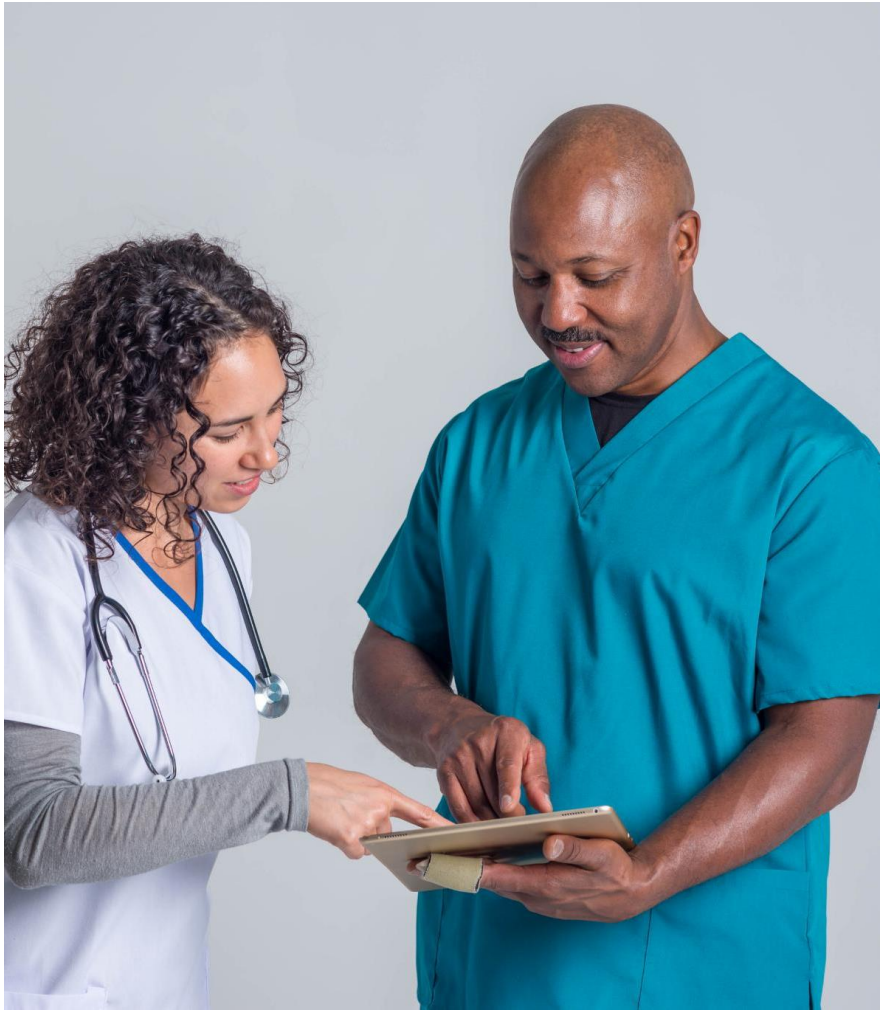

Designing Trials with Patients to Reduce Burden & Strengthen GCP Compliance & Inspection Readiness

EMPOWERING HEALTHCARE COLLABORATION FOR FUTURE IMPROVEMENTS

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Why This Matters NOW

THE PROBLEM

- Rising trial complexity
- Recruitment/retention failures
- Protocol deviations & dropouts
- Data quality gaps
- Feasibility underestimated

REGULATOR FOCUS

- ICH E8(R1): Meaningful patient impact
- ICH E6(R3): CtQ & quality by design
- FDA's Patient-Focused Drug Development (PFDD): Patient-informed design
- Risk-based oversight
- Documented feasibility

THE SOLUTION

- **Patient-centered trial design**
- **Reduce burden at source**
- **Build feasibility evidence**
- **Create inspection-ready narratives**
- **Strengthen consent & protection**

Today's Journey

1. **Regulatory Landscape**
   ICH E8, E6(R3), FDA, EMA
2. **Evidence Base**
   Research on patient engagement impact
3. **5-Step Framework**
   Operational roadmap for implementation
4. **KPIs & Metrics**
   Inspection-defensible quality measures
5. **Evidence Pack**
   Compliance narrative & documentation

