Comprehensive Summary of Site Engagement Literature

Key Themes

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Overview of Contents

Budgets/Budget Negotiation

SUMMARY OF SITE NEEDS/CONCERNS

- Lengthy & burdensome process
- FMV databases may not reflect true work effort for all that is involved with a given procedure
- Holdback payments
- Study cancellations during the start-up process
- Budgets don't account for a number of personnel hours spent completing training

SITE PREFERENCES

- Budgets that capture all required elements to fulfill protocol compliance, including training requirements
- Online, transparent, platform to facilitate budget negotiations; Streamlined, transparent budget negotiation process
- Eliminate holdback payments
- Improve the three most under-funded line items: start-up costs, screen failure reimbursements, severe adverse reaction reporting
- Improve funding for closeout costs, monitoring visits, study cancellations
- Flexible - willing to modify budgets
- Similar studies with the same sponsor should consider the previously approved budget to avoid protracted contract budget negotiations

CRA Quality/CRA Turnover

SUMMARY OF SITE NEEDS/CONCERNS

- Lack of competent CRAs
- High CRA turnover
- CRA leave of absence: CRAs is often not replaced immediately or at all, leaving study milestones such as Green Light on hold until CRA returns
- Lack of consistency across CRAs when they change mid-study

SITE PREFERENCES

- CRAs who come to the site to work with use & not against us & the trial
- How CRA turnover is handled & communicated is a more important & actionable Attribute of maintaining positive relationships with sites than is the turnover itself be proactive in communication about personnel changes
- Ensuring CRAs are knowledgeable about the study
- Have professional, knowledgeable & well-trained monitors/CRAs

Clinical Trial Supplies

SUMMARY OF SITE NEEDS/CONCERNS

- Delayed supplies (particularly during pandemic)
- Frustration with lack of communication/notification of shipments or delays
- Poor communication/expectations around the management or return of unused supplies

SITE PREFERENCES

- Provide timely drug/clinical trial supply availability
- Maintain open & transparent communication regarding shipments/delays
- Options for direct shipment to subject home (where appropriate)
- Provide clarity around expectations for unused supplies

Communication

SUMMARY OF SITE NEEDS/CONCERNS

- Poor communication & organization
- Significant problem is the lack of visibility to the Green Light status
- Communication is a key issue to improving site operating efficiency
- Last minute schedule changes (this was specifically sites as challenge for CRUs but broadly applies to all sites)

SITE PREFERENCES

- Clear lines of communication & support throughout entire life cycle & especially after study is completed
- Have a single point of contact for communication/escalation & resolution of issues
- Improve response times to queries
- Maintain open, transparent communication
- Platforms are more beneficial if they have an API to link to site's internal solutions

ESG/Sustainability

We were unable to locate any references related to environmental, social, governance (ESG) or sustainability related topics as pain points, areas of focus or concerns for sites.

SUMMARY OF INDUSTRY CONCERNS

- Remote monitoring to reduce CRA travel
- Frequency of shipments sent/received related to studies (e.g. lab samples, ancillary supplies)
- Study supply waste (many sponsors want to work with sites/CROs to reduce waste such as lab kits that are ordered but never used & need to be destroyed)
- General

NOTES/OPPORTUNITIES FOR FURTHER EXPLORATION

- If CRAs need to travel, accommodate longer hours at the site per visit to reduce the number of individual visits (and travel) to the site
- How does this impact the site? Trade-offs for ESG vs. site resource demands worth it - why or why not?
- Are there opportunities to reduce?
- What does this look like from the site's perspective?
- This is a challenge because if you want to reduce the number of shipments noted in the bullet above, larger orders could be placed, but then this increases waste
- JIT ordering reduces supply waste but increases shipments. This is a tricky balance.
- How do these impact site storage? Inventory management? Manual v. automatic tracking of expiration dates? Other considerations?
- How does ESG factor into their strategies or initiatives?
- How do they think about ESG?
- How can Sponsors/CROs collaborate with sites on any of these initiatives that would be valuable to both entities?

Good Comprehensive Summary of Site Concerns

The below table provides a good summary of global site concerns, many of which have been captured in the prior tables from other sources.

