GUIDELINE: OPTIMAL SITE INPUT FOR DECENTRALIZED TRIAL ELEMENTS

I. INTRODUCTION

The purpose of this guideline/toolkit is to gain and incorporate site input regarding DCT methods during trial planning to improve trial design for optimal patient inclusion, to support site adoption of decentralized trial elements and to align stakeholders for success.

II. PROJECT OBJECTIVES

- Create an easy to implement, customizable process to seek & react to input from sites without adding significant* time to protocol development and study launch.
- Increase site input to trial planning to decrease adoption barriers for DCT methods.
- Increase sponsor awareness of site needs to enable DCT adoption
- Enable clinical trial teams to understand site needs and concerns when DCT methods are used in trials

*goal of no more than 2 weeks added to the process

III. CATEGORIES OF INPUT

1) **Prior to Protocol Finalization**

Timing: As soon as possible during trial planning to **allow for protocol edits and the company's protocol approval process.**

Goals of this category include:

- Understanding patient burden
- Understanding site burden and resources needed
- Site feedback to DCT elements that will help patient inclusion/recruitment/retention by including DCT elements
- Allow enough time post-input for protocol finalization and vendor selection re DCT elements

2) **Prior to Site Selection for Alignment and Adoption of DCT**

Timing: As soon as possible during site feasibility and **prior to site selection**

Goals Prior to Site Selection (protocol is already defined – this is for logistics, alignment, expectations):

- To understand site capabilities, experience and willingness for using central DCT vendors and elements vs. site tools already available
- Understanding concerns and logistical or resourcing challenges at the site
- Take into account any PI/Site budget considerations
- To align study teams and vendors to support sites in DCT adoption

Note: Sponsors may use one or both categories for each study and/or program.

IV. QUESTION BANK

Attached in Appendix A is a question bank that is divided into three categories: 1) prior to protocol finalization 2) prior to site selection and 3) both. Sponsors may use questions in the bank that best fit into their company site outreach processes and relevant study feedback desired. The timing of these questions is important and will be critical during the planning process. Feedback from sites indicates that they often learn about decentralized elements late in the process, commonly introduced at the PI meeting. Sponsors following this guideline will help align all stakeholders involved in a clinical trial or program.

V. HOW TO OBTAIN FEEDBACK

Depending on time-frame available, budget, background knowledge, existing resources (e.g. connection to site adboards), different methods and approaches can be implemented:

- **Site Advisory Boards** - to collect structured, high-quality feedback from clinical trial sites (ideally from study coordinators, i.e. people who will be close to the DCT operational implementation)
- **Survey and Questionnaires** - sent to investigators and coordinators prior to protocol development or during feasibility assessments
- **Outside firms** - especially for unbiased insights, broader reach, or specialized expertise
- **Interviews and focus groups** - in-depth discussions with site staff
- **Trial Simulations** – to collect site feedback on technology usability (e.g. eConsent, telehealth), site readiness for decentralization
- **Site Feasibility Visits**
- **Site Initiation Visits (SIVs)*** - Capture early impressions of protocol complexity.
- **Monitoring Reports*** - Identify recurring issues or bottlenecks
  *only applicable if amendment planned to include DCTs

VI. USES OF SITE FEEDBACK

Feedback can be used to adjust the study plan/protocol or to better align and logistically plan for DCT elements. Sponsors may or may not adjust the protocol based on their own company goals. The guideline recommendation is to provide a summary of site feedback, and any actions taken from it, to the sites and all study team stakeholders, including CROs and vendors involved.

1) **Category - Protocol Input/Potential Changes**

   Adjust protocol based on feedback to optimize patient inclusion or remove barriers

   Examples:

   - *Visit Schedule- options for remote/home health visits*
   - *Optimize for patient population and preferences-willingness to participate*
   - *Optimize for site adoption of DCTs*
   - *Protocol Simplification – Remove or adapt unnecessary procedures or visits*
   - *Direct-to-Patient shipments or interactions, wearables/digital health tools*

2) **Category - Alignment and Adoption of DCT**

Translate feedback regarding operational adjustments (e.g. technology, DCT services) and corresponding training material and change management or alignment

Examples:

- *Technology Selection - Choose tools that sites find intuitive and reliable or allow them to use their own tools*
- *Training Materials - Tailor based on site-reported gaps or confusion*
- *Site Resourcing/Expectations – align early on between site and Sponsor*
- *Site Budgeting – understand the activities at the site level to ensure incorporated in the budget*
- *Vendor Enablement/Engagement – Share site feedback with multi-stakeholders to set them up for success*

VII. SHARING OF FEEDBACK TO STAKEHOLDERS AND SITES

1.) **Stakeholders:** Sites, KOLs, Sponsor study team, DCT vendors, CRO, and other vendors interacting with DCT elements

2.) Communication:

a. Decisions around DCTs – any summary information that drove Sponsor decisions and any final decisions that have been made. Also include critical summary feedback that will affect the conduct of the study for both the sites and the vendors.
b. Any DCT elements that affect primary and secondary objectives/endpoints of the protocol.
c. Expectations of sites as it relates to interaction with DCT elements/providers
    i. Eg. Communication plans, help desks, responsibilities between vendor and sites
d. Training materials and information
e. Benefit/risk assessment to patient for using DCT
f. E6/r3 considerations

3.) Visuals: Appendix B contains options for including visuals to outline DCT elements for sites and patients to understand easily how and when these elements occur throughout the study.

VIII. SUMMARY

As the industry is improving in understanding patient populations and their journey, the mindset of patient inclusion has been adjusted. Decentralized trials have increased possibilities for inclusion of patients that may not have otherwise participated in clinical trials. This guideline is intended to help Sponsors best prepare for Site Input during trial planning and better adoption at the site level of decentralized trial elements. Timing and suggested feedback methods are outlined to set all stakeholders up for success in the DCT journey.

APPENDIX A

Revised DCT Site Questions - Sorted by Timepoint

Question	Category	Timepoint
Have you used [this DCT capability] at your site?	Design	Timepoint 1: Prior to Protocol Finalization
What challenges has your site experienced in the past with the incorporation of {this DCT element] into studies in the past?	Design	Timepoint 1: Prior to Protocol Finalization
What strategies have been successful/helpful for your site in incorporating [this DCT element] into studies in the past?	Design	Timepoint 1: Prior to Protocol Finalization
What deviations would you predict may increase (or decrease) as a result of the incorporation of [this DCT element]? If increased, how could this be mitigated?	Design	Timepoint 1: Prior to Protocol Finalization
Would incorporation of any DCT capabilities not proposed help achieve enrollment or retention goals?	Design	Timepoint 1: Prior to Protocol Finalization
Will incorporation of [this DCT element] help your site achieve participant enrollment goals? If no, why not?	Design	Timepoint 1: Prior to Protocol Finalization
Is it feasible/beneficial to use [this DCT element] at the study timepoints indicated? If no, why not?	Design	Timepoint 1: Prior to Protocol Finalization
Does [this DCT element] make sense in the context of this particular protocol. If no, why not?	Design	Timepoint 1: Prior to Protocol Finalization
Would use of [this DCT element] have a positive impact on your study participants? If no, why not?	Design	Timepoint 1: Prior to Protocol Finalization
Would use of [this DCT element] have a positive impact on your study staff? If no, why not?	Design	Timepoint 1: Prior to Protocol Finalization
Are your participants more/less likely to comply with protocol	Design	Timepoint 1: Prior to Protocol Finalization

requirements and remain in this trial if [this DCT capability] was offered? If no, why not?		
I would like to communicate with patients during the trial via XXX (phone calls, video calls, emails, SMS, communication in the app, in person), (scale 1-5 from strongly agree to strongly disagree)	Both	Both Timepoints
What barriers do you see to [targeted patient population] using [this DCT element]	Both	Both Timepoints
What barriers do you see to your study staff using [this DCT element]	Both	Both Timepoints
I feel comfortable participating in trials using XXXX (DCT element) (scale 1-5 from strongly agree to strongly disagree)	Both	Both Timepoints
What is your expectation of sponsor support for [this DCT capability]?	Implementation	Timepoint 2: Prior to Site Selection
What logistical barriers does your site have to the incorporation of [this DCT element] at the timepoints indicated?	Implementation	Timepoint 2: Prior to Site Selection
What is your process for training patients on [this DCT capability]?	Implementation	Timepoint 2: Prior to Site Selection
Which of the planned capabilities is your site trained on implementing? [Provide a list]	Implementation	Timepoint 2: Prior to Site Selection
Are there roles within your site that support [this DCT capability] - e.g. direct-to-patient shipping?	Implementation	Timepoint 2: Prior to Site Selection
Do you have the infrastructure/workflow at your site to use [this DCT capability]?	Implementation	Timepoint 2: Prior to Site Selection
Do you work with outside partners to support [this DCT capability - e.g. Home Health Nursing or remote biospecimen collection]?	Implementation	Timepoint 2: Prior to Site Selection
Does your contracting process support use of DCT? (has time impact on workload for the SC, PI and other site staff been determined?)	Implementation	Timepoint 2: Prior to Site Selection
Are there particular vendors for [this DCT capability] that your site has worked with in the past? What made the experience positive/negative?	Implementation	Timepoint 2: Prior to Site Selection