The Current State

Trials are becoming harder to deliver & harder to defend

Common Challenges at Inspection

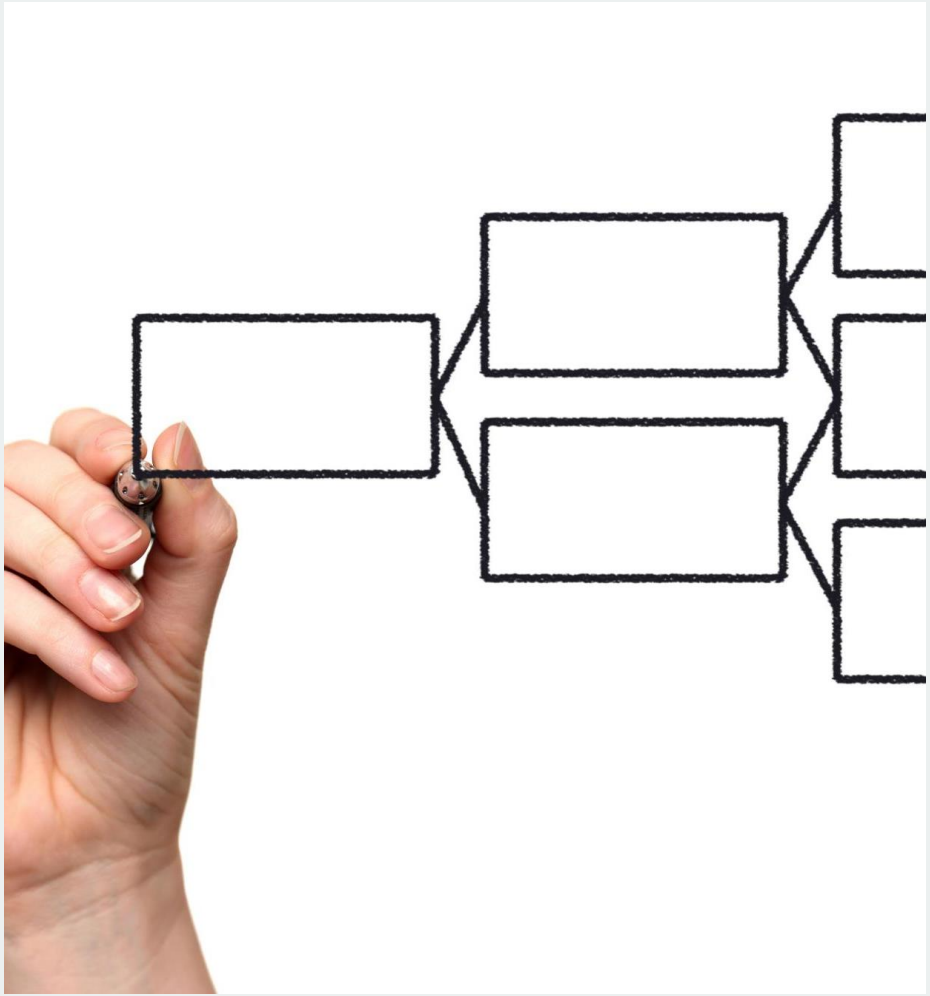
- Protocol deviations linked to burden or feasibility
- Missed visits or assessments due to dropout
- Incomplete diary data or ePRO submissions
- Lengthy, hard-to-read informed consent forms
- Insufficient evidence of risk-based quality management
- No documented link between design & participant needs

Inspection Finding Patterns

Of these findings, the majority could have been prevented with patient-centered design and burden assessment.

What Regulators Expect

A shift toward quality by design and operational feasibility



ICH AND REGULATORY DIRECTION

ICH E8(R1) [2021]

- Quality by Design (QbD) for trials
- Critical-to-Quality (CtQ) factors
- Feasibility as a design requirement
- Meaningful patient impact focus
- Systematic risk identification

ICH E6(R3) STEP 5 [Jan 2025]

- Proportionate quality management
- CtQ identification & monitoring
- Quality Tolerance Limits (QTLs)
- Risk-based monitoring plans
- Documented design rationale

FDA & EMA Expectations

FDA PFDD Guidance

Methods to Identify What Is Important to Patients
(Final, January 2025)

- Stepwise patient engagement methods
- Patient experience data integration
- Decision-logging frameworks
- Encourages early patient involvement

EMA Reflection Paper

Patient Experience Data in Clinical Trials
(Published, September 2025)

- Patient involvement across lifecycle
- Patient experience as evidence
- PRO/eCOA data integrity expectations
- Supports proportionate design

Patient Engagement Fundamentals

Evidence-based rationale and critical framing

Evidence Base: What Research Shows

BMJ 2018	PPI associated with improved recruitment & retention
CTTI	Meaningful partnership improves trial relevance & data quality
EClinical Medicine 2024	Consent readability linked to participant retention
SPIRIT-PRO 2023	Patient-informed PRO design improves measurement validity
TransCelerate	Early patient input reduces feasibility failures & improves adherence

Critical Framing: What Patient Engagement IS & ISN'T

Patient Engagement IS:

- A method to achieve QbD outcomes
- A way to identify authentic CtQ factors
- Risk-anticipation & burden assessment
- An audit trail for compliance
- An inspection defense strategy

Patient Engagement ISN'T:

- A standalone GCP requirement
- A checkbox exercise
- Only about diversity or representation
- Driven by social responsibility alone
- Something done in isolation from QA/RA

The 5-Step Framework

- **Inspection-defensible approach to patient-centered design**

Step 1: Plan & Govern Patient Partnership

- Engagement charter & formal scope
- Governance structure & decision approvals
- Stakeholder mapping (patients, sites, internal)
- Decision-logging process & templates
- Timeline & resource allocation