Source: 2014 SCRS White Paper: The Quest for Site Quality & Sustainability Perspections, Principles and Best Practices

Factors Contributing to Lower Levels of Satisfaction

Site Related Factors	Protocol/Sponsor/CRO Related Factors
	Protocol • Poorly written protocols; too many gray areas • Protocols that do not match real world practices • Overly complex and burdensome protocols
Personnel • Inconsistency across staff (e.g., coordinators) • Staff turnover • Understaffed/under-resourced • Workload burdens from accepting too many trials for site's capacity • Physician disinterest • Inexperienced personnel • Large diverse staff making it difficult to ensure consistency and excellence	**Personnel** • Staff turnover; frequent changes in monitors • Slow responsiveness • CRAs who manage multiple protocols and don't know a given protocol well
Systems/Processes • Failure to follow SOPs • Lack of an internal audit system • Lack of formal QA program • Lack of proactivity in certain areas ; reactive vs. proactive culture • Lack of sharing of best practices and learnings amongst staff • Lack of a risk detection or risk mitigation strategy	**Processes/Communication** • Site needs are dismissed, sponsor demands are increasing • Inconsistent messages from various parties involved (sponsor, CRO, CRAs, etc.) • Sponsors putting emphasis and pressure on enrollment versus quality • Variation in sponsor/CRO rules and interpretations • Managing overwhelming amount of email communication and knowing what is important to focus on
	EDC • EDC system that doesn't match protocol • Sponsors who change expectations around data entry and definitions of queries causing confusion and rework • Slow response time to query clarifications
Training • Poor or insufficient training of staff • Lack of training plan or effective training programs • Insufficient time to reinforce training • Lack of good training programs within the industry on how to best monitor quality	**Training** • Information given at Investigator Meeting is not in the protocol • Poorly trained CRAs (lack of clinical and clinical research knowledge) • Different interpretations depending on who is asked • Delivery methods of training (e.g., webinars versus face-to-face)
	Site Support • Lack of site support particularly at start-up • Budgets and timelines that are too tight
	Vendors • Too many and poorly trained outside vendors

Overall Sponsor/CRO/Site Relationship

SUMMARY OF SITE NEEDS/CONCERNS

- Sites don't feel like a partner
- Sponsor-site relationships are better than sponsor-CRO relationships (but both could improve)
- Overall administrative burden based on sponsor/CRO processes

SITE PREFERENCES

- Sites want their expertise to be acknowledged & solicited (protocol design, workflow, etc)
- Have professional medical staff in clinical operations
- Sites would prefer to have insight or input into vendor selection. It impacts the participation experience for sites & patients, as well as the regulatory review process.
- Communicate to sites why not able to incorporate their feedback (if solicited)

Payments/Payment Terms

SUMMARY OF SITE NEEDS/CONCERNS

- Quarterly payment terms
- End of trial reconciliation is lengthy, burdensome & frustrating process

SITE PREFERENCES

- Monthly payment terms (90% of sites say this is very or extremely important)
- Sites want to be paid within 30 days of data entry with detailed report to allow sites to reconcile line items per study
- Electronic funds transfer for payment
- Access to the site's financial information in payers' electronic systems
- Automatic payment with reduced need for manual invoicing

Protocol Complexity/Design

SUMMARY OF SITE NEEDS/CONCERNS

- Protocol complexity & intensity of execution requirements continue to grow & impact site operations and patient recruitment/retention
- Multiple amendments
- Pragmatic study design is essential & may be overlooked by inexperienced staff on the sponsor side

SITE PREFERENCES

- Protocol quality & design
- Realistic studies & realistic expectations
- Design patient-friendly protocols
- Develop protocols in which scientific rationale aligns with clinical practice realities
- Solicit site feedback on draft protocol with focus on operational feasibility
- Protocols that require minimal amendments
- Flexible - willing to modify protocols

Recruitment/Retention

SUMMARY OF SITE NEEDS/CONCERNS

- Untimely patient stipend reimbursement
- Patients incur uncompensated costs in terms of time & convenience when utilizing telehealth & other solutions
- Sites experiencing higher costs associated with patient diversity expectations (per recent FDA guidance)

SITE PREFERENCES

- Provide payment for patient stipends
- Support sites with booking travel/transportation assistance
- Adjust patient compensation to accommodate burdens associated with telehealth solutions
- Provide adequate funding for patient recruitment
- Set realistic goals on recruitment
- Provide support in the DE&I space (analysis, education, awareness building, implementation)

