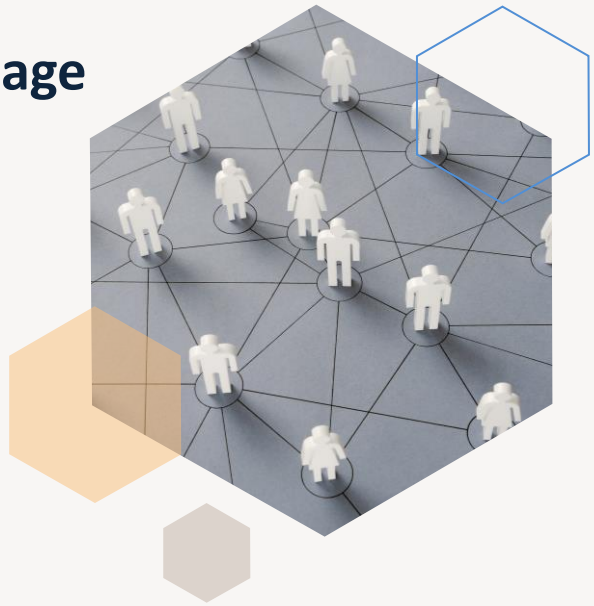
Study Start Up & The Village It Takes [a multi-faceted perspective]



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Objective

The purpose of this presentation is to present a general overview to study start up and the multiple layers that come with it. This presentation will dive into different perspectives while diving into a general over view of '10 Steps in Study-Up'

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Domain 5: Study and Site Management

Domain 8: Communications and Teamwork

Acknowledgement: Domains pulled from the JTF Core Competency Framework for Clinical Research Professionals

Heads Up! Interactive Activity!

What words come to mind when you hear study-start up?

Chat Storm!

10 Steps in Study Start Up – General Overview

Step 1	Step 2	Step 3	Step 4	Step 5
Identify Sites	Contact Sites/Assess Initial Interest	Execute the CDA	Conduct Feasibility	Pre-Study Visit or Screening Visit

Step 6	Step 7	Step 8	Step 9	Step 10
Initial Clinical Trial Agreement (CTA)	Negotiate the CTA	Regulatory Documents and Critical Submissions	Site Initiation Visits	Wrap-Up Study Start Up

Acknowledgement: The Oracle 10 Step Article was used as a tool to guide the presentation in a ten-step process. Some steps may be called different names at different institutions. The article will not be referenced on each slide, but the link may be obtained here for future reference

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https://www.oracle.com/a/ocom/docs/industries/life-sciences/10-steps-clinical-startup-eb.pdf

Step 1.

~1-2 Weeks

Identify Sites

Sponsor/Lead Team Perspective

Objective: Find sites that can enroll in the study protocol

- Use screen failure data
- Use physician directories
- Use internal databases

Site Perspective/Impact

The research team at site should start communicating as early as possible once identified by the sponsor. Site should review the study and respond in timely manner.

- Does this fit your site portfolio?
- Can your site enroll efficiently?
- Does your screen failure data reflect anything pertinent to being an efficient enrolling site?

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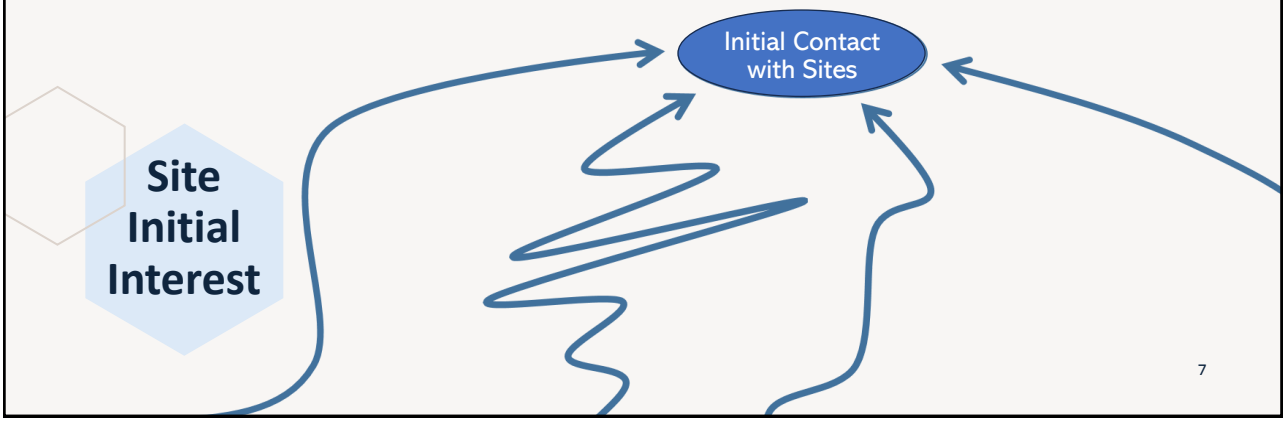
Sometimes the way sites receive questions about interest feels like this…



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Start involving core research teams as early as steps 1 & 2

Step 2.

