pressure Unit	
		SYSBP_VSORRESU
2.3	Diastolic Blood Pressure	
		DIABP_VSORRES
2.4	Diastolic Blood Pressure Unit	
		DIABP_VSORRESU
2.5	Blood Pressure Position	☒ (PRONE) Prone ☐ (SEMI-RECLUMENT) Semi-Recumbent ☐ (SITTING) Sitting ☐ (STANDING) Standing ☐ (SUPINE) Supine
		BP_VSPOS

Clinical Trial Database schema, edit checks, etc.



Algorithm, Analysis, & Report Output Selection



Each **SOA**, at the time of authoring the Protocol, is operationally defined and machine-actionable

Adapted from CDISC's website, link: <https://www.cdisc.org/kb/ecrf/vital-signs>

Streamlined customer experience



Clinical Scientists

It is easier for me to incorporate insights into proposed study designs because I receive them earlier in the process.



Data Management

I can begin downstream startup sooner based on a structured design concept and accelerate data collection operations (EDC build).



Medical Writers

I save time writing and editing the protocol because I can rapidly generate portions of it in a consistent and high-quality manner.



Single source of truth



Common standards



Automation of operations



E2E Connectivity across functions



Design aids and tools



Development Team

I'm able to create planned visit schedules when the structured design concept is stabilized earlier.



Outsourcing Managers

I can manage vendors more effectively using cost analysis based on the reports generated.

The background is a complex, abstract network of thin, light blue lines radiating from a central point, creating a starburst effect. Interspersed among these lines are numerous translucent, spherical nodes of varying sizes. These spheres have a blue base color with iridescent, rainbow-like highlights on their surfaces, giving them a three-dimensional, crystalline appearance. The overall composition suggests a digital network or a molecular structure.

Tackling a Digital Protocol Project

Governance



Key Responsibilities:

Executive Committee:

- Provide strategic direction & intent

Steering Committee:

- Oversight and guidance to DPS working teams

Program Management Office:

- Manage overall project direction & execution
- Ensure alignment with Steering Committee & workstream leads

Program Functional Leadership:

- Manage and deliver; promote adoption

Workstreams:

- Each workstream will have delivery leads supported by business & technical resources
- Sub-teams within workstreams will be defined as necessary

Collaboration:

- Provide partner support to drive workstreams and ensure program success through program governance

Digital Protocol Project Workstreams

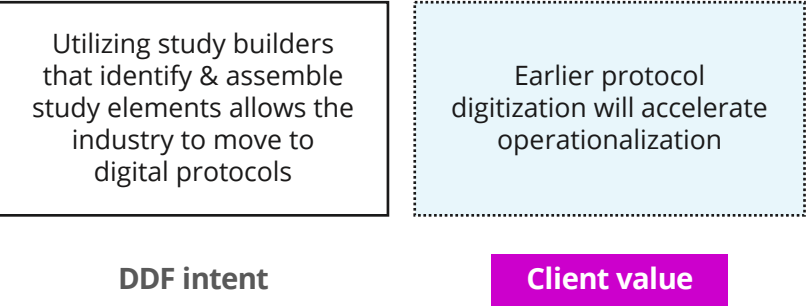
R = Responsible
A = Accountable
S = Supporting
I = Informed

Workstreams	Description
1 Program Management	• Manages overall project management, cross-workstream orchestration, and day to day project delivery • Program structuring, timelines, and financials
2 Standards: Digital Protocol Foundations	• Digital protocol foundations will define, reconcile, and coordinate the protocol foundation definitions across R&D functions • Workstream will develop a strategy to incorporate defined protocol foundation elements and establish the roadmap for capabilities
3 Database Build	• Lay the core technical foundation for EDC build • Generate initial EDC build or database spec • Align on future state integrations/integrations • Pilot capabilities as they become available and provide learnings
4 Protocol Optimizations	• Integration • Deliver activities related to data management, protocol optimization
5 Change Management	• Facilitate organizational change management • Change management strategy, aligned to business implementation

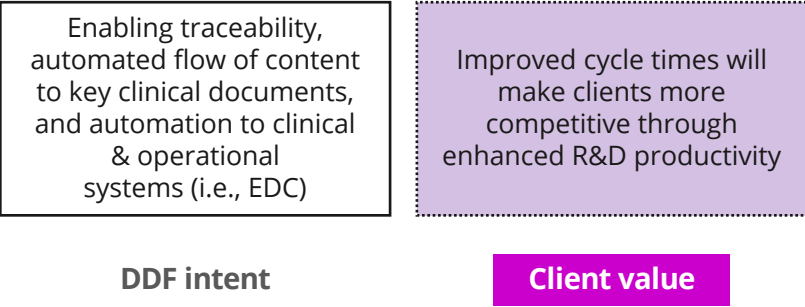
A team, completely aligned, dedicated to achieving specific outcomes, and committed to meeting deadlines.
We communicate clearly, adapt efficiently, document decisions & honour commitments.