SCRS Site Payment Recommendations

The below table provides a good summary of current site payment recommendations:

Burdens Identified	Initial Recommendations
1. Contract Terms: Payment Frequency	Payment within 30 days
2. Contract Terms: Pay When Paid	In contracts where a "pay when paid" clause is included, the clause is limited to only cases were the sponsor has filed for bankruptcy
3. Payment Back-Up Information	Each payment will be accompanied by a report to include the protocol name and number, investigator name, details of each payment line item including subject initials, visit number, visit date and procedures outlined if the payment is for items outside the visit
4. Holdback Payments	Eliminate holdbacks
5. Dispute Resolution	All parties to the contract should include within their standard study documents an escalation process and contact information

Table 1 Identification of Significant Burdens on Sites by the Current Site Payments Practices

Source: 2016 SCRS White Paper: Site Payment

Site Business Sustainability

SUMMARY OF SITE NEEDS/CONCERNS

- **Lack of study opportunities**
- **Lack of visibility to pipeline**

SITE PREFERENCES

- **Share pipeline with sites**

Site Initiation/Start-Up Process

SUMMARY OF SITE NEEDS/CONCERNS

- Pressure for site activation prior to contract execution (& impact to site payments)

SITE PREFERENCES

- *N/A - site preferences were not specifically voiced in the literature reviewed*

Site Staffing/Resourcing

SUMMARY OF SITE NEEDS/CONCERNS

- Maintaining site resources, especially CRCs
- High CRC/SC turnover
- Good CRCs are recruited by sponsors/CROs
- Recruiting CRCs with IT expertise is problematic(different skill sets)
- New roles are emerging requiring different hiring practices/personnel profiles & competencies (in general, and particularly with hybrid/DCT models)
- General workforce challenges & demand outpacing the supply of qualified site staff
- Lack of diverse workforce reduces inclusion of diverse patient populations

SITE PREFERENCES

- More training & support to develop cultural competency
- Racial & ethnic representation among the research workforce is essential in reducing barriers to clinical study volunteer participation among historically underrepresented populations
- DEI-specific materials and SOPs

Site Quality/Performance Metrics

SUMMARY OF SITE NEEDS/CONCERNS

- Lack of transparency/visibility to site's performance

SITE PREFERENCES

- Access to site "report cards"/performance metrics

Technology

SUMMARY OF SITE NEEDS/CONCERNS

- Sites don't want to bear full responsibility for investing in & providing technology for DCT & hybrid trial
- Too many systems with different processes & login credentials
- It is not unusual for site staff to access > 20 systems over a single day (although on average they touch ~5 systems per day or week)
- Too much redundant training on standard technologies
- Systems are incompatible, requiring duplicate data entry across systems
- Multiple stakeholders involved to obtain activation to systems
- Sites spend too much time resolving queries using RBM compared to traditional approaches
- Across 12 different technologies, less than 50% of the sites feel very proficient in using the systems

SITE PREFERENCES

- Adjust budgets to accommodate extra work effort associated with training (patients, staff) and troubleshooting associated with technologies
- Sponsors should allow sites to use their technology & not force sponsor-provided technology on them
- Single sign on capabilities
- Single point of data entry across systems
- Share RBM metrics with sites
- Integration across systems
- All sites to use their own tools/templates (e.g. Delegation Log) where possible
- Provide uncomplicated CRF design
- Easy to use technology

Trainings

SUMMARY OF SITE NEEDS/CONCERNS

- Eliminate redundant training
- Improve quality of training
- Increase training volume impacts time available to manage studies (sites report 10-12 hours per study for month 1)
- Access to systems based on training completion delays recruitment

SITE PREFERENCES

- Sites prefer Face to Face meetings
- Sites want inspection support training
- Tailor site training to different roles/experience levels (one size does not fit all)
- Provide adequate training support
- Training platform where site staff training can be tracked & monitored from the data of completion to system access

Literature Reviewed (2011-2023)

This document summarizes key themes from a comprehensive literature search related to Sponsor/CRO-Site Relationships. It reflects high level site needs and concerns along with site preferences identified in the clinical research industry literature from 2011 through 2023.

Click on the listed reference to access the original source.

