

ACCELERATING COVID-19 THERAPEUTIC INTERVENTIONS AND VACCINES (ACTIV)



Innovations Quick Reference Guide

Version 1.0

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1.0 Overview

Many of the solutions outlined in this guide are for virtual, digital, online technology solutions or innovations that are becoming increasingly relevant in the COVID-19 clinical trial environment. This is not meant to be a comprehensive list of solutions for clinical trials in general, rather these innovations may help with expeditious and efficient clinical trial execution in the COVID-19 environment.

The ACTIV Clinical Trial Capacity Working Group developed detailed Innovation playbooks for: e Clinical Outcome Assessment (COA); eConsent; Home Nursing; Remote Source Data Verification (SDV); and Site Training/Tools.

The scope of this guide includes the following subject areas partitioned according to four stages of clinical trial operations (Planning, Start-Up, Execution, Close-Out).



- Trial Participants: Recruitment, Enrollment, Assignment, Communications
- Site Identification, Training, Management, Communication
- Data Collection, Management, Analysis
- Remote execution solutions
- Laboratory Functions
- Investigational medicinal product (IMP) Management
- Centralized Operations

1.1 Planning



- **Trial Participants: Recruitment, Enrollment, Assignment, Communications**
 - Enrollment modelling tools
 - Clinical trial setting: out-patient, decentralized; in-hospital
 - Considerations: Applicable to all clinical trials. Early and effective enrollment modelling will help to enable predictable, efficient clinical trial execution
 - Potential solutions/vendors: Clinical Research Organization (CRO) tools, multiple vendors
 - Standardized recruitment plan and materials (details on volume, intensive care unit (ICU)/non-ICU, etc.)
 - Considerations: Applicable to all clinical trials. Early and effective enrollment modelling will help to enable predictable, efficient clinical trial execution
 - Adaptive recruitment planning capability, incl Age / Ethnic / geography / health care worker cohorts
 - Clinical trial setting: vaccine
 - Considerations: Clinical Trial planning for adaptive / master protocols where it is intended to adjust treatment arms / add new treatments etc.
 - Potential solutions/vendors: CRO tools

- Alignment with national efforts to meet public health needs
 - Clinical trial setting: out-patient, decentralized; vaccine
 - Considerations: Clinical Trial planning in a volatile environment, e.g. where infection rates vary over time / geography. Enabling access to increasing patient populations through national / public registries.
 - Potential solutions/vendors: Verily, DCRI HERO registry
- Vaccine awareness campaigns
 - Clinical trial setting: vaccine
 - Considerations: Critical for higher patient volume Phase II / Phase III vaccine trials.
- Site feasibility (Process, Technology)
 - Clinical trial setting: out-patient, decentralized; in-hospital
 - Considerations: Effective feasibility assessment crucial for all trials to ensure realistic enrollment planning and projection
 - Potential solutions/vendors: CRO tools, multiple external vendors
- **Site Identification, Training, Management, Communication**
 - Data science to track emerging disease peaks for targeting recruitment efforts
 - Clinical trial setting: vaccine
 - Considerations: Clinical Trial planning in a volatile environment, e.g. where infection rates vary over time / geography. Identifying disease prevalence in the future to enable accurate planning.
 - Potential solutions/vendors: Microsoft, Google, Academics
 - Site resourcing & site grants (Process, Technology)

“clinical trial cost benchmarking tools and budgeting applications that are critical to achieving more cost-effective clinical trials”

 - Considerations: Applicable to all trials, particularly global trials to ensure cost effectiveness but also competitiveness in an already crowded field.
 - Potential solutions/vendors: GrantPlan
 - Central databank for barred sites tracking
 - Clinical trial setting: in-hospital setting
 - Considerations: Applicable to all trials.
 - Coordinated community engagement plan (more pertinent for out-patient protocol)
 - Clinical trial setting: in-hospital
 - Considerations: Applicable to trials focused on out-patient / asymptomatic / pre-symptomatic populations. Early and effective community engagement will enable better patient engagement, enrollment and retention.
 - Potential solutions/vendors: CRO solutions
 - Virtual site planning
 - Clinical trial setting: out-patient, decentralized
 - Considerations: Applicable to trials focused on out-patient / asymptomatic / pre-symptomatic patients, particularly in a situation where patient movement becomes restricted (Lock-down)
 - Potential solutions/vendors : Science 37, Lightship, Medable