Step 2: Journey Mapping & Burden Assessment

Journey Map Covers:

- Enrollment & consent process
- Visit frequency & duration
- Assessments & data collection
- Study medication administration
- Diary/ePRO requirements
- Follow-up & off-study procedures

Burden Assessment Against:

- ICH E8 'meaningfulness' factors
- Site feasibility & staffing
- Participant accessibility & transportation
- Informed consent comprehension
- Data quality risks
- Retention predictors

Step 3: Turn Insights Into Controlled Decisions

INSIGHT-TO-DECISION LOG (Example Format)

INSIGHT	Patients reported weekly diary burdensome (n=12/15); difficulty remembering entries
DESIGN CHANGE	Shift to eCOA app with daily prompts, push notifications, & weekly reminder calls
CTQ LINK	Primary endpoint depends on diary compliance; app reduces forgotten/late entries
RATIONALE	Balances frequency with accessibility; maintains data integrity while reducing burden
MONITORING	Track eCOA completion vs. targets; monthly feasibility survey; site feedback review

✓ Clear audit trail • ✓ Structured reasoning • ✓ Regulatory-defensible • ✓ Scope management

Step 4: Set Quality Tolerance Limits (QTLs) & KPIs

QTL/KPI Domains (Burden-Linked)

Adherence & Feasibility	Visit compliance, diary completion, protocol adherence
Data Quality	Primary endpoint completeness, query rates, timeliness
Informed Consent	Comprehension, re-consent frequency, deviations
Operations	Recruitment/retention trends, screen failure reasons, amendments

Step 5: Build Your Inspection Evidence Pack

EVIDENCE PACK COMPONENTS

1. Executive summary & design philosophy statement
2. Engagement governance charter & decision logs
3. Journey map & burden assessment findings
4. CtQ identification & QTL rationale
5. Patient & site feedback (compiled, anonymized)
6. QTL performance data (actual vs. threshold)
7. Recruitment, retention, and compliance trends
8. Lessons learned & continuous improvement log

TODAY'S JOURNEY

Real-World Impact

Concrete measures that support compliance

Real-World Measures: How Patient-Centered Design Drives Compliance

Real-Trial Impact Summary

Trial A (Oncology)				
Screen failure	23%	→	12%	↓ 48%
Early dropout	18%	→	9%	↓ 50%
Protocol deviations	31%	→	14%	↓ 55%
Trial B (Diabetes)				
Diary completion	62%	→	91%	↑ 47%
Missing primary data	8%	→	1.2%	↓ 85%
Trial C (Cardiology)				
Feasibility amendments	18%	→	3%	↓ 83%

Getting Started

Practical next steps for implementation

Quick-Start Implementation Checklist

MONTH 1: Setup	Executive sponsorship • Pilot trial selection • Engagement lead assignment • Governance charter
MONTH 2: Engage	Patient advisory group formation • Journey mapping workshop • Burden assessment • CtQ identification
MONTH 3: Design	Insight-to-Decision logs • QTL definition • Protocol updates • Site training
ONGOING: Monitor	Patient/site feedback review • QTL performance tracking • Steering committee meetings • Lessons learned

Ready-to-Use Toolkits & Resources

TransCelerate P-PET	*Journey mapping, engagement governance, decision logging*
FDA PFDD Methods	*Stepwise patient engagement framework & documentation*
CTTI Recommendations	*Best practices from multi-sponsor trial network*
GCTP Custom Templates	*Therapy-specific tools & AI-powered synthesis*
ICH E8(R1) & E6(R3)	*Regulatory foundations for QbD & CtQ*

Key Takeaways

1. Patient engagement is now regulatory expectation, not optional
2. It's a method to achieve quality-by-design & CtQ mandates
3. 5-step framework provides inspection-defensible roadmap
4. Real data shows improved recruitment, retention & data quality
5. Tools are available; implementation is straightforward
6. Start with one pilot; scale systematically

Thank You

Key Takeaway for Your Organization

- Patient-centered trial design is no longer a 'nice-to-have.' It's a regulatory expectation that, when implemented systematically, becomes your strongest inspection defense.
- Start today with a single pilot.
- Document everything.
- Build your evidence pack.
- By the time inspectors arrive, you'll have a compelling narrative of thoughtful, feasibility-informed design.

Questions?

Where to Find Resources

TransCelerate P-PET	*www.transceleratebiopharma.org*
FDA PFDD Guidance	*www.fda.gov/drugs*
CTTI Recommendations	*www.ctti-clinicaltrials.org*
ICH Guidelines	*www.ich.org*
GCTP Custom Tools	*www.gctp.consulting*
Journal Articles	*BMJ, EClinicalMedicine, SPIRIT*

Ready to Get Started?

Next Steps:

- 1. Select a pilot trial (single study or program)
- 2. Assign an engagement lead (QA or Clinical Ops)
- 3. Download TransCelerate P-PET toolkit
- 4. Schedule kick-off meeting with patient & site reps
- 5. Build your evidence pack as you go

5-Step Framework at a Glance