Incorporating Patient-Centric Sampling in Clinical Trials - Protocol Template Text

Guidance for use of this document

When including patient-centric sampling in a clinical study, the following suggested template text can be incorporated into the study protocol. The sections of the protocol are indicated as CAPITALISED HEADINGS and the suggested wording is set out for each. Text in brackets [] indicates where appropriate insertions/deletions are to be made. Instructions and guidance text appear in green font. This document is not intended to be exhaustive.

SCHEDULE OF ACTIVITIES

Intervention	Notes
Participant contact	Staff to contact participants within 1 day after clinic visit to ensure [blood sampler] devices were collected and picked up by the courier Staff to contact participants within 1 day after home sample collection to understand whether sample was successfully collected
Patient-centric sampling device collection	
[Blood sampler] patient-centric sampling device (in clinic)	Collect prior to administration of study intervention. [Number] [blood sampler] devices to be collected in clinic
[Blood sampler] patient-centric sampling device (at home)	[Number] [blood sampler] devices to be collected within [time period]
Device collection failure assessment	Collect information when the device(s) fails to collect the full volume of blood

INTRODUCTION

Patient-Centric Sampling

Smaller collection volumes are critical in vulnerable populations such as [pediatrics and oncology] due to blood volume collection restrictions. To meet this demand, alternative sampling technologies have been developed and approved for collecting biological samples for clinical use. These approaches, termed patient-centric sampling (PCS), reduce sample volume, reduce pain associated with collection, and may enable collection outside of planned clinical visits. Providing opportunities to collect samples remotely can reduce patient burden and enable patients to enrol in clinical studies without being geographically co-located with clinical sites [Dockendorf, et al., 2019]. The need to develop remote sampling capabilities was highlighted during the disruption in clinical studies from the COVID-19 pandemic [Brown, et al., 2021]. Finally, the ability to collect samples outside the traditional clinic visit allows

interrogation of biological changes that occur outside the logistical constraint of clinical site visits. Historically, new sampling technology has been successfully implemented across the pharmaceutical industry in multiple clinical studies for PK analysis [Kothare, P. A., et al., 2016; Li, C. C., et al., 2018]. Dried blood spot (DBS) microsampling applications for drug quantitation are well accepted and specific considerations for validation of DBS assays are included in regulatory bioanalytical method validation guidance documents [Food and Drug Administration, 2018; European Medicines Agency, 2023; ICH, 2023]. New devices such as the [blood sampler] provide high sample quality without the pain associated with [fingerstick based collection methods / standard phlebotomy]. [[Sponsor name] has experience implementing these new approaches across several clinical studies in [disease state] for drug level measurements. It is desirable to assess these novel technologies to determine the utility of these approaches for applications beyond PK.]

HYPOTHESES, OBJECTIVES, AND ENDPOINTS

Suggested wording to add to the text in the "Hypothesis, Objectives, and Endpoints" section of the study protocol;

Objectives	Endpoints
Primary	
Secondary	
Tertiary/Exploratory	
Objective: To evaluate the ability of [PK / molecular (genomic, metabolic, and/or proteomic) / biomarker / safety panels] data from patient-centric sampling, collected in the clinic and at home, to replicate molecular data obtained from traditional blood collection. or Objective: To establish the relationship between the [PK / molecular (genomic, metabolic, and/or proteomic) / biomarker / safety panels] data from patient-centric sampling and traditional blood collection, collected in the clinic and at home.	[PK / molecular (genomic, metabolic, and/or proteomic) / biomarker / safety panels] using traditional blood collection and patient-centric sampling. Correlation between patient-centric sampling and traditional blood collection data.
Objective: To evaluate patient-centric sampling device use, feasibility of collection, and accuracy of collecting these samples both at the clinic and at home.	Compliance in use of device Device performance Quality of samples collected

Objectives	Endpoints
	Sample volumes collected

STUDY DESIGN

Scientific Rationale for Study Design

This study will also evaluate the potential of patient centric sampling to obtain blood samples to conduct [PK / multi-omic disease analyses]. Reduction of collected blood volumes and the ability to have 'at-home' collection using this approach may allow incorporation of new translational and biomarker technologies into clinical care in the future. The recent advent of the COVID-19 pandemic has highlighted the need for reliable at-home blood collection approaches such as the patient-centric sampling device that is incorporated into this study.

STUDY ASSESSMENTS AND PROCEDURES

Administrative and General Procedures

Patient-centric Sampling Device

[Number] [blood sampler] devices will be used to obtain capillary blood samples from participants' [arms or fingers]. The [blood sampler] device collects a [dried sample on an absorptive material or liquid blood sample that can be further processed to plasma or serum]. The device [adheres to the skin of participant's upper arm and a delicate vacuum to flow blood into the tool or uses lancets to pierce the skin from which blood is collected]. Instructions on the use of the [blood sampler] devices will be provided in the laboratory manual.

Device failures (i.e., lancet does not pierce skin, or device does not collect blood) or adverse events (AEs) directly related to the [blood sampler] devices should be communicated to the Sponsor by the investigator. Additionally, AEs involving the devices should be recorded on the appropriate eCRF. Refer to the laboratory manual for additional details.

Timepoints for the collection of these samples can be found in the schedule of activities (SoA). Please refer to the laboratory manual for detailed instructions on sample collection, storage, and shipment.

Pharmacokinetics

Blood samples will be collected for the determination of [analyte] concentrations and PK parameters.