1.2 Start-Up

Planning
Section 1.1

Start-Up
Section 1.2

Trial Execution
Section 1.3

Trial Close-out
Section 1.4

- **Trial Participants: Recruitment, Enrollment, Assignment, Communications**
 - Point of care enrollment
 - Clinical trial setting: out-patient, decentralized, vaccine
 - Considerations: To facilitate rapid enrollment in a manner that is least burdensome to subjects
 - Potential solutions/vendors: Walmart clinics, CVS Minute Clinics, Walgreens
 - eConsent
See detailed ACTIV eConsent Innovation Playbook
 - Randomization solutions (Process, Technology, Service)
 - Clinical trial setting: out-patient, decentralized, in-hospital
 - Considerations: Applicable to all trials. Adaptive solutions will be required for larger/master protocols; Integration with Clinical Database will enable streamlined flow of data and reduce downstream data cleaning requirements
 - Potential solutions/vendors: Cenduit
- **Site Identification, Training, Management, Communication**
 - Remote initiation visit, start up, and tracking of sites
 - Considerations: Effectively tracking site initiation and planning process is critical to enabling efficient study start-up. Digital tools will help to streamline the flow of information and also ensure downstream audit-readiness.
 - Potential solutions/vendors: Veeva Systems Inc. (SiteVault), Zoom (initiation visit), Gbalto (Oracle), Smartsheet, Medidata
 - Site trainings for investigators, site nurses, point of care nurses, etc.
 - Clinical trial setting: out-patient, decentralized; in-hospital; vaccine
 - Considerations: Traditional site-training tools and modalities can be ineffective and cumbersome. Targeted digital training can provide online just-in-time training that reduces the burden on site personnel yet enables effective performance management.
 - Potential solutions/vendors: Teckro, CRO tools
 - Site communication, Investigator portal (Technology)
 - Clinical trial setting: in-hospital
 - Considerations: Effective, online communication tools are particularly important in the dynamic, fast-moving COVID-19 environment where standard of care is changing rapidly, new treatment arms are being added to trials etc. Being able to communicate fast and effectively with global clinical trial sites will be crucially important.
 - Potential solutions/vendors: Transcelerate SIP, DrugDev, Novatis Connect

- Central site databank for "reusable" (across studies) site documents (e.g. CVs, FDs, etc.) to use under defined criteria (age, no change)
 - Clinical trial setting: in-hospital
 - Considerations: Supports the ability to remotely manage site performance, particularly in a situation where clinical research associate (CRA) movement is compromised. Critical to ensuring future audit-readiness
 - Potential solutions/vendors: Veeva Vault, Documentum, Transcelerate SIP
- **IMP Management**
 - Drug Handling (Service)
 - Clinical trial setting: out-patient, decentralized; in-hospital
 - Considerations: Effective drug management capabilities will be important in an adaptive situation when treatment arms are being added to a master protocol. Will also be critical to ensure effective control especially when investigational product or comparator may be in short supply.
 - Potential solutions/vendors: CRO tools, Fisher Clinical Services
- **Centralized Operations**
 - Centralized Institutional Review Board (IRB) (Service)
 - Clinical trial setting: out-patient, decentralized; in-hospital
 - Considerations: Important to enabling rapid study-startup
 - Potential solutions/vendors: Advarra, Western
 - Electronic data capture (EDC) solution (Technology)
 - Clinical trial setting: out-patient, decentralized; in-hospital
 - Considerations: Important to identify solutions that can be deployed rapidly, that can be supported globally and that can be scaled to enable high volume data collection. Also critical to ensure selection of robust good clinical practice (GCP)-compliant tools that will help ensure downstream audit readiness.
 - Potential solutions/vendors: Medidata, Oracle, Veeva, and many more smaller vendors

