SAMPLE CASE STUDY #1

Note: The information and resources in this case study are educational in nature and are not intended to constitute legal advice.

You are the PI for a team of clinical researchers that is applying for a grant to undertake a study enrolling subjects in rural areas spread over four separate states (states A, B, C, and D) who have tested positive for COVID-19. Study participant identification, screening, enrollment, and retention will be conducted from four hubs: University A for state A, and Universities B, C, and D (subcontracted study sites) for their states.

Participants will be both English and Spanish speakers. All study activities, including screening and enrollment, will be conducted entirely remotely, without any in-person clinic visits.

The threshold study criterion is that all participants will have tested positive for COVID-19. Full inclusion criteria have not yet been finalized (e.g., time frame since positive test), but cohorts would include participants who use tobacco, participants who use marijuana, participants who use both, and participants who use neither.

The following remote monitoring technology devices will be provided to study subjects (University A will serve as the central technology vendor contact):

1. Kit for remote capillary blood self-collection
2. Smart watch/similar fitness wearable
3. Smart scale
4. Pulse oximeter
5. Blood pressure monitor
6. Home spirometry kit

The team is considering whether to permit participants to use their own existing home monitoring technology devices in the above categories if desired.

The study aim is to monitor participants for possible long COVID and to identify an association between tobacco and/or marijuana use and long COVID. However, a significant parallel primary deliverable of the study will be to provide data that will help lead to the development of strategies to successfully recruit and retain rural participants in a fully remote study that includes patient-reported outcomes, remote patient monitoring, and remotely obtained biospecimens.

You are seeking regulatory information for the research team regarding FDA-related issues.

<u>General/broad issues/questions:</u>

1. Does FDA regulate any part of this study?
2. If so, how?
3. If not, why not?

Specific issues/questions:

- How, if at all, would the FDA be involved in the use of the proposed remote technology devices in this study? Are IDEs (Investigational Device Exemptions) required?
- If the FDA does not regulate this particular study, would it be involved in future research evolving from the parallel primary deliverable described above? If so, under what general circumstances would the FDA be involved in that type of research?

Responses

1. **Does FDA regulate any part of this study?**	
1.1 If so, how?	**See below**
1.2 How, if at all, would the FDA be involved in the use of the proposed remote technology devices in this study? Are IDEs required?	The FDA likely would be involved, and an IDE application would be required, only if a) one or more of the selected devices is investigational (i.e., not cleared or approved as may be required by its FDA classification type) and intended for marketing, AND b) the IRB deems those devices to be of SR (Significant Risk) in the setting of the proposed research. In its guidance document "Digital Health Technologies for Remote Data Acquisition in Clinical Investigations" (December 2023, final guidance), FDA noted that devices intended only for use in clinical investigations—rather than intended for marketing—are typically exempt from requirements that might otherwise apply, including premarket clearance (510(k)) or premarket approval (PMA) requirements for devices that are not yet cleared/approved, as long as the investigation/study otherwise complies with applicable requirements under 21 CFR 812.2(b) regarding non-significant risk devices used in clinical research (e.g., labeling, IRB approval, informed consent, etc.) The guidance document also notes that any DHT (Digital Health Technology) devices used in clinical research that is under FDA jurisdiction (which is not the case here; see the next question's discussion section below) must be shown to be "fit for purpose" as demonstrated through the following factors and processes, described in detail in the guidance document. CONSIDERATIONS WHEN USING DIGITAL HEALTH TECHNOLOGIES IN CLINICAL INVESTIGATIONS

	A. Selection of a Digital Health Technology and Rationale for Use in a Clinical Investigation B. Digital Health Technology Description in a Submission C. Verification, Validation, and Usability Evaluations of Digital Health Technologies D. Evaluation of Endpoints Involving Data Collected Using Digital Health Technologies E. Statistical Analysis and Trial Design Considerations F. Risk Considerations When Using Digital Health Technologies G. Record Protection and Retention H. Other Considerations When Using Digital Health Technologies During a Clinical Investigation The guidance document does recommend that investigators also consider using the above processes to enhance study reliability for any clinical research using remote digital technology even if the study does not involve an FDA-regulated "test article." FDA also has separate "qualification" programs that are intended to support the development of DHT tools for use in assessing medical products, where developers of those tools may choose to pursue qualification of their DHT as either a Drug Development Tool (DDT) or a Medical Device Development Tool (MDDT) for a specific context of use. Such a qualified tool may be relied upon in multiple clinical investigations to support submissions for drugs or biological products (if qualified as a DDT) or devices (if qualified as an MDDT) without having to repeat studies that supported the qualification. In the guidance document, the FDA also discusses the possibility and effects on research data of using a BYOD (Bring Your Own Device) approach. The guidance notes as follows: "Allowing participants to use their own DHTs or other technologies with which they are already familiar may potentially reduce the burden of using additional DHTs or other technologies provided by the sponsor. However, allowing participants to use their own DHTs may not be appropriate for DHTs that are customized or highly specialized for specific uses.... Sponsor-provided DHTs or other technologies to support their operation should be available as an option to ensure

	that participants who do not bring their own are not excluded from the clinical investigation for that reason. Sponsor-provided telecommunication services should also be made available as needed so that participants who have no or limited access to these services are not excluded from the clinical investigation."
1.3 If not, why not?	This study is not seeking to establish (or supplement) the safety and efficacy of an FDA-regulated "test article," which is the only time the FDA itself regulates a study. As discussed above, in the device arena, the FDA would not actively regulate a study involving a non-SR device even if that device was investigational and a test article (note that FDA would still regulate the device itself but would not normally be involved in the study phase).
2. **If the FDA does not regulate this study, would it be involved in future research evolving from the parallel primary deliverable described above? If so, under what general circumstances would the FDA be involved in that type of research?**	1) The FDA would be involved as described above regarding any SR investigational device used in a future study. 2) The FDA also would be involved in a future study that is under an IND (Investigational New Drug filing, involving a drug or biologic that is seeking either initial approval or supplemental approval). Its involvement in this type of study would involve either CDER (Center for Drug Evaluation and Research) or CBER (Center for Biologics Evaluation and Research), depending on whether the study focuses on a drug or a biologic. CDRH (Center for Devices and Radiological Health) might also be involved in an IND study if SR investigational devices are used in the study.