APPENDIX B – USE OF ICONS TO ILLUSTRATE DCT ELEMENTS

Procedures	Screening day -7 to -1	Enrollment/Baseline Visit 1, Day 1 +/- 1 day	Visit 2 Day 7 +/- 1 day	Visit 3 Day 14 +/- 1 day	Visit 4 Day 21 +/- 1 day	Visit 5 Day 28 +/- 1 day	Visit 6 Day 35 +/- 1 day	Visit 7 Day 42 +/- 1 day	Visit 8 Day 49 +/- 1 day	Visit 9 Day 56 +/- 1 day	Visit 10 Day 63 +/- 1 day	Visit 11 Day 70 +/- 1 day	Visit 12 Day 77 +/- 1 day	Visit 13 Day 84 +/- 1 day	Safety Follow-up Day 150 +/- 21 days	At Failure
Informed Consent																
Demographics & Medical History	X															
Randomization		X														
AE Review			X	X												
Con Med Review	X	X	X	X	X	X	X	X	X	X	X	X	X	X		
Physical Exam Including Height & Weight)	X	X			X			X			X			X	X	X
Vital Signs	X	X			X			X			X			X	X	X
Weight																
Blood Pressure	X	X			X			X			X			X	X	X
Hematology	X	X			X			X			X			X	X	X
*Serum Chemistry	X	X			X			X			X			X	X	X
Pharmacokinetic Assays		X			X			X			X			X		
12-Lead EKG	X	X			X			X			X			X		
Mobile EKG																
KCCQ-12 & EQ-5D																
**Administer IND8765		X			X						X			X		
***Administer IND309					X			X			X			X		
Complete CRFs	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X

*includes albumin, AP, total bilirubin, BUN, calcium, chloride, creatinine, AST, ALT, sodium
**via infusion, 2hrs
***oral, to be administered 4hrs (+/- 30min) following completion of IND8675 infusion, titrated weekly by EKG and weight as described in protocol section 6.3

Icon	DCT Method	Category	Noun Project Search Terms	Notes
DIGITAL & REMOTE ENGAGEMENT				
	eConsent	Digital	"digital signature" "document sign" "tablet signature"	Pen/signature on digital device
	eCOA / ePRO	Digital	"mobile survey" "patient report" "health survey"	Mobile phone with questionnaire
	Telemedicine Visit	Remote	"video call" "telemedicine" "telehealth"	Video camera with medical symbol
	Remote Patient Monitoring	Remote	"remote monitoring" "patient monitoring" "health tracking"	Heart rate with connectivity symbol
	Digital Sensors / Wearables	Digital	"wearable device" "fitness tracker" "smartwatch"	Smartwatch or wristband
HOME & LOCAL SERVICES				
	In-Home Nursing	Home Services	"home health" "house nurse" "home care"	House with medical cross
	Local Phlebotomy	Home Services	"blood draw" "phlebotomy" "blood test"	Blood drop with test tube
	Local Radiology / Imaging	Home Services	"medical imaging" "x-ray" "radiology"	X-ray or scan image
	Direct-to-Patient Shipment	Logistics	"home delivery" "package delivery" "shipping"	Package with delivery arrow
CLINICAL ASSESSMENTS & DATA				
	HCP Assessment / Standard of Care	Clinical	"doctor exam" "clinical assessment" "stethoscope"	Stethoscope or medical exam
	EMR/EHR Integration	Data Flow	"medical records" "EHR" "health data"	Document with medical symbol
	Lab Assessments	Clinical	"laboratory" "lab test" "test tube"	Test tube or beaker