~1-2 Weeks

Site Initial Interest

Sponsor/Lead Team Perspective

Objective: Track initial interest and assess site capabilities

- Consider the phase of the trial, size of the sponsor, or enrollment goal
- Clear and transparent conversations with the sites

Site Perspective/Impact

Site receives communication in a variety of ways

- Online surveys via a platform such as REDcap
- Through an already established network
- Direct email communication to an established site PI

Some additional documents that may accompany this step

- Brief synopsis of the protocol
- A Confidential Disclosure Agreement (CDA) ready for initiation

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Step 3.

~4-6 Weeks

Execute the CDA

Sponsor/Lead Team Perspective

Objective: Obtain signed Confidential Disclosure Agreement to distribute full protocol to sites

- Incorporate SOPs
- Create and disseminate CDAs in bulk to sites and investigators

Site Perspective/Impact

Key Take Away – *be sure to consult legal as early as possible after receiving the CDA – this is not a PI signature role!*

- Executed Confidential Disclosure Agreements are usually pivotal to obtaining a full protocol
- Start developing questions within the key research team and departments that may participate in the study

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Step 4.

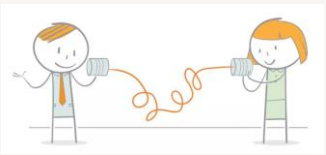
~4-6 Weeks

Conduct Feasibility

Sponsor/Lead Team Perspective

Objective: Send & obtain a completed Site Feasibility Questionnaire

- Obtain data to see if the site is a good fit
- Have an organized method of distributing the same questionnaire in bulk



Site Perspective/Impact

REVIEW-REVIEW-REVIEW THE PROTOCOL CAREFULLY

- PI, CRC, and site staff should review the protocol to assess the feasibility
- Review trial design; single or multicenter, open-label, or randomized and double-blind
- Review patient population at site to meet the screening and enrollment goals
- Ensure a completed Site Feasibility Questionnaire gets sent to the sponsor

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Step 4. Conduct Feasibility continued

**** Be realistic in your screening and enrollment goals****

Feasibility Survey

- Review protocol, schedule of assessments, and procedure requirements
- Review Investigator Brochure (IB), pharmacy manual, and investigational product administration (if applicable)
- Review lab manual for lab collection, processing, shipping, PK and Biomarker sample collection if applicable and dry ice requirement

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DISSECT the Protocol

- Carefully assess the protocol specific eligibility criteria - ***pay attention*** to all key inclusion criteria
- Be realistic in providing screening and enrollment projection to the sponsor-some trials has screen failure rate up to 50 % - (i.e epilepsy trials)
- Look for challenges in the study design that is not logistically feasible

Some questions you may want to ask

- Does the study team have prior experience and other contacts in the area?
- Does the site have the right equipment as required per protocol or if sponsor will provide the equipment? (e.i weighing scale for IP)
- Does the site have sufficient staffing and resources to meet the protocol requirements?
- Will there be additional training needed for the research team?

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** Involve departments early**

- Other Departments To Consider
  - Radiology
  - Ophthalmology
  - Infusion Centers
  - Nursing Resources
  - Emergency Departments
  - ***Any applicable department the study will touch***

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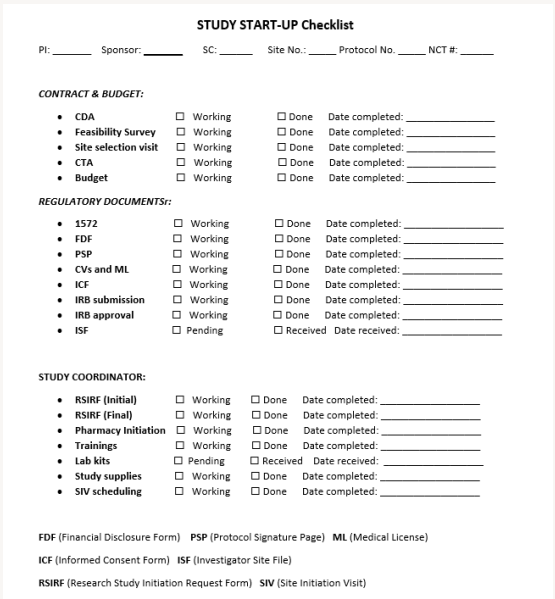
Example of a study start up checklist



STUDY START-UP Checklist

PI: _____ Sponsor: _____ SC: _____ Site No.: _____ Protocol No. _____ NCT #: _____

CONTRACT & BUDGET:

- **CDA** ☐ Working ☐ Done Date completed: _____
- **Feasibility Survey** ☐ Working ☐ Done Date completed: _____
- **Site selection visit** ☐ Working ☐ Done Date completed: _____
- **CTA** ☐ Working ☐ Done Date completed: _____
- **Budget** ☐ Working ☐ Done Date completed: _____