1.3 Trial Execution



- **Trial Participants: Recruitment, Enrollment, Assignment, Communications**
 - Pre-screening solutions
 - Clinical trial setting: out-patient, decentralized; in-hospital
 - Considerations: Pre-screening solutions have been shown to increase enrolment speed. Suggest consideration for outpatient and vaccine trials
 - Potential solutions/vendors: Reify (for US)
 - Increasing the pool of volunteers (ResearchMatch) + marketing campaigns
 - Clinical trial setting: out-patient, decentralized; in-hospital
 - Considerations: To ensure adequate and timely supply of patients to sites and to help speed-up trial enrolment

- Patient portal/helpdesk
 - Clinical trial setting: vaccine
 - Considerations: For high volume trials, where patients need to be followed for a long period of time, digital/online solutions or a helpdesk will enable more accurate follow up and data collection
 - Potential solutions/vendors: TrialBee
- Recruitment
 - Digital recruiting platforms
 - Clinical trial setting: out-patient, decentralized
 - Considerations: Digital / Social media recruitment tools may provide alternative access to higher patient volumes. May become more important as disease prevalence begins to fall-off. May be a critical avenue for higher volume vaccine trials
 - Potential solutions/vendors: Novartis Digital Recruiting (NDR)
 - Social Media and other Digital Media Assets, Community engagement
 - Clinical trial setting: out-patient, decentralized; vaccine
 - Considerations: Digital / Social media recruitment tools may provide alternative access to higher patient volumes. May become more important as disease prevalence begins to fall-off. May be a critical avenue for higher volume vaccine trials
 - Potential solutions/vendors: Verily, Antidote, CRO tools
- Electronic health record (EHR)-based recruitment workflow methods
 - Clinical trial setting: in-hospital
 - Considerations: EHR driven direct emails and patient portal messages can augment traditional recruitment strategies. Query modules, screening lists and notification components of EHRs, if available, may be useful to investigators.
 - Potential solutions/vendors: REDCap
- Trial Feedback Questionnaire (TFQ)
 - Clinical trial setting: out-patient, decentralized; in-hospital
 - Considerations: By surveying patients who have participated in trials, learnings can be used to improve the experience of future trial participants, thereby improving enrollment and retention rates.
- **Site Identification, Training, Management, Communication**
 - Site Training
 - *See detailed ACTIV Site Training/Tools Innovation Playbook*
 - Guidance documents for virtual/remote handling of sites (Process)
 - Clinical trial setting: out-patient, decentralized; in-hospital
 - Considerations: This will be critical during the acute phase of the pandemic when CRA movement is limited. Clear procedures that define how sites should be managed remotely will be key to ensuring strong performance and compliance and to protecting future audit readiness.
 - Help-desk/call center for sites
 - Considerations: Applicable to all trials, particularly during acute pandemic when CRA movement is limited. Also important for more complex / master / adaptive protocols.

- Site cockpit for site level performance management
 - Clinical trial setting: in-hospital
 - Considerations: Applicable to all trials. Understanding site performance early will enable study teams to close down poor enrolling sites earlier and focus resources where they can add most value.
- **Data Collection, Management, Analysis**
 - DSMB data review (Technology, Service)
 - Clinical trial setting: in-hospital
 - Considerations: Central DSMB solution important to enable early and effective safety management over the entire ACTIV portfolio
 - Potential solutions/vendors: Veeva DSMB modules, CRO service
 - Data Collection Platform for PRO data (surveillance, symptom tracking, etc.)
 - Clinical trial setting: out-patient, decentralized; in-hospital; vaccine
 - Considerations: Applicable to out-patient/vaccine trials where long-term follow up is required.
 - Potential solutions/vendors: MyCap mobile app or similar tool designed for longitudinal interaction with participant
 - High-throughput data management / analytics capability
 - Considerations: Applicable to vaccine trials specifically where high data volumes will be received and require to be processed in rapid turnaround times.
 - Potential solutions/vendors: CRO tools, Veeva, Medidata, Oracle
 - **Remote Source Data Verification (SDV)** (Technology)
 - *See detailed ACTIV Remote Source Data Verification (SDV) Innovation Playbook*
- **Remote execution solutions**
 - Home nursing solutions
 - *See detailed ACTIV Home Nursing Innovation Playbook*
 - Sensors - Pulse oximetry in the home - other sensors, to monitor patients post discharge
 - Clinical trial setting: out-patient, decentralized; vaccine
 - Considerations: Applicable to out-patient trials. Should be considered in a situation where patient movement is restricted.
 - At-home blood collection devices
 - Clinical trial setting: out-patient, decentralized; vaccine
 - Considerations: Applicable to out-patient trials. Should be considered in a situation where patient movement is restricted.
 - Potential solutions/vendors: Seventh Sense
 - Diaries, possibly eCOA, potentially with imaging to collect injection site reactions (BYOD)
 - *See detailed ACTIV eCOA Innovation Playbook*
 - Telemedicine
 - Clinical trial setting: outpatient, decentralized; vaccine
 - Considerations: Applicable to out-patient trials. Should be considered in a situation where patient movement is restricted or where the ability of traditional trial sites to access patients becomes a limiting factor.
 - Potential solutions/vendors: Medable, Verily, Veeva