SOURCE	DATE	TITLE
Clinical Leader	October 2016	SCRS: Site/Sponsor Relationship Needs Improvement
Clinical Leader IQVIA White Paper	Unknown	Investigator Payments - A Critical Component in Bayer's Sponsor of Choice Strategy & Top 10 Global Pharma Company Dramatically Improves Site Payments in Drive To Become Sponsor of Choice
Clinical Leader	December 2016	What do sites really want from sponsors and CROs? ACRP/Avoca survey explains
Clinical Leader	July 2022	Tips for Clinical Trials Sponsors to Cultivate Meaningful Relationships with Sites
SCRS White Paper	August 2017	Site Budget Development and Payment Systems: A Call for Transparency from Clinical Research Sites
SCRS White Paper	April 2017	Site Payments and Patients Reimbursements: A Global Perspective
SCRS White Paper	February 2019	Financial Barriers to Site Sustainability, Patient Experience & Overall Trial Success
SCRS White Paper	October 2012	Better Payment Term for Sites - An Industry Imperative
SCRS White Paper	October 2014	The Quest for Site Quality and Sustainability: Perceptions, Principles and Best Practice
SCRS White Paper	October 2016	Site Payment
SCRS White Paper	October 2016	Study Site Dashboard
SCRS White Paper	March 2014	An Industry in Crisis: The Escalating Cost to Society of Our Inability to Sustain the Performance of Clinical Research Sites Today and Into the Future
SCRS White Paper	October 2014	Responsible Site Management Best Site Practices

Literature Reviewed (2011-2023), *cont.*

SOURCE	DATE	TITLE
SCRS White Paper	2022	The 2021 Site Landscape Survey: A Year in Flux
SCRS White Paper	September 2019	Impact Assessment of eClinical Technologies and Industry Initiatives on Sites
SCRS White Paper	July 2020	Sites Speak Out on Clinical Trial Technology Overload: An SCRS Survey
SCRS White Paper	2022	Sites Perspectives on Decentralized Trials
CenterWatch	January 2023	Sanofi, IQVIA Took Top Spots on Reputation with Sites Last Year (2022)
CW Weekly	January 2023	Sites Name Tech Acceptance as Essential Factor in Selection of Sponsors, Survey Finds
CenterWatch	2021	Global Site Relationship Benchmark Survey Report - For CROs
CenterWatch	2021	Global Site Relationship Benchmark Survey Report - For Sponsors
Applied Clinical Trials	March 2023	Assessing Investigative Site Outlook and Operating Experience Post-Pandemic
Applied Clinical Trials	May 2022	Improving Diversity in Clinical Trial Volunteer Participation by Addressing Racial and Ethnic Representation Among the Clinical Research Workforce
Applied Clinical Trials	March 2023	DIA Europe Forum - Creating an Impact for Patients and Our Planet - Advancing Drug Development Towards a More Sustainable, Carbon-neutral and Circular Model
ACRP	2019	Technology Competency in Clinical Research: ACRP/ Forte Research Systems White Paper
ACRP	2020	The Impact of Increases Technology Use on the Clinical Research Workforce: ACRP White Paper
ACRP	2020	An Assessment of the Adequacy of the Clinical Research Workforce: ACRP/Teconomy Special Report

Literature Reviewed (2011-2023), *cont.*

SOURCE	DATE	TITLE
DIA Journal (TIRS)	May 2022	Tufts CSDD Survey: Global Investigative Site Personnel Diversity and Its Relationship with Study Participant Diversity
DIA Journal (TIRS)	May 2011	Tuft CSDD Survey: Factors Influencing Investigative Site Willingness and Ability to Participate in Clinical Trials
DIA Journal (TIRS)	2017	Assessing Study Start-Up Practices, Performance, and Perceptions Among Sponsors and Contract Research Organizations
DIA Journal (TIRS)	2017	Hot Button Protocol and Operational Issues Between Sponsors and Sites in Clinical Pharmacology Studies: A Moderated Forum Session
Slide Share	January 2021	Glass, H. Payment Practices, FMV, and Study Performance. Retrieved from https://www.slideshare.net/mariejcpa/payment-practices-fmv-and-study-performance-harold-glass
Trials	2019	Criteria for site selection in industry sponsored clinical trials; a survey among decision-makers in biopharmaceutical companies and clinical research organizations
Clinical Trials	2011	Factors Influencing Investigative Site Willingness and Ability to Participate in Clinical Trials