REGULATORY DOCUMENTSr:

- **1572** ☐ Working ☐ Done Date completed: _____
- **FDF** ☐ Working ☐ Done Date completed: _____
- **PSP** ☐ Working ☐ Done Date completed: _____
- **CVs and ML** ☐ Working ☐ Done Date completed: _____
- **ICF** ☐ Working ☐ Done Date completed: _____
- **IRB submission** ☐ Working ☐ Done Date completed: _____
- **IRB approval** ☐ Working ☐ Done Date completed: _____
- **ISF** ☐ Pending ☐ Received Date received: _____

STUDY COORDINATOR:

- **RSIRF (Initial)** ☐ Working ☐ Done Date completed: _____
- **RSIRF (Final)** ☐ Working ☐ Done Date completed: _____
- **Pharmacy Initiation** ☐ Working ☐ Done Date completed: _____
- **Trainings** ☐ Working ☐ Done Date completed: _____
- **Lab kits** ☐ Pending ☐ Received Date received: _____
- **Study supplies** ☐ Working ☐ Done Date completed: _____
- **SIV scheduling** ☐ Working ☐ Done Date completed: _____

FDF (Financial Disclosure Form) **PSP** (Protocol Signature Page) **ML** (Medical License)

ICF (Informed Consent Form) **ISF** (Investigator Site File)

RSIRF (Research Study Initiation Request Form) **SIV** (Site Initiation Visit)

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Heads Up! Interactive Activity!

Chat Storm!

What inclusion/exclusion challenges have you experienced during feasibility assessments?

What ancillaries do you always involve?

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Step 5.

~8-12 Weeks

Pre-Study Visit

Sponsor/Lead Team Perspective

Objective: Schedule a pre-study visit as soon as possible to confirm the site's eligibility to conduct the study.

Site Perspective/Impact

Make sure the major players of your team are available for the pre-study visit.

- Give the team enough time to prepare and schedule properly
  - *Do not give in to the pressure to rush and get up and rolling the fastest*
- Have realistic deadlines for next steps after the pre-study visit
- Have an after-action report template to discuss what went well and what did not go well during the visit

Be clear, concise, and transparent about the goals for both sponsor and

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Step 6.

~4-20 Weeks

Initial Clinical Trial Agreement (CTA)

Sponsor/Lead Team Perspective

The CTA is the legal binding agreement between the sponsor and the site. It assigns important functions between sponsor and site.

Site Perspective/Impact

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Step 7.

~4-12 Weeks

Negotiate the CTA

Sponsor/Lead Team Perspective

Objective: Obtain a signed Clinical Trial Agreement as quickly as possible to open the site to enrollment

Site Perspective/Impact

- Financial Commitments
- Responsibilities
- Obligations
- Risk Allocation

Negotiate and advocate for the work you will be doing

**Optimistic Reminder! Very rare the original CTA gets accepted verbatim **

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** Do not be afraid to ask questions**

Budget Considerations

- Research team effort or time
- Investigator oversight
- Examinations
- Trainings
- Pharmacy
- Ancillary Support

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** Do not be afraid to ask questions**

Commonly Missed Financial Considerations

- Site overhead
- Payment terms
- Document translation fees
- Monitoring visits
- Dry ice
- Amendment processing

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Heads Up! Interactive Activity! [Chat Storm or Speak Up!]

Chat Storm!

What part of the CTA negotiation is your least favorite?

Any CTA negotiation wins you would like to share?

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Step 8.

~6 Weeks

Regulatory Documents and Critical Submissions

Sponsor/Lead Team Perspective

Objective: Get all required documents submitted as quickly as possible for an IRB submission

Site Perspective/Impact

- Systematic approach of submission to sponsor and IRB
- Process and track the submissions of:
  - Protocol
  - Informed consent/patient cards
  - FDA Form 1572 and Financial disclosures
  - Sign CVs of site staff and medical licenses
  - Training Certifications
  - Equipment calibration record
- Remember the 'Essential Documents' Categories
  - FDA regulations and human subject protection laws
  - Institutional Review Board/Ethics Committee
  - Standard Operation Procedure requirements

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** Needs to occur before participant enrollment**

Step 9.

~ Varies

Site Initiation Visits

Objectives for both Site and Sponsor

- Ensure understanding of the protocol and Good Clinical Practice requirements
- Review recruitment plan and discuss any last details to enroll participants
- Site has received all equipment and updated copies of study manuals
- Site staff has access to all the vendors including EDC, IWRS. Lab portal, and training sites

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Heads Up! Interactive Activity!

Step 10.

~ 22-66 Weeks

Wrap Up!

Chat Storm!

What have your site's 'pain points' been in study start up?

Any other challenges or successes?

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Conclusion

Running a clinical trial, and getting the study start up complete takes a village of people working together!

Do not be afraid to ask the hard questions, and use the resources you have.

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Thank you!

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