How does the Transcelerate DDF initiative align?

Digitized Protocols



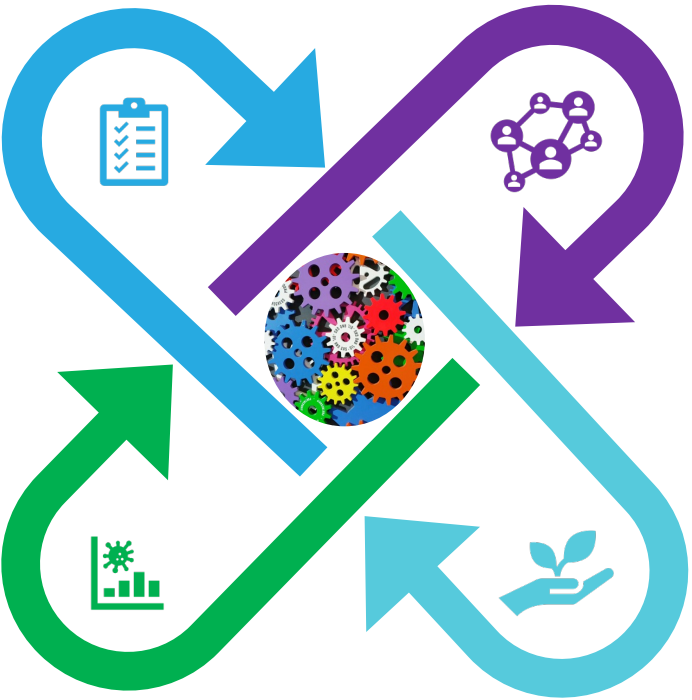
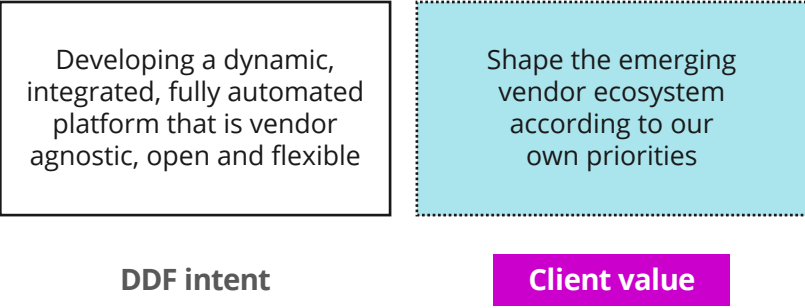
Connectivity of Data and Processes



Advanced Analytics



Open and Flexible Platform



Key factors that will ensure a successful program delivery

1. **Business value & end users:** Digital protocol drives strong business value (e.g., compliance, collaboration, cost, cycle time) while keeping the end users in mind
2. **Future ready architecture:** Build a modern architecture with best-in-class product solutions, aligned with Client principles
3. **Optimized delivery:** Deliver the solution in a timely manner addressing user requirements and integrating across multiple vendor partners
4. **Data migration & integration:** Deliver a robust data migration, integration strategy and execution considering legacy environments as well as upstream and downstream system & process dependencies
5. **Tested & validated:** Deliver a thoroughly tested and validated solution in accordance with Client SOPs
6. **Change management & training:** Drive accelerated user adoption through a comprehensive change management, business process redesign and training