[blood sampler device] samples (venous blood and capillary blood) will be collected for analysis of [analyte] concentrations. Subjects will be asked to collect some [blood sampler device] samples themselves [at home / in-clinic / at home and in-clinic]. A survey will be used to obtain feedback from the subjects on the self-collection of blood samples.

Biomarkers

To identify novel biomarkers, the following biospecimens to support exploratory analyses of cellular components (e.g., protein, RNA, DNA, metabolites) and other circulating molecules will be collected from all participants as specified in the SoA:

- Blood for genetic analysis
- Blood for biomarker analysis
- Blood for plasma biomarker analysis
- Blood for RNA analyses
- Blood for ctDNA analyses
- Dried whole blood from [blood sampler] device
  or
  Liquid whole blood from [blood sampler] device
- Archival or newly obtained tissue collection
- Unscheduled sample collection if breakthrough event observed during trial participaton

Sample collection, storage, and shipment instructions for the exploratory biomarker specimens will be in the laboratory manual. A survey will be used to obtain feedback from the subjects on the self-collection of blood samples

Consent and Collection of Specimens for Future Biomedical Research

In order to optimize the research that can be conducted with future biomedical research specimens, it is critical to link participants' clinical information with future test results. In fact, little or no research can be conducted without connecting the clinical study data to the specimen. The clinical data allow specific analyses to be conducted. Knowing participant characteristics like sex, age, medical history and intervention outcomes are critical to understanding clinical context of analytical results.

To maintain privacy of information collected from specimens obtained for future biomedical research, the Sponsor has developed secure policies and procedures. All specimens will be single-coded per ICH E15 guidelines as described below.

At the clinical study site, unique codes will be placed on the future biomedical research specimens. This code is a random number which does not contain any personally identifying information embedded within it. The link (or key) between participant identifiers and this unique code will be held at the study site. No personal identifiers will appear on the specimen tube.

Participant Identification Card

All participants will be given a participant identification card identifying them as participants in a research study. The card will contain study-site contact information (including direct telephone numbers) to be used in the event of an emergency. The investigator or qualified designee will provide the participant with a participant identification card immediately after the participant provides documented informed consent. At the time of intervention randomization, site personnel will add the treatment/randomization number to the participant identification card.

The participant ID card also contains contact information for the emergency unblinding call center so that a health care provider can obtain information about study intervention in emergency situations where the investigator is not available.

Procedures

Study procedures should be completed as close to the prescribed/scheduled time as possible. Procedures will be performed in the following order of proximity (below) with regard to the prescribed time. These procedures can be done prior or after the time point. For this study the

blood sample for [analyte] is the critical parameter and needs to be collected as close to the exact time point as possible.

1. Blood collection for [analyte]
2. [Blood sampler device] sampling
3. Laboratory safety tests
4. Vital signs
5. Physical examinations
6. Weight
7. Meals

The exact time at which a procedure is performed must be recorded on the electronic case report forms (eCRF). The order of priority can be changed during the study with joint agreement of the Investigator and the Sponsor Clinical Monitor.

Any non-scheduled procedures required for urgent evaluation of safety concerns take precedence over all routine scheduled procedures.

Blood Samples for [Analyte] Assay

For all subjects, blood samples for determination of plasma [analyte] will be collected and processed according to the details to be provided in a separate laboratory manual at scheduled time points as indicated in the schedule of activities.

For all subjects, [blood sampler device] samples (venous blood and capillary blood) for determination of [analyte] will be collected and processed according to the details to be provided in a separate laboratory manual at scheduled time points as indicated in the schedule of activities. Subjects will be asked to collect some [blood sampler device] samples themselves. A survey will be used to obtain feedback from the subjects on the self-collection of blood samples.

References

Brown L, Byrne RL, Fraser A, Owen SI, Cubas-Atienzar AI, Williams CT, et al. Self-sampling of capillary blood for SARS-CoV-2 serology. Sci Rep. 2021;11:7754.

Dockendorf MF, Murthy G, Bateman KP, Kothare PA, Anderson M, Xie I, et al. Leveraging digital health technologies and outpatient sampling in clinical drug development: a phase I exploratory study. Clin Pharmacol Ther. 2019;105(1):168-76.

European Medicines Agency. ICH M10 on bioanalytical method validation - Scientific guideline, 2023. https://www.ema.europa.eu/en/ich-m10-bioanalytical-method-validation-scientific-guideline.

Food and Drug Administration. Bioanalytical method validation: guidance for industry. Silver Spring, MD. 2018. https://www.fda.gov/regulatory-information/search-fda-guidance-documents/bioanalytical-method-validation-guidance-industry.

ICH guideline M10 on bioanalytical method validation and study sample analysis – Step 5. 2023. https://www.ema.europa.eu/en/ich-m10-bioanalytical-method-validation-scientific-guideline#current-version-9785.

Kothare PA, Bateman KP, Dockendorf M, Stone J, Xu Y, Woolf E, et al. An integrated strategy for implementation of dried blood spots in clinical development programs. AAPS J. 2016;18(2):519-27.

Li CC, Dockendorf M, Kowalski K, Yang B, Xu Y, Xie I, et al. Population PK analyses of ubrogepant (MK-1602), a CGRP receptor antagonist: enriching in-clinic plasma PK sampling with outpatient dried blood spot sampling. J Clin Pharmacol. 2018;58(3):294-303.