- **Laboratory Functions**
 - Commercial pharmacy partnership for testing/blood draw
 - Clinical trial setting: vaccine
 - Considerations: Applicable to out-patient trials. Should be considered in a situation where patient movement is restricted.
 - Potential solutions/vendors: LabCorp, Quest
 - Lab management
 - Clinical trial setting: out-patient, decentralized; in-hospital
 - Considerations: Robust arrangements should be put in place to ensure laboratory data is effectively controlled. Particularly important for vaccine trials with long-term serology assessments.
 - Potential solutions/vendors: LabCorp, Q2 Quest
- **IMP Management**
 - Home IMP solutions (rapid supply chain to move IMP to target locations efficiently)
 - Clinical trial setting: out-patient, decentralized; vaccine
 - Considerations: Applicable to out-patient trials. Should be considered in a situation where patient movement is restricted.
 - Potential solutions/vendors: Fisher
 - Collaboration with local pharmacy chains for testing/drug supply (Service)
 - Clinical trial setting: out-patient, decentralized; in-hospital
 - Considerations: Applicable to out-patient trials. Should be considered in a situation where patient movement is restricted.
 - Potential solutions/vendors: Verily, RITE Aid
- **Centralized Operations**
 - Clinical Trial Management System (CTMS) (Technology)

Used to manage maintain and manage planning, performing and reporting functions, along with participant contact information, tracking deadlines and milestones.

 - Clinical trial setting: in-hospital
 - Considerations: Applicable to all trials. Robust CTMS capabilities required to manage planning and reporting activities.
 - Potential solutions/vendors: IMPACT (Parexel), Veeva, Oracle, Medidata
 - Central Operations Center
 - Clinical trial setting: out-patient, decentralized; in-hospital
 - Considerations: Effective, online communication tools are particularly important in the dynamic, fast-moving COVID-19 environment where standard of care is changing rapidly, new treatment arms are being added to trials etc. Being able to communicate fast and effectively with global clinical trial sites will be crucially important.
 - Potential solutions/vendors: Novartis Connect, Transclerate SIP, DrugDev Site Portal
 - Study mission control center for overall study management (e.g., Novartis SENSE)
 - Clinical trial setting: out-patient, decentralized; in-hospital
 - Considerations: Particularly applicable for larger trials or complex / master protocols to ensure transparency of clinical trial performance and to empower leadership to make early and effective decisions.

- Simple Digital Mobile Applications designed with Clinicians or Prospective Patients as central users (e.g. awareness, decision tools) – this is one of our service line items in RIC and they're pretty fast to build out for testing/implementation (with limited level of site specificity)
 - Clinical trial setting: out-patient, decentralized; in-hospital
 - Considerations: To ensure seamless and frictionless information flow from patients

1.4 Trial Close-Out



- Remote close-out visits
 - Considerations: Applicable for all trials, particularly during acute-phase of the pandemic when CRA movement is limited
- Collaborative / Structured authoring tools
 - Considerations: Applicable for all trials, to streamline report writing process and enable rapid submission and approval
- Pre-populating standard CSRs
 - Considerations: Applicable for all trials, to streamline the submission process and reduce the lag from LPLV to submission.