Design &
Configuration



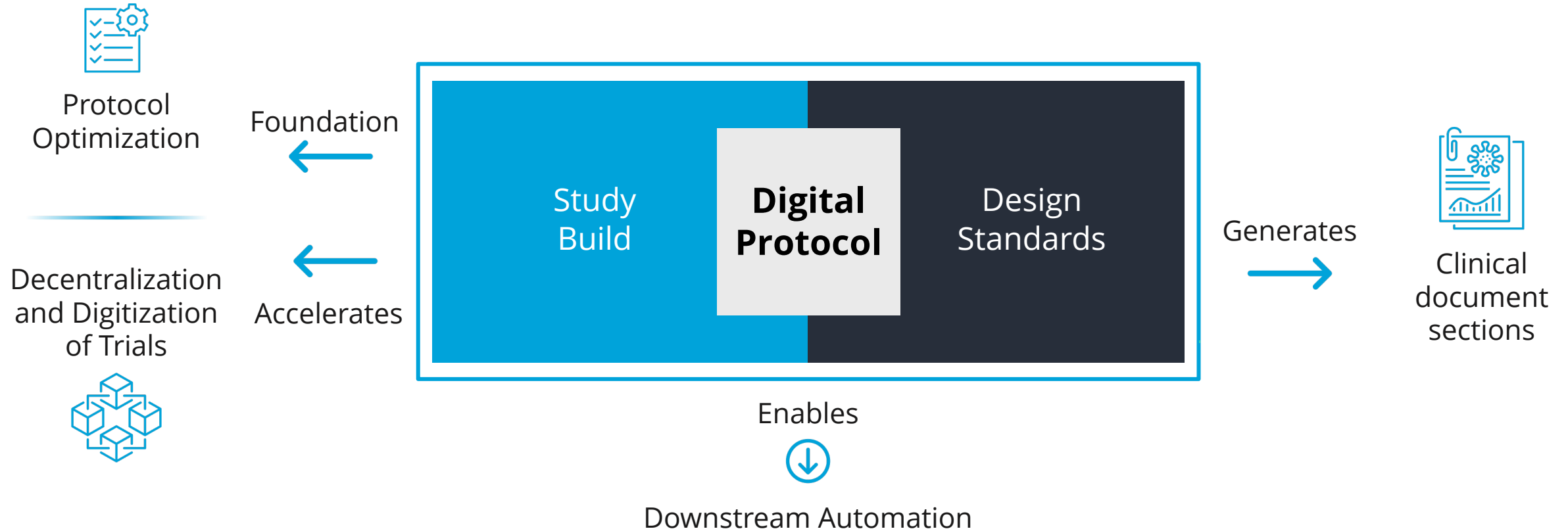
Pilots &
Proofs of Concepts



Exec. Sponsorship &
Benefits Tracking

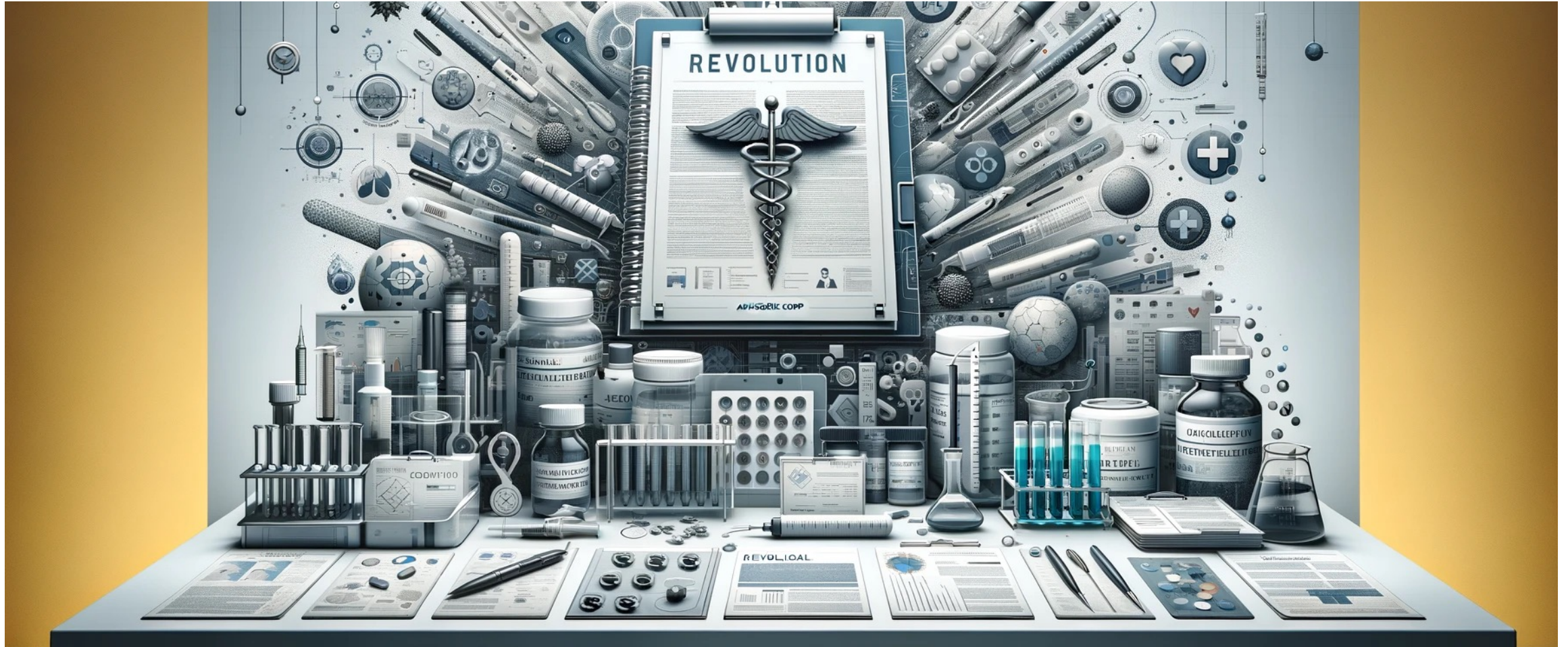
Wrap up

The protocol: Center of our universe



Implement a digitally connected solution that optimizes the clinical trial process

To revolutionize an industry, start at the beginning; for clinical trial research this is the protocol





The future transformed for the benefit of everyone.

Intelligent solutions empowering collaboration
and life-enhancing science.

Contact Bill Qubeck @

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