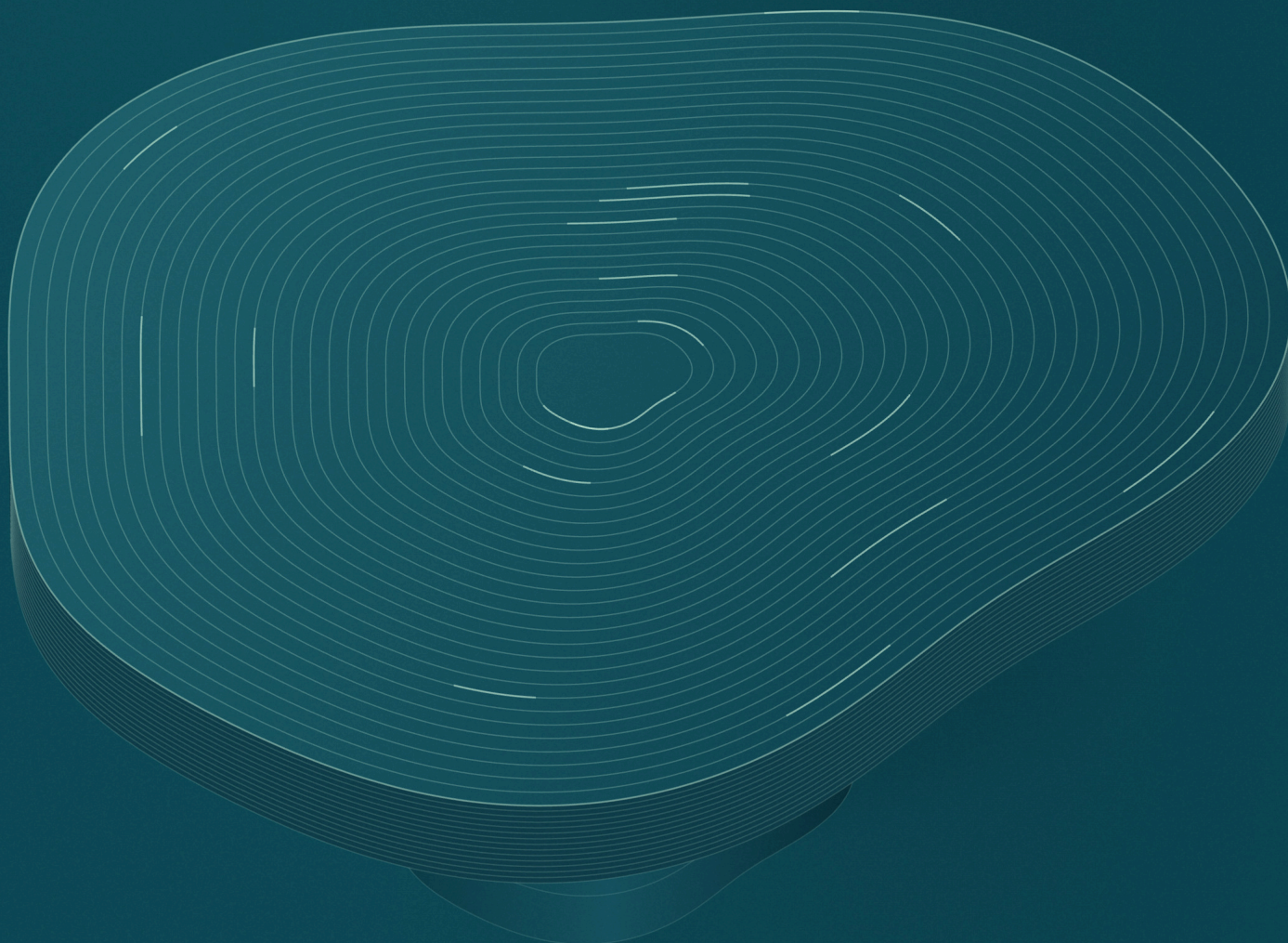




OPHTHALMOLOGY CLINICAL TRIAL OPERATIONS

Advancing Clinical Trial Operations in Ophthalmology

A peer-to-peer discussion forum for clinical trial leaders



HOSTED BY

Dr. Arshad M. Khanani

Director of Clinical Research, Sierra Eye Associates

PARTICIPATING ORGANIZATIONS

Sierra Eye Associates · REGENXBIO · 4D Molecular Therapeutics · Perfuse Therapeutics · Character Biosciences · Tilda Research

ABOUT THE ROUNDTABLE

A peer-to-peer forum for clinical trial leaders

A senior leaders’ discussion of the operational pain points in ophthalmic clinical trials, and of where the field is heading over the next decade.

PARTICIPANTS

AK

Arshad M. Khanani, MD
Director of Clinical Research
Sierra Eye Associates

HOST

AN

Anahita Nikzad
VP of Clinical Operations
REGENXBIO

KM

Kim Maplestone
Chief Clinical Operations Officer
4D Molecular Therapeutics

MC

Michelle Chen
VP & Head of Clinical Development
Perfuse Therapeutics

—

Anonymous, MD
Head of Development
Ophthalmology biotech

ANONYMIZED*

SH

Somayeh Honarmand
VP of Clinical Science
Character Biosciences

RY

Ram Yalamanchili
Founder & CEO
Tilda Research

CONTENTS

01	Vendor and CRO management	05
02	Data quality at the source	07
03	Redundancy and site burden	09
04	AI in clinical operations	12
05	Monitoring and SDV	16
06	What excites leaders	18
—	Recommended actions	20

NOTES

*In some instances, names and companies of individuals are anonymized due to corporate policy.

Some quotations have been lightly edited for readability while preserving the speaker’s meaning.

EXECUTIVE SUMMARY

The conversation converged on a consistent set of themes.

Senior leaders discussed the operational pain points in ophthalmic clinical trials and where the field is heading. Three operational themes dominated, followed by a candid assessment of AI.

01 MOST-CITED FRICTION

Vendor and CRO management

Particular concern over the post-COVID erosion of monitoring quality and high CRA turnover. Participants described monitoring reports reduced to checklists, source data verification that still depends on flying people to sites to confirm a single data point, and a pervasive lag between data entry at the site and actionable insight for the sponsor.

02 ENDPOINT INTEGRITY

Data quality at the source

Especially the primary endpoints in retina trials: best-corrected visual acuity (BCVA) and imaging. Several leaders argued the industry under-invests in protecting these endpoints in real time, while the patient is still in the chair and errors can still be corrected.

03 AVOIDABLE WORK

Redundancy and site burden

Repeated pre-study visits (PSVs), duplicative document requests, and feasibility questionnaires sent to sites the CRO already knows well. Multiple sponsors shared concrete tactics for pushing back: grandfathering known sites, waiving PSVs, and going straight to site initiation.

ON AI

The group was candid: adoption in their own trials remains limited today, but appetite has shifted dramatically in the past two to three quarters.

The group discussed where AI is already delivering ROI: trial master file (TMF) processing, essential document packages, monitoring visit report analysis, and investigational product accountability. TMF is a lagging indicator, while the real leverage sits upstream with the CRA and document intake.

The session closed with agreement that the most valuable near-term uses are real-time quality checks at the point of data entry, reduced site burden, and stronger AI fluency across organizations.

KEY REFRAMING

“The TMF workflow is actually a lagging indicator. The leading indicator is the CRA.”

Ram Yalamanchili, Tilda Research

The numbers behind the discussion.

~60%

of document work at therapeutically focused CROs need not even happen: the information already exists.

Tilda Research benchmarking · Section 03 (page 9)

~3.5M

documents a year at one benchmarked partner. 45% of that volume requires rework: duplicates and errors.

Tilda Research benchmarking · Section 04 (page 14)

5–10

monitors cycled through a single high-enrolling site in a brief window.

Participant accounts · Section 01 (page 6)

2–3

quarters in which appetite for AI has shifted dramatically.

Group discussion · Section 04 (page 12)

WHERE AI IS ALREADY DELIVERING ROI

Areas the group identified, with TMF chosen as a beachhead for its fast return.

- ✓ TMF processing
- ✓ Essential document packages
- ✓ Monitoring visit report analysis
- ✓ Investigational product accountability

MOST VALUABLE NEAR-TERM USES, AS AGREED

- 1 **Real-time quality checks**
at the point of data entry
- 2 **Reduced site burden**
fewer redundant visits and document requests
- 3 **Stronger AI fluency**
across organizations

Adoption in participants' own trials remains limited today. The caution voiced throughout: AI is only worthwhile if it demonstrably improves quality **and** lowers cost.

SECTION 01

Vendor and CRO management

Asked to name their top operational pain points, nearly every participant began with the challenge of managing vendors and CROs.

For leaner biotechs, the friction is often structural: they must rely on external partners to mirror their own standards of excellence, but that original intent frequently erodes as it moves toward the site level.

The group identified the root of the failure as communication rather than technical expertise. Strategic priorities are clear to business development but vanish before reaching the teams actually performing the work.

Anahita Nikzad of REGENXBIO described this disconnect as a primary source of frustration, observing that messages pass through so many intermediaries that their substance is lost by the time they reach the field.

IN BRIEF

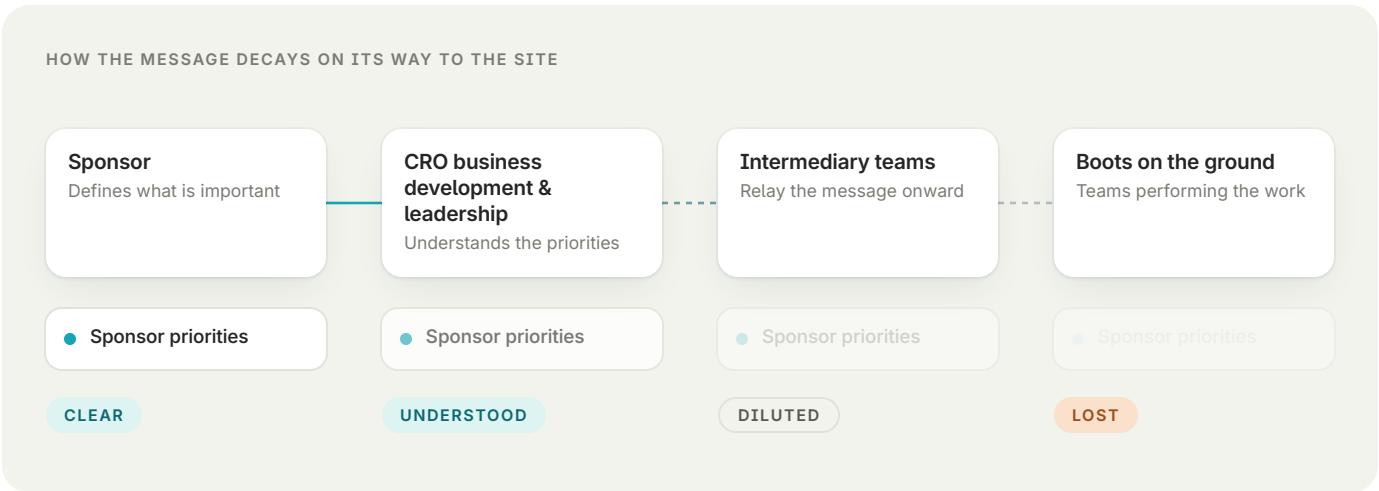
Vendor and CRO management was the most-cited source of friction in the room.

The failure is one of communication, not technical expertise.

“A big problem is just communication and messaging within external partner teams. We’re able to convey what’s important to us and their business development and leadership understands it, but by the time it gets to the boots on the ground that message is lost.”

AN

Anahita Nikzad
VP of Clinical Operations, REGENXBIO



Schematic of the communication chain described by participants. The substance of sponsor priorities is lost as it passes through intermediaries.

SECTION 01

Vendor and CRO management · continued

Kim Maplestone of 4D Molecular Therapeutics, who runs a best-in-class multi-vendor model across two major Phase 3 programs, pointed specifically to the post-pandemic deterioration of monitoring quality. High turnover, she noted, has hollowed out the expertise within these teams.

“We’ve seen a reduction of expertise and quality in the monitoring teams... we’ve seen tremendous CRA turnover on every single CRO we’ve used.”

KM

Kim Maplestone
Chief Clinical Operations Officer, 4D Molecular Therapeutics

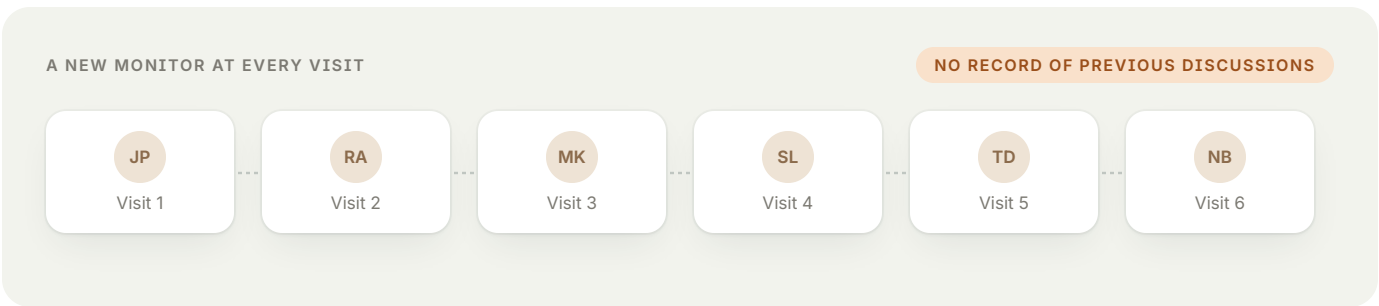
The direct consequence is a breakdown in oversight. When high-enrolling sites cycle through five to ten monitors in a brief window, institutional memory disappears. Reports that should provide actionable insight have been reduced to checklists that, as Kim noted, fail to convey anything meaningful.

Arshad affirmed this from the site’s perspective, describing the disruption of meeting a new monitor at every visit who has no record of previous discussions and asks repetitive questions.

“As a site, it’s dreadful to meet a new monitor every visit. Then they don’t know what the last one did. They ask you the same question, they don’t read the notes from the last one.”

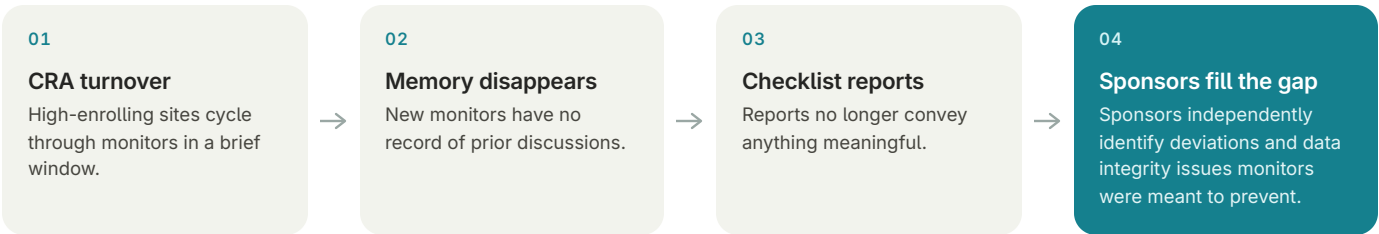
AK

Dr. Arshad Khanani
Director of Clinical Research, Sierra Eye Associates



Schematic. Participants described high-enrolling sites cycling through five to ten monitors in a brief window.

FROM CHURN TO FORMALITY: THE CONSENSUS VIEW



SECTION 02

Data quality, endpoints, and the real-time lag

The conversation repeatedly returned to the integrity of data at the source, driven by its direct impact on primary endpoints: the ultimate arbiter of a trial’s success or failure.

A fundamental friction exists because clinical sites are primarily patient-care environments rather than data-processing centers. Consequently, burdened staff often relegate data entry to the bottom of their priority list. This delay creates a persistent gap, where sponsors make decisions based on information that lags significantly behind the clinical reality at the site.

Participants also observed that the tracking of these critical endpoints remains an antiquated, manual exercise, often relying on spreadsheets for safety and efficacy oversight rather than point-of-care systems that could validate data in real time.

Somayeh Honarmand of Character Biosciences articulated the gravity of these delays, noting that the core mission of clinical research, evaluating therapeutic efficacy, is compromised when data entry is sluggish or imprecise. She suggested that sponsors can mitigate this by clearly identifying the most critical CRF pages, allowing sites to focus their limited bandwidth accordingly.

ENDPOINTS AT STAKE

BCVA

Best-corrected visual acuity, often the primary endpoint in retina trials.

Imaging

Vulnerable to reading-center rejection after the patient has left.

“Sites are so busy seeing patients and doing the assessments that data entry sort of falls to the last of tasks to do...”

SH

Somayeh Honarmand
VP of Clinical Science, Character Biosciences



Schematic of a site visit as described by participants. Imaging errors caught after treatment cannot be corrected; delayed data entry means sponsors act on lagging information.

SECTION 02

Data quality, endpoints, and the real-time lag · continued

Imaging was cited as a particularly vulnerable area: a reading center’s rejection of an image after a patient has already departed imposes an avoidable burden on both the participant and the site. Arshad highlighted the finality of these errors within the clinic.

“At a site level right like I look at every image taken but sometimes the image is bad and [you need to] go retake it because after you treat the patient you cannot reimage them.”

AK

Dr. Arshad Khanani
Director of Clinical Research, Sierra Eye Associates

The group also challenged the efficacy of traditional source data verification (SDV). Jennifer, Head of Development at an ophthalmology biotech, detailed a proactive strategy where the company dispatches its own personnel to perform mini-audits alongside CRO monitors.

ESCAPING EXHAUSTIVE SDV
Discrepancies in visual acuity and blood pressure, observed in sponsor-run mini-audits alongside CRO monitors.

Remarkably, even with exhaustive SDV, discrepancies in vital measures, including visual acuity and blood pressure, still escape the notice of standard monitoring teams. Her takeaway was that the solution is not more oversight layers, but rather a commitment to continuous, high-touch training that accounts for the reality of constant site staff turnover.

PROTECTING BCVA AND IMAGING

	TODAY	WHAT PARTICIPANTS CALLED FOR
ENDPOINT OVERSIGHT	● Spreadsheets for safety and efficacy oversight	✓ Point-of-care systems that validate data in real time
VERIFICATION	● Manual, retrospective source data verification	✓ Quality checks while the patient is still in the chair
SITE FOCUS	● Burdened staff leave data entry to last	✓ Sponsors identify the most critical CRF pages
OVERSIGHT MODEL	● More oversight layers	✓ Continuous, high-touch training as site staff turn over

THE COLLECTIVE REALIZATION

The field’s most vital endpoints, best-corrected visual acuity and imaging, are far too critical to depend on manual, retrospective verification methods.

SECTION 03

Redundancy, site burden, and PSVs

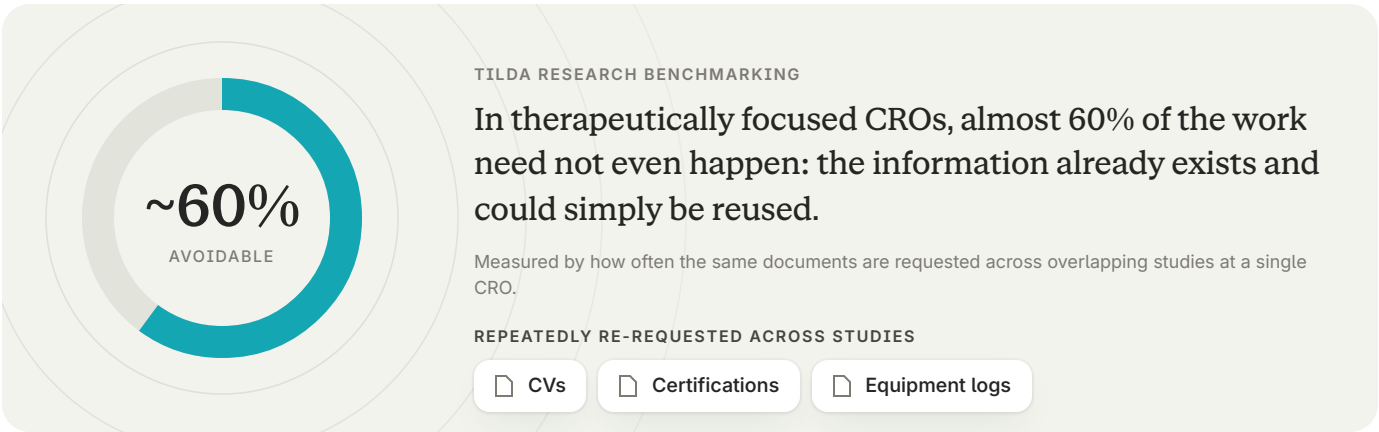
A substantial and lively portion of the conversation centered on redundant activity that inflates cost and exhausts sites without improving quality.

Arshad described the frustration of repeated pre-study visits. The clearest example is the repeated PSV performed at sites a CRO already knows well, often as a box-checking exercise tied to internal process rather than any genuine qualification need.

From the site’s perspective, being asked to undergo a fresh PSV while already running dozens of studies with the same CRO is both baffling and burdensome. Participants noted that these visits have steadily expanded in scope, with some now resembling full initiation visits that walk line by line through the protocol, despite the relevant information already living in site and CRO records.

Ram Yalamanchili of Tilda Research offered hard numbers from benchmarking that quantify the scale of the duplication.

IN BRIEF
Redundancy is not an unavoidable cost of doing business, but a large and addressable inefficiency.



That finding reframes redundancy not as an unavoidable cost of doing business but as a large and addressable inefficiency. It lent weight to the sponsors’ own frustrations about repeated requests for CVs, certifications, and equipment logs.

SECTION 03

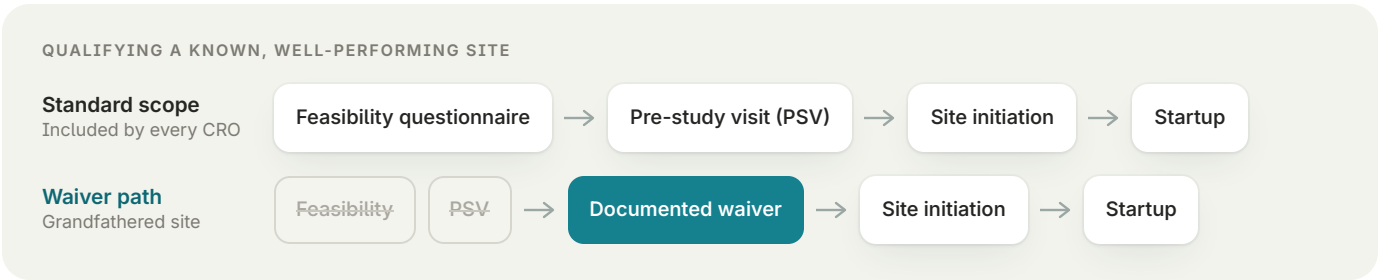
Redundancy, site burden, and PSVs · continued

Encouragingly, several sponsors shared concrete tactics that have actually moved the needle on reducing this burden. The most direct came from Anahita, who declined feasibility questionnaires and pre-study visits outright for sites already active on her studies.

“Every CRO includes PSVs as standard scope with a new trial regardless of extensive history with these sites. If we have worked with a site before and choose to work with them again based on good performance, we don’t need to requalify them. In that case, we say ‘No, thank you’ to PSVs and request to move the site straight to startup.”

AN

Anahita Nikzad
VP of Clinical Operations, REGENXBIO



THE SPONSOR PLAYBOOK IN PRACTICE

AN

Anahita Nikzad
REGENXBIO

Declined feasibility questionnaires and PSVs outright for sites already active on her studies; secured a documented waiver to proceed straight to initiation.

KM

Kim Maplestone
4D Molecular Therapeutics

Adopted the same waiver approach on her second Phase 3 program after a more cautious first study, and confirmed it saved considerable time.

SH

Somayeh Honarmand
Character Biosciences

Pushes CROs to grandfather known sites and substitute lighter-touch contact for full visits, though CROs routinely push back to satisfy their own process checkboxes.

SECTION 03 Redundancy, site burden, and PSVs · continued

The burden ultimately lands on sites working with multiple CROs that do not coordinate. Jennifer captured the absurdity of process for process's sake with an example of dispatching a CRA across the country to verify one data point near database lock.

“A single BCVA change had to deploy a person to fly over to a site to say, ‘Oh, you said 68. Okay, this is 68.’”



Jennifer
Head of Development, ophthalmology biotech

CONSENSUS

The responsibility belongs with the large CROs, who hold extensive site data they could mine far more effectively. The duplication persists largely because internal teams do not share information across studies.

SECTION 04

The state and trajectory of AI in clinical operations

When the discussion turned to AI, participants were honest about how little is genuinely in production within their own trials today.

Several individuals noted that even where CROs claim to use AI, they see no efficiency gain, and that their own companies’ efforts remain at the pilot stage or have not yet started. The group was candid about the gap between enthusiasm and reality, grounding the more optimistic discussion that followed in a realistic baseline rather than vendor promises.

IN BRIEF
A realistic baseline, not vendor promises.

TODAY

Little is genuinely in production

- Adoption within participants’ own trials remains limited.
- Even where CROs claim to use AI, participants see no efficiency gain.
- Their own companies’ efforts remain at the pilot stage or have not yet started.

APPETITE

Shifted dramatically

2–3 quarters

The period over which appetite for AI has changed, driven by an economic forcing function in large-pharma contracts.

Ram described where Tilda has found early, defensible value. He explained that Tilda builds “AI Teammates” that operate in two modes: oversight for sponsors who outsource to vendors, and execution support for the clinical operations teams doing the work.

TILDA’S AI TEAMMATES OPERATE IN TWO MODES

Oversight

For sponsors who outsource to vendors



Execution support

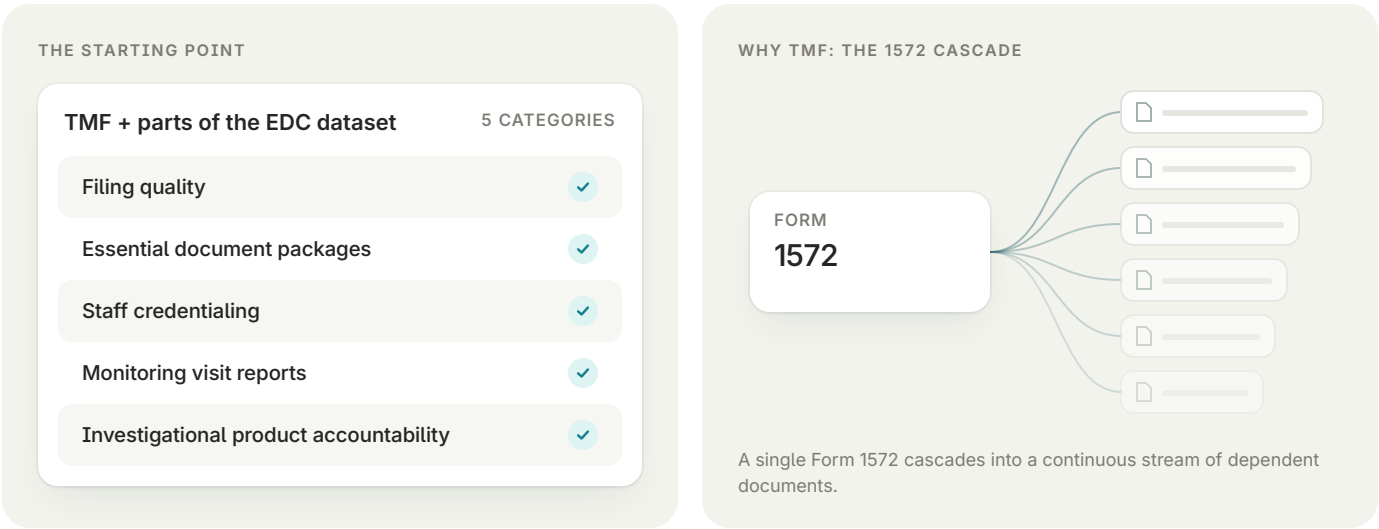
For the clinical operations teams doing the work

The choice of the TMF as a beachhead was deliberate because it offers fast ROI, a logic that Anahita independently endorsed when she noted how a single Form 1572 cascades into a continuous stream of dependent documents.

SECTION 04

The state and trajectory of AI in clinical operations · continued

The starting point was the TMF and parts of the EDC dataset, broken into categories spanning filing quality, essential document packages, staff credentialing, monitoring visit reports, and investigational product accountability.



The most resonant idea of the session was Ram’s reframing of where the leverage actually sits. Benchmarking a partner that processes roughly 3.5 million documents a year, he found that 45% of that volume is rework in the form of duplicates and errors that cannot be fixed at the TMF level, because the failure originates upstream. His conclusion inverted the industry’s usual focus.

THE SESSION’S MOST RESONANT IDEA

Fix quality where documents originate, not where they are filed.

“The TMF workflow is actually a lagging indicator. The leading indicator is the CRA.”

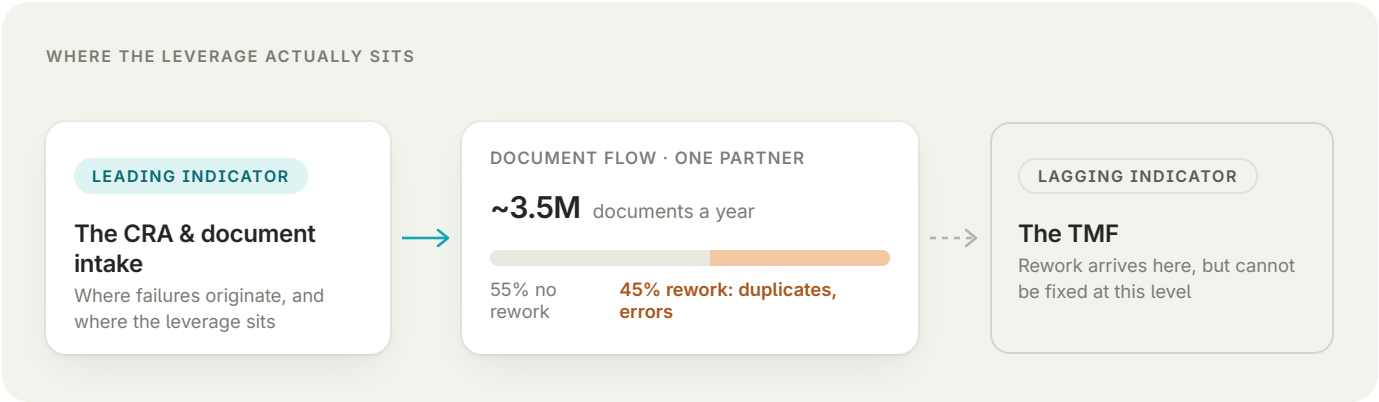
RY

Ram Yalamanchili

Founder & CEO, Tilda Research

SECTION 04

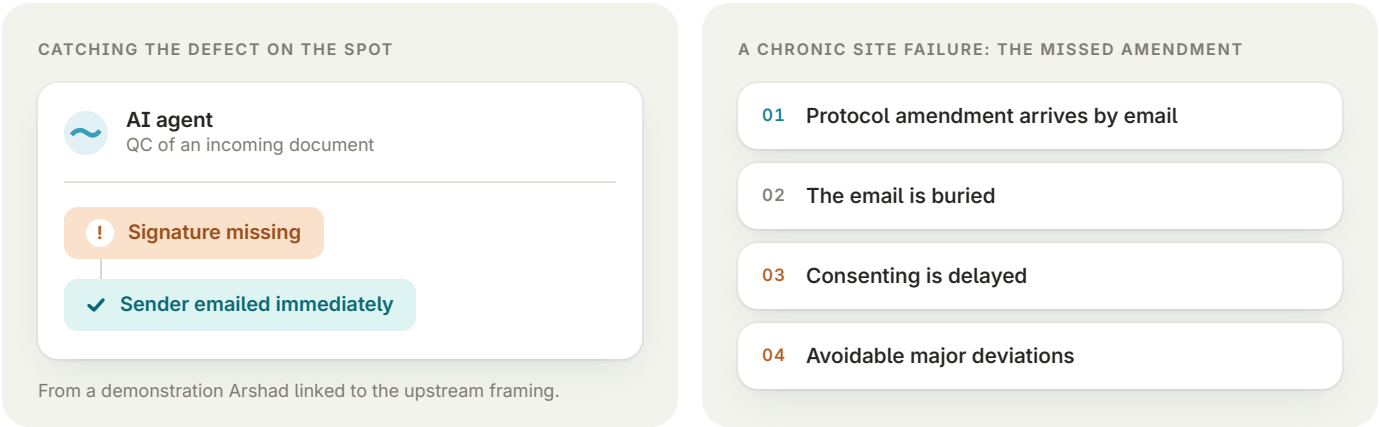
The state and trajectory of AI in clinical operations · continued



Benchmark of one partner's document volume, as described by Ram Yalamanchili. Bar drawn to scale.

This upstream framing connected directly to the failures described by the group. Arshad linked it to a demonstration in which an AI agent QC's an incoming document and immediately emails the sender when a signature is missing, catching the defect on the spot.

He extended the use case to missed protocol amendments, a chronic site failure in which a buried email leads to delayed consenting and avoidable major deviations.



SECTION 04

The state and trajectory of AI in clinical operations · continued

WHY NOW

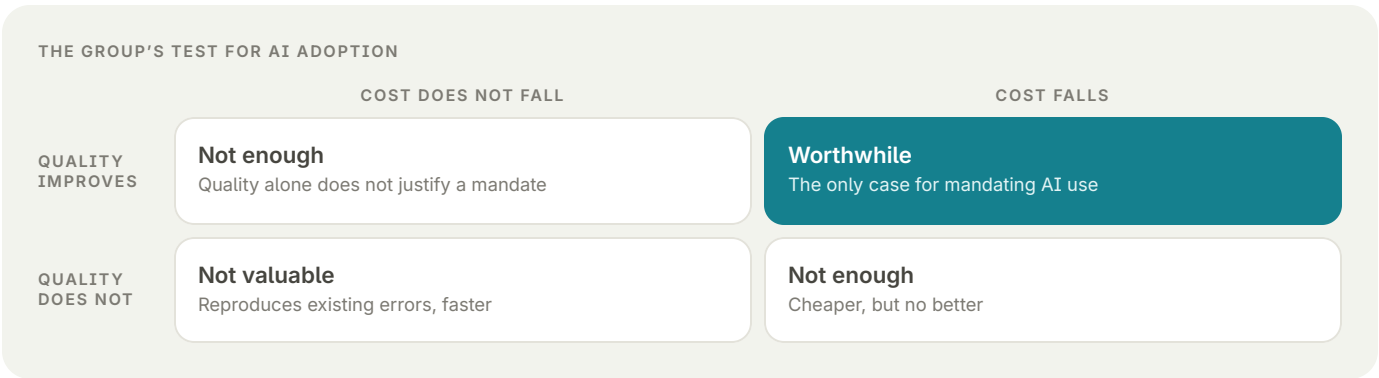
Ram explained that the appetite for AI has changed due to an economic forcing function: large-pharma contracts using AI efficiency rebates, in which sponsors demand decelerating rather than escalating pricing.

The group's caution, voiced sharply by Kim, was that mandating AI use is only worthwhile if it demonstrably improves quality and lowers cost. Arshad agreed, warning against AI adoption that simply reproduces existing errors faster: if quality does not improve and cost does not fall, the technology is not valuable.

FORCING FUNCTION

AI efficiency rebates in large-pharma contracts.

Pricing expected to decelerate, not escalate.



SECTION 05

Rethinking monitoring and SDV

The group discussed to what extent AI can meaningfully change monitoring and source data verification (SDV), or whether human site visits remain unavoidable.

Jennifer observed that even in 2026, a person must still verify every data point, which she took as evidence of an unresolved gap between the systems that should be talking to one another. The group expressed disbelief that the industry still flies people across the country to confirm single values that software could reconcile.

She went on to offer a precise and high-value use case for AI: longitudinal consistency checks that flag clinically implausible changes between visits. She also pointed to the value of robust edit checks that fire queries automatically at the moment of entry.

TWO USE CASES RAISED

Longitudinal consistency checks between visits.

Edit checks that fire queries automatically at entry.

LONGITUDINAL CONSISTENCY CHECK

ILLUSTRATIVE

MEASURE	VISIT 1	VISIT 2	VISIT 3	AI TEAMMATE
Slit-lamp finding				! Finding disappears
Refraction				! Implausible swing

A slit-lamp finding that disappears from one visit to the next, or a refraction that swings impossibly, is exactly the kind of discrepancy a rotating CRA may never catch, but an AI teammate comparing against prior visits would surface immediately.

SECTION 05

Rethinking monitoring and SDV · continued

Michelle Chen of Perfuse Therapeutics identified the parallel opportunity in pre-screening for difficult-to-recruit diabetic retinopathy trials, where screen-fail rates run extremely high, while naming the central validation gap that remains.

“The gap is between whether or not these AI scores are actually matching what the reading center had scored.”

MC

Michelle Chen
VP & Head of Clinical Development, Perfuse Therapeutics

THE EMERGING CONSENSUS: A SENSIBLE DIVISION OF LABOR

WELL SUITED TO AI NOW

Real-time, rules-and-pattern work at the point of entry

● Image gradeability

● Endpoint plausibility

● Document completeness

NOT YET

Human or formally validated involvement, for now

● Reading-center concordance

● Certain regulatory verifications

The value is greatest not in replacing the site visit wholesale but in catching errors while they can still be fixed, before the patient leaves and the opportunity closes.

SECTION 06

What excites leaders about the future

Closing the session, Arshad asked each participant what excites them about the future of retinal clinical development. The responses clustered around real-time quality at the source and the broader acceleration of treatment options.

AN Anahita Nikzad

Instant imaging feedback

Lets a site send a patient home with confidence rather than recalling them for a quality failure.

KM Kim Maplestone

Elevating the primary endpoint

The industry must elevate how it treats its most important endpoint.

J Jennifer

Real-time EDC mining

Questioning implausible endpoint values as they are entered, though coordinators often do not enter data at the point of care.

SH Somayeh Honarmand

The science itself

New treatment options for patients, and data integrators that match protocols to patients.

MC Michelle Chen

Efficiency and consistency

Concrete near-term wins, including AI-assisted generation of case report forms from a protocol.

RY Ram Yalamanchili

Alignment, and AI fluency

The collective alignment in the room as an indicator of progress; tooling gives little ROI without a workforce able to integrate it.

“Remembering that our primary endpoint is often BCVA, we have put more focus on the quality and oversight of that endpoint and how it is collected at sites.”

KM

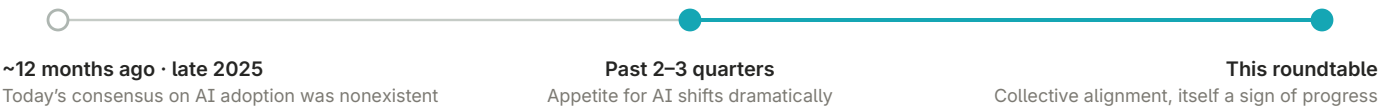
Kim Maplestone

Chief Clinical Operations Officer, 4D Molecular Therapeutics

SECTION 06

What excites leaders about the future · continued

A RAPID SHIFT IN SENTIMENT



The group agreed on the necessity of organizational AI fluency, with Ram arguing that advanced tooling provides little ROI unless paired with a workforce capable of strategic integration.

“At the end of the day, the goal of this discussion is to explore how we can bring innovative treatment options to patients by overcoming operational challenges, protecting the primary endpoints of clinical studies, strengthening collaboration between sponsors and sites, and ultimately reducing the cost of drug development through greater efficiency and the effective use of technology.”

AK

Dr. Arshad Khanani
Director of Clinical Research, Sierra Eye Associates

RECOMMENDED ACTIONS

Recommended actions

The following actions are drawn directly from the discussion, recognizing that most require collaboration across sites, sponsors, and CROs.

FOR SPONSORS

- 1 Eliminate redundant site qualification.**
Follow the example of grandfathering known, active sites by waiving feasibility questionnaires and PSVs in favor of documented waivers and direct site initiation.
- 2 Require proof of impact for AI usage.**
Structure multi-year services agreements that mandate AI use where it demonstrably improves quality and lowers cost, rather than requiring AI for its own sake.
- 3 Prioritize the endpoints that matter.**
Direct sites to the highest-priority CRF pages and elevate the rigor around BCVA and imaging, including more frequent certification and real-time delta checks.
- 4 Strengthen independent oversight where warranted.**
Consider supplementing CRO monitoring with sponsor-deployed mini-audits at high-enrolling sites, paired with ongoing (not one-time) training as staff turns over.

FOR CROs

- 5 Mine existing data to reduce duplicate requests.**
Reuse documentation already collected across overlapping studies rather than re-requesting CVs, certifications, and equipment logs. Benchmarking suggests a large share of this work is avoidable.
- 6 Restore substance to monitoring.**
Move beyond checklist-only monitoring reports, address CRA turnover and continuity, and ensure data management and monitoring functions coordinate to avoid duplicative queries to PIs.
- 7 Enable knowledge-sharing within governance limits.**
Explore redacted, AI-supported internal databases so site-performance intelligence can be reused across teams without breaching sponsor confidentiality.

FOR THE INDUSTRY

- 8 Invest in AI fluency.**
Build organizational capability to use and integrate AI into everyday workflows, recognizing that tooling alone does not create value without skilled users. Tilda Research's free masterclass for clinical research leaders is one route; see the back cover.

FREE MASTERCLASS

AI Foundations for Clinical Research Leaders

To help build AI fluency across the industry, Tilda Research offers a free masterclass for clinical research leaders, completed by hundreds of industry professionals.



HOSTED BY
Ram Yalamanchili
Founder & CEO, Tilda Research

Register for free

tilda.bio/ai-masterclass

ABOUT TILDA RESEARCH

Tilda Research builds AI Teammates that execute clinical operations workflows end-to-end, inside the existing eClinical stack, with the team's full oversight.

AI Teammates for the trial master file and site & study management are live, with study monitoring and finance & payments to follow. Built for sponsors and CROs.

AI TEAMMATES EXECUTING ACROSS

300+

Studies

10,000+

Sites

45

Countries